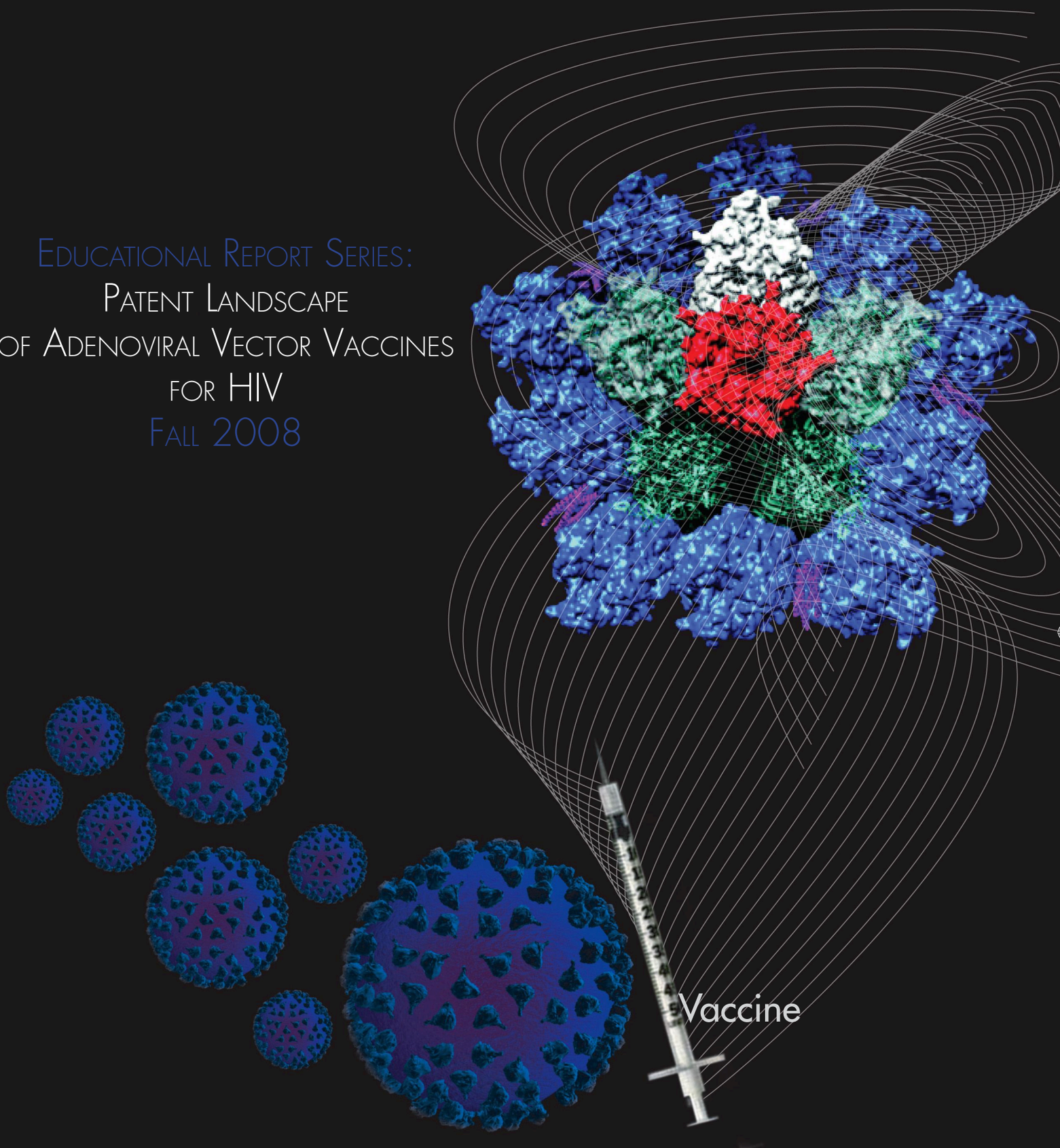
Educational Report Series:

Patent Landscape of Adenoviral Vector Vaccines for HIV

Fall 2008



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FRANKLIN PIERCE LAW CENTER EDUCATIONAL REPORT: PATENT LANDSCAPE OF ADENOVIRAL VECTOR VACCINES FOR HIV



FALL 2008

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A special thanks to Dr. Kerri Clark of Public Intellectual Property Resources for Agriculture (hereinafter PIPRA) without whom this project would not have been possible.

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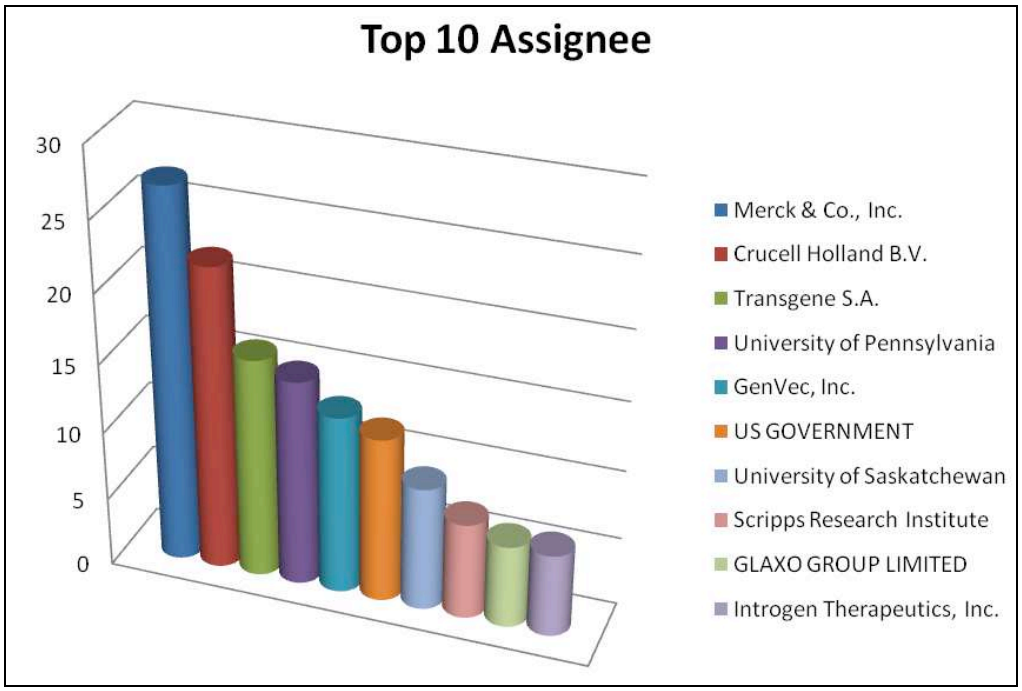
Table of Contents

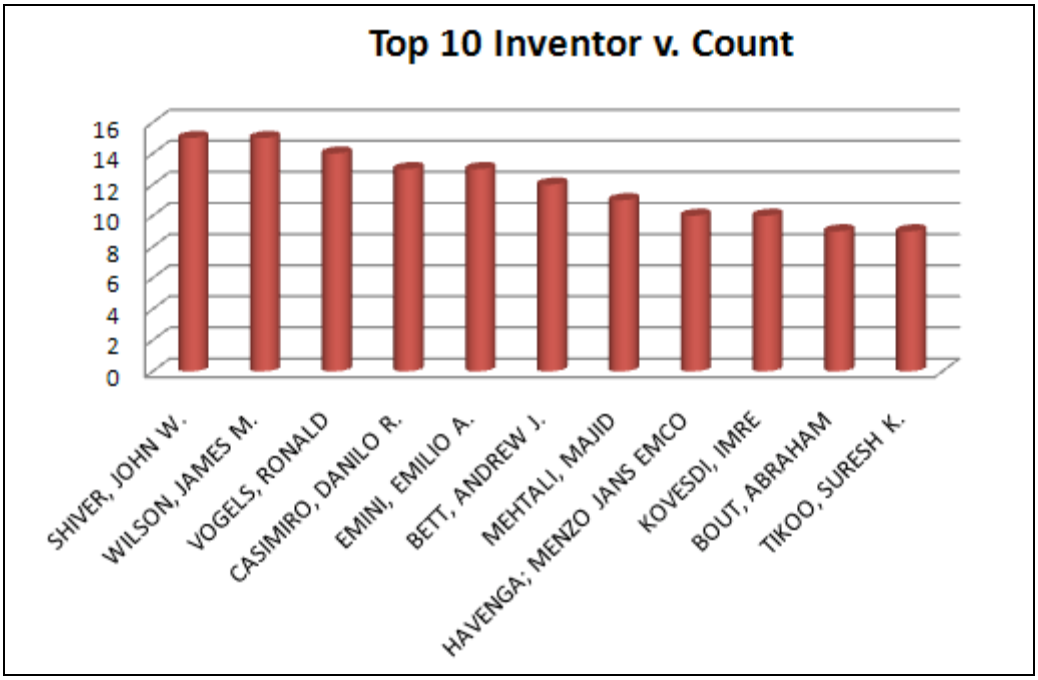
Executive Summary 1
Disclaimer 5
I. About the Technology 6
1. Adenovirus Biology 6
1.A. Adenovirus Biology Overview 6
1.B. Adenovirus Replication 10
1.C. Adenovirus Infection 13
2. Vaccine Vectors 15
2.A. Adenovirus Uses Other Than Cancer and HIV 15
2.B. Methods for Production of Adenovirus Vectors 17
2.C. Strategies to Attack Pre-existing Immunity 20
2.C.1. From Drawbacks to Merits 20
2.C.2. Adenovirus Immunogenecity Mechanism 20
2.C.3. Problems of Pre-existing Antivector Immunity 21
2.C.4. Strategies to Attack Pre-existing Immunity 21
3. HIV Vaccines 23
3.A. Using the Adenovirus Vector as an HIV Vaccine 23
3.B. Measuring Cellular Immune Responses Against HIV-1 Antigens 24
3.C. Selecting Vaccine Antigens and Potential for Cross-Clade Immune Responses 26
3.D. Current Progress for HIV Vaccines Using Adenovirus Vector – Clinical Trials 27
3.D.1. Clinical Trial Overview 27
3.D.2. Current Clinical Trial for HIV Vaccine Using Adenovirus Ad5 Vector. 27
3.D.2.a. Merck Research 28
3.D.2.a.i Merck's Phase II Trial 29
3.D.2.a.ii. Merck's Phase IIb Trial 29
3.D.2.b. VRC Research 29
3.D.2.b.i. VRC Phase I Trial 29
3.D.3. Other Clinical Trials Using Vectors Other Than Human Ad5 Vector 30
3.D.3.a. Clinical Trial Using Human Adenovirus Vector Other Than Ad5 by IAVI. 30
3.D.3.b. Clinical Trial Using Nonhuman Primate Adenovirus by IAVI 31
3.E. Future Approaches Towards Developing an Adenovirus-based Vaccine 31
3.E.1. Major Alternative Approaches 31
3.E.2. Prime-Boosting Regimens 32
3.E.3. Adenoviral Vectors from Rare Human Serotypes 32
3.E.4. Nonhuman Primate Studies. 33
3.E.5. Adenoviral Vectors from Nonhuman Serotypes 34
3.E.6. Chimeric Adenoviral Vectors and Making Adenoviral Vectors 34
II. Patent Search Methodology and Results 36
1. Patent Search Methodology 36
2. Patent Search Tables 39
2.1 Search #1 39
2.2 Search #2 42
2.3 Search #3 44
3. Patent Search Results Spreadsheet Summary 55
3.1 Categorization Summary 55
3.2 Master Spreadsheet 58
4. Patent Search Analytics 91
4.1 Search Analysis through MicroPatent, Aureka®, Patent Insight Pro®. 91
4.1.1 MicroPatent® Results. 91
4.1.2 Aureka® ThemeMap® Results. 93
4.1.3 Patent Insight Pro® Results. 96
4.1.3.1 Top 5 Assignees. 97
4.1.3.2 Top 5 Inventors. 104

4.2 Final Search Analysis after Adjusting Assignee names. 111
4.2.1 Patent Count vs. Country. 111
4.2.2 Patent Count vs. Publication Date. 112
4.2.3 Patent Count vs. Filing Date. 113
4.2.4 Patent Count vs. Main IPC Class. 114
4.2.5 Patent Count vs. Derwent Main Class. 115
4.2.6 Patent Count vs. Derwent Mannual Code. 116
4.2.7 Patent Count vs. US classification 117
4.2.8 Patent Count vs. Assignee. 119
4.2.9 Patent Count vs. Inventor. 120
Appendix A: Scientific Papers 122
Appendix B: Description of Patent Databases Used in this Report 146
Appendix C: Definitions U.S. Classifications 150
Appendix D: Definitions IPC Classifications 152
Appendix E: Derwent Classifications 153
Appendix F: Chemical Patents Index (CPI) Manual Codes 154
Appendix G: Current Clinical Trials (as of November 2008) 155
Appendix H: Authors' *Curriculum Vitae* 163
Appendix I: MicroPatent Summary Report for Relevant Patents 180

EXECUTIVE SUMMARY



This figure illustrates the patent count by assignee for the patent landscape for Adenovirus Vaccine Technology for HIV. The top assignees include Merck and Crucell Holland.



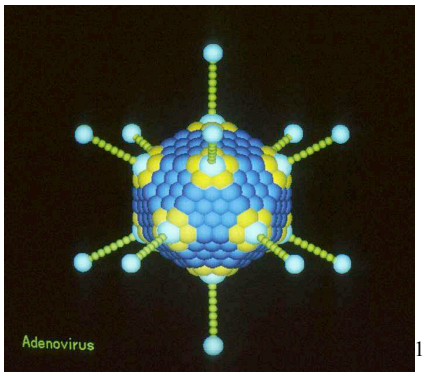
This figure illustrates the patent count by inventor for the patent landscape for Adenovirus Vaccine Technology for HIV. The top inventors include Shiver, Wilson and Vogels.

Value Added Features

This Report enhances previous Pierce Law Patent Landscape Reports Series by adding innovative capacity building features including:

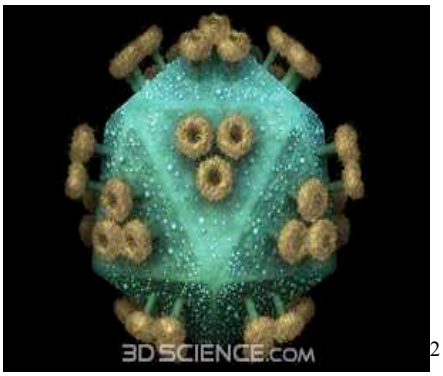
1. Due to the complexity of the subject, the limited timeline for completion of this project and the use of the acquired data by PIPRA, the need for more in-depth technical expert opinion was required. As such, Dr. Dan Barouch was consulted regarding the nature of this project. Dr. Barouch is an Associate Professor at Harvard University. He has conducted research and written numerous papers regarding HIV vaccines using adenovirus vectors.
2. A much greater pool of non-patent, scientific literature was utilized to establish appropriate keywords, inventors and assignees to facilitate patent mining.
3. Due to the complexity and broad nature of the project, a greater pool of patents was reviewed.
4. Due to the complexity of the subject matter, it was necessary to divide teams to specialize in certain aspects of the technology. Each team was assigned a sub-specialty and mined for patents using keywords, inventors, assignees and classification schemes specific to that aspect of the technology.
5. Greater organization of team members resulted in a team leader overseeing two students, a project leader overseeing the team leaders and two professors overseeing the entire project.
6. Introduced use of new patent analytic tools (e.g. Aureka® and Patent Insight Pro® which enable enhanced analyzing of data).
7. Determined and utilized Derwent® Manual Code.
8. Compared and contrasted data obtained by our mining methods with PIPRA collaborator Dr. Kerri Clark. Determed patents unique to Dr. Clark and those unique to the Pierce team. Determined patent documents common to both search efforts.

Scope of the Technology Analyzed



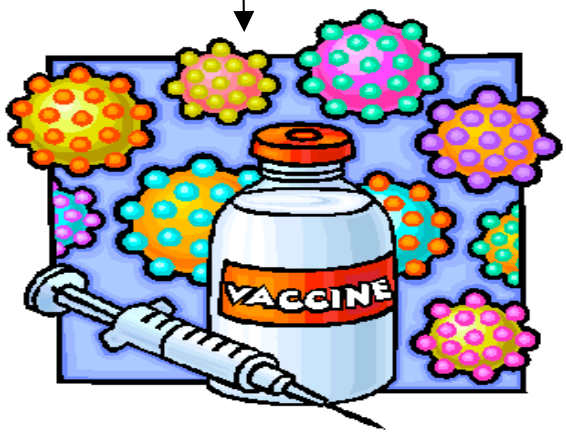
[1]

Adenovirus



[2]

HIV



[3]

Currently the use of adenoviruses as a vaccine carrier for such diseases as HIV is being extensively studied. However, the pre-existing immunity in humans has become a major hurdle when using the adenovirus in such a fashion. As such, research into such a vaccine carrier involves the deletion of one or all of the adenovirus genes. The deletion of E1, E2, E3 and 34 are often referred to as first generation, second generation and

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[1] Adenovirus, http://upload.wikimedia.org/wikipedia/commons/0/0b/Adenovirus.jpg (last visited Dec. 4, 2008).

[2] 3dScience: HIV, http://www.3dscience.com/3D_Images/Biology/Viral/HIV/HIV_Green.php (last visited Dec. 4, 2008).

[3] Another Shot of Rohail, http://images.google.com/imgres?imgurl=http://sabahkamal.files.wordpress.com/2007/03/vaccine.jpg&imgrefurl=http://sabahkamal.wordpress.com/2007/03/11/another-shot-for-rohail/&usg=__eDBIHHth6NoabgG1G1X3t6I0834=&h=306&w=311&sz=17&hl=en&start=2&sig2=24x_7kO9JrfDPce6-yjTiQ&um=1&tbnid=xNPfVnCwmDjyDM:&tbnh=115&tbnw=117&ei=o9g3SafcNaaUeID76IkD&prev=/images%3Fq%3Dvaccine%26um%3D1%26hl%3Den%26rlz%3D1T4GGLF_enUS292US292%26sa%3DN (last visited Dec. 4, 2008).

"gutless," depending on which gene(s) have been deleted. The purpose of this patent landscape study was to search, identify and categorize patent documents that are relevant to the research, development and distribution of a Adenoviral vector based HIV vaccine.

DISCLAIMER

This is an educational report and is neither inclusive nor comprehensive. Rather, it is an informational resource to facilitate a better understanding of the international patent literature landscape with regard to Adenovirus vaccines for HIV.

This report is not a list of all potentially relevant patent documents. It is not a Freedom to Operate (FTO) opinion. Furthermore, this report does not reach the level of a FTO analysis, but instead constitutes an educational presentation of potentially relevant information.

While the search engine utilized in this project are extensive, it is likely that the entire spectrum of patent documents was not obtained utilizing the various search strategies and methods articulated herein. Therefore, it is not the supposition of this team that all relevant patent documents were discovered during the creation of this report.

As the team members are not experts in the field of Adenovirus vaccines for HIV, it is also highly possible that the categorization of the patent documents found, coded and compiled are incomplete. The team cannot guarantee that these patent documents were evaluated at the level of expert scientific sophistication.

Due to the limited time frame (15 weeks) imposed upon this project, the number of patent documents evaluated was established by this constrained schedule, the overall semester demands, and the general press of business. As such, additional patents may have been available for evaluation, but without the necessary time, they may not have been considered.

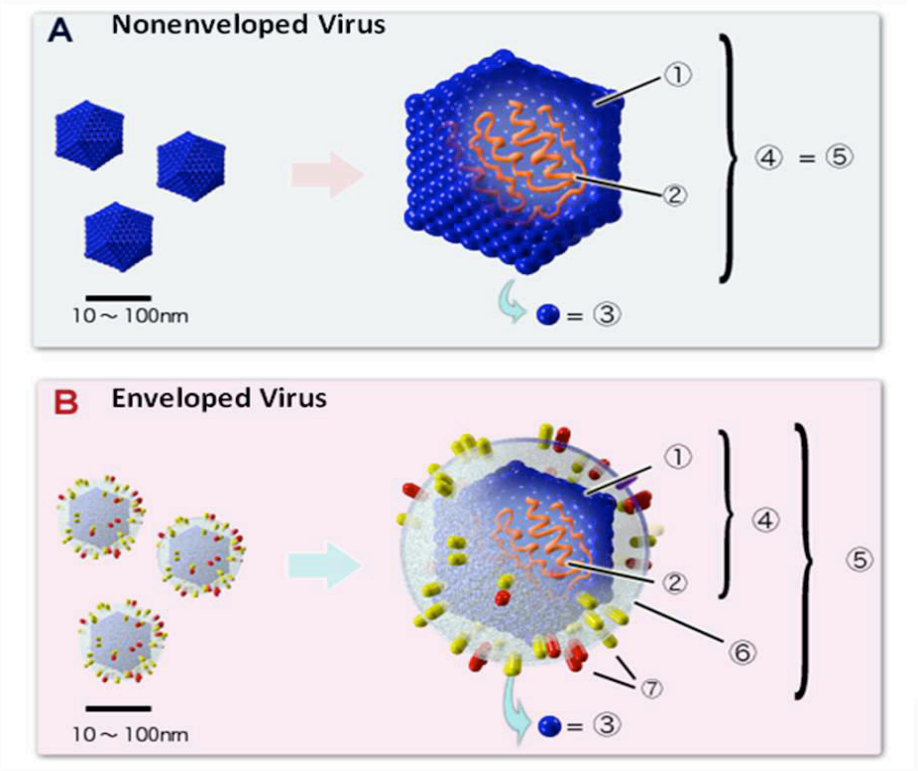
Again, this report should not be viewed as a FTO analysis but instead constitutes an educational report.

I. About the Technology

1. Adenovirus Biology

1.A. Adenovirus Biology Overview

Adenoviruses were first isolated from cultures of human adenoid tissue (tissue located at the back of the nose, above the tonsils) and were discovered in 1953.[4] Adenoviruses are non-enveloped, icosahedrally symmetric double-stranded DNA viruses with a genome of ~ 34-43 kb.[5] See Figure 1. They are associated with acute upper respiratory tract infections as well as gastrointestinal and ocular disease in normal hosts.[6]



1. **Capsid**: The protein shell of the virus.
2. **Nucleic acid**: DNA/RNA.
3. **Capsomer**: An individual unit of the Capsid.
4. **Nucleocapsid**: The genome of the virus and the protein coat that surrounds it.
5. **Virion**: A complete virus particle with its DNA or RNA core and protein coat as it exists outside the cell. Also called a viral particle.
6. **Envelope**: Made of phospholipids and proteins, but include some viral glycoproteins.
7. **Spike** Proteins that contain oligosaccharide chains covalently attached to their polypeptide side-chains.

Figure 1[7]

[4] Samuel K. Campos & Michael A. Barry, *Current Advances and Future Challenges in Adenoviral Vector Biology and Targeting*, 7(3) GENE THERAPY 189, 189 (2007).
[5] Dan H. Barouch & Gary J. Nabel, *Adenovirus Vector-Based Vaccines for Human Immunodeficiency Virus Type 1*, 16(2) HUMAN GENE THERAPY 149, 149 (2005) (discussing the applicability of adenovirus vectors to the immunization of HIV); Nia Tatsis & Hildegund C. J. Ertl, *Adenoviruses as Vaccine Vectors*, 10(4) MOLECULAR THERAPY 616, 616 (2004) (discussing the biology of adenoviruses).
[6] Barouch et al., *supra* note 5, at 149.
[7] Virion, http://upload.wikimedia.org/wikipedia/commons/3/30/Virion.png (last visited Dec. 4, 2008).

The adenovirus capsid is composed primarily of 240 homotrimeric Hexon capsomers with twelve Penton capsomers located at each of the twelve fivefold axes of symmetry. See Figure 2. The capsid of the virus contains three major proteins: Hexon, Fibers, and Penton Base proteins. The Hexon protein provides structural support, but differs in size and immunological properties between serotypes. It is comprised of approximately 1,000 residues, which form three identical large polypeptide chains.[8] The Fiber protein of adenovirus exhibit high homology among serotypes and occurs as a trimer on the surface of the capsid.

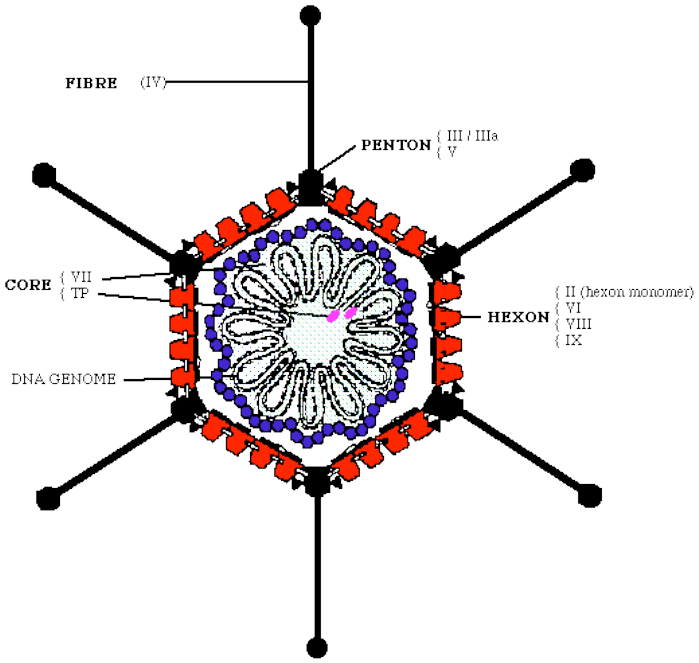


Figure 2[9]

The Fiber proteins are anchored to the capid by the Penton Base proteins, which occur as a pentamer. Together with the Fiber protein, it is responsible for the attachment of the virus to cell surfaces.[10]

The capsid is stabilized by several minor scaffolding proteins: VI, VIII, IX, IIIa, and IVa2. Protein VI is located beneath the hexons in the viral capsid. When the virus enters the host cells, the lowered pH causes destabilization of the capsid, which liberates protein VI and promotes membrane disruption.[11] Proteins VIII and IX are thought to aid in stabilization and/or assembly of the virion.[12] Protein IIIa is associated with the Penton Base and is critical to major late mRNA and protein expression.[13] Protein IVa2 plays a role in viral DNA packaging and is a transcriptional activator of the major late promoter. Research suggests that the IVa2 protein

[8] Hans Jornvall et al., *The Adenovirus Hexon Protein*, 256(12) J. BIOLOGICAL CHEMISTRY 6181, 6181 (1981).
[9] MicrobiologyBytes, *Adenoviruses*, http://www.microbiologybytes.com/virology/Adenoviruses.html (last visited Dec. 3, 2008).
[10] Luci Karayan et al., *Structural and Functional Determinants in Adenovirus Type 2 Penton Base Recombinant Protein*, 71(11) J. VIROLOGY 8678, 8678 (1997).
[11] Christopher M. Wiethoff et al. , *Adenovirus Protein VI Mediates Membrane Disruption Following Capsid Disassembly*, 79(4) J. VIROLOGY 1992, 1997 (2005).
[12] MicrobiologyBytes, *supra* note 6.
[13] Magnus Molin et al., *Unscheduled Expression of Capsid Protein IIIa Results in Defects in Adenovirus Major Late mRNA and Protein Expression*, 83 VIRUS RESEARCH 197, 197 (2002).

plays a role in viral DNA packaging and that a functional interaction between IVa2 and the rest of adenovirus packaging machinery is serotype specific.[14] See Figure 3.

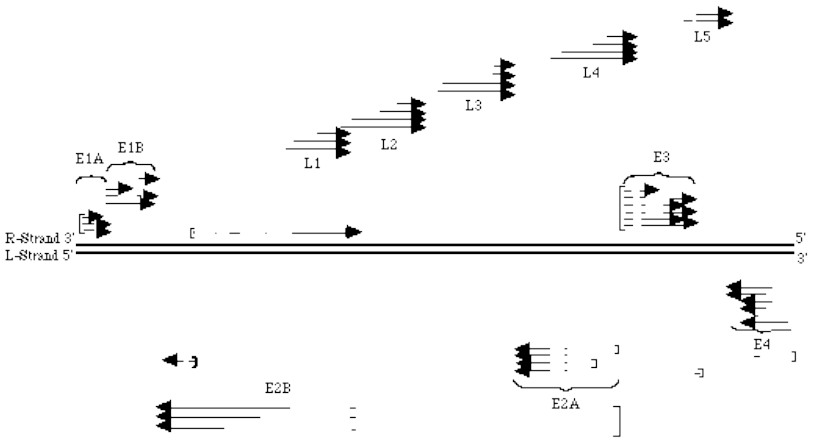


Figure 3[15]

The core of adenoviruses contains four key proteins: Terminal Protein, V, VII, and Mu. The Terminal Protein is covalently attached to the ends of the genome strand. Protein V and VII are non-covalently associated with the genome forming a chromatin-like substance and the latter is believed to form a link between the viral DNA-core protein complex and the viral capsid.[16] Protein Mu is believed to help condense DNA. However, Mu has a precursor protein, preMu, works with protein V to demonstrate nuclear and nucleolar targeting. preMu may also be capable of modulating splice-site selection.[17]

As previously stated, the genome of adenovirus is approximately 34-43kb and forms double-stranded DNA. To conserve space, it encodes polypeptides from both DNA strands and uses alternative splicing and different polyadenylation sites. Its genome carries five early genes: E1A, E1B, E2, E3, and E4.[18] The E1A gene induces

[14] Wei Zhang & Michael J. Imperiale, *Requirement of the Adenovirus IVa2 Protein for Virus Assembly,* 77(6) J. VIROLOGY 3586, 3586–87 (2003).
[15] MicrobiologyBytes, *supra* note 9.
[16] MicrobiologyBytes, *supra* note 12.
[17] T. W. R. Lee et al., *Precursor of Human Adenovirus Core Polypeptide Mu Targets the Nucleolus and Modulates the Expression of E2 Proteins*, 85 J. GENERAL VIROLOGY 185, 185–95 (2004).
[18] Tatsis et al., *supra* note 5, at 616–17.

expression of other viral early genes.[19] The E1B gene delays host cell lysis during viral replication and after replication is complete, it induces apoptosis and controls the export of viral transcripts.[20] Deletion of E1 results in viruses that are severely impaired in their ability to replicate and allows for the insertion of approximately 5.1kb of new DNA.[21]

The E2 gene encodes DNA-binding proteins and a polymerase and is essential for virus replication. Conversely, the E3 gene is not essential for virus replication, but is involved in blocking Fas-mediated apoptosis. This gene allows the virus to escape immunosurveillance by reducing expression of major histocompatibility complex class I determinants. E3 is expressed at a late state of viral replication and encodes a protein, the Adenovirus Death Protein, which promotes death of the infected cell and thus releases the virus particles.[22] The E4 gene encodes seven proteins that affect transcription and affect host cell functions, including proliferation and apoptosis (in part by degrading p53). This gene is essential for nuclear export of viral RNA.[23]

Adenoviruses are species specific. Their taxonomic family is Adenoviridae and there are four genera: Siadenovirus, Aviadenovirus, Atadenovirus, and Mastadenovirus. Each genus is serologically distinct from the others and there is great variation among the genera, especially regarding the size of the genomes and the virion surface proteins. The Siadenvirus genus has only two known members: Frog adenovirus 1 and Turkey adenovirus 3. This genus only affects amphibians (frogs) and birds (turkey, pheasant, and chicken). The Aviadenovirus genus infects birds only and its genome is approximately 20% - 45% larger than the other genera in the family. The Atadenovirs genus has a broad range of hosts (snake, duck, opossum, ruminant, etc) and all of the affected classes are vertebrates. The Mastadenovirus genus infects mammals only. There are at least fifty-one antigenicaly unique serotypes or species categorized into six subgenera (A-F).[24]

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[19] Alan J. D. Bellett et al., *Control Functions of Adenovirus Transformation Region ElA Gene Products in Rat and Human Cells*, 5(8) MOLECULAR & CELLULAR BIOLOGY 1933, 1933 (1985).
[20] Yue Liu et al., *Adenovirus E1B 55-Kilodalton Oncoprotein Inhibits p53 Acetylation by PCAF*, 20 MOLECULAR & CELLULAR BIOLOGY 5540, 5540 (2000).
[21] X. Danthinne & M. J. Imperiale, *Production of First Generation Adenovirus Vectors: a Review*, 7 GENE THERAPY 1707, 1707–08 (2000).
[22] Shimon Efrat et al., *Adenovirus Early Region 3 (E3) Immunomodulatory Genes Decrease the Incidence of Autoimmune Diabetes in NOD Mice*, 50(5) DIABETES 980, 983 (2001).
[23] Catarina Hemstrom et al., *Adenovirus E4-Dependent Activation of the Early E2 Promoter is Insufficient to Promote the Early-to-Late-Phase Transition*, 65(3) J. VIROLOGY 1440, 1440 (1991).
[24] M. Benko, VIIIth *Report of the International Committee on Taxonomy of Viruses* (Jan. 2007), *available at* http://www.vmri.hu/~harrach/AdVtaxlong.htm.

This virus is genetically very similar to the host cells which it infects. Antivirals have generally been ineffective against adenovirus infection. The vaccine against adenovirus is live, oral and attenuated in the intestine. Vaccines are administered to the military but not available for general use because of concern about the live vaccine's oncogenic potential and the level of attenuation achieved in children. Adenoviruses can lead to serious and sometimes fatal infections such as meningioencephalitis and pneumonia, especially in children and individuals with compromised immune systems.[25] See Figure 4.

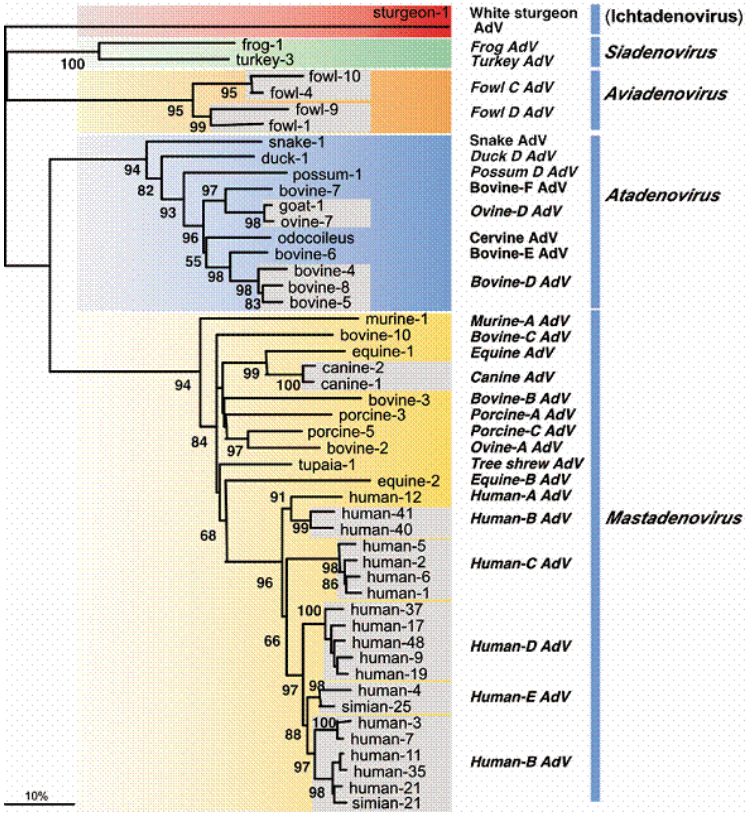

Figure 4[26]

1.B. Adenovirus Replication

A single virus particle (called virion) essentially lacks all the necessary components that are present in cells to reproduce. They are therefore completely dependent on the host cells for this function. Viruses of the family *Adenoviridae* are no different. They use the host cells own replication machinery (DNA polymerase, DNA binding protein etc.) to reproduce the viral DNA in the cell.[27]

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[25] Tatsis et al., *supra* note 5, at 616–18.
[26] Benko, *supra* note 24.
[27] TOPLEY AND WILSON'S MICROBIOLOGY AND MICROBIAL INFECTIONS, VOLUME 1: VIROLOGY 75–91(9th ed., Oxford Univ. Press 1998).

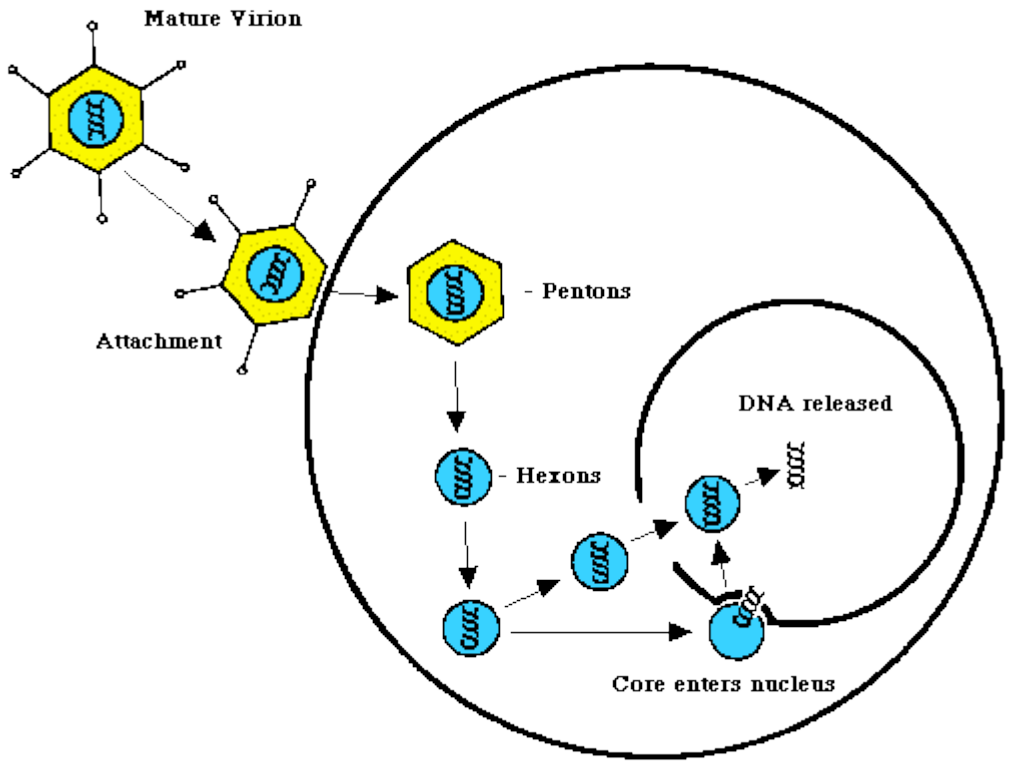

Figure 5: Adenovirus cell infection.[28]

Replication is divided into 2 phases: early and late. The late phase starts upon onset of DNA replication. Before and independently of genome replication, immediate early and early mRNAs are transcribed from the input DNA. Transcription of the Adenovirus genome is regulated by virus-encoded trans-acting regulatory factors. Products of the immediate early genes regulate expression of the early genes. Early genes are encoded at various locations on both strands of the DNA.[29] See Figure 5.

The first mRNA/protein to be made (~1h after infection) is E1A. This protein is a trans-acting transcriptional regulatory factor whose precise mode of action is not known (not a DNA-binding "transcription factor") but is necessary for transcriptional activation of early genes. The protein is also capable of activating transcription from a variety of other viral and cellular promoters and shows no sequence-specificity, rather a modification of the cellular environment. E1A is considered the "immortalizing" protein of Adenoviruses.[30]

"E" mRNA/proteins are made during the early phase. "L" mRNA/proteins are made during the late phase.[31] Refer to Figure 3 (above).

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[28] Alan Cann, *Welcome to Microbiologybytes*, www.microbiologybytes.com (last visited Dec. 3, 2008).
[29] J. Flint & T. Shenk, *Viral Transactivating Proteins,* 31 ANNUAL REVIEW OF GENETICS 177, 192. (1997).
[30] John W. Shiver & Emilio A. Emini, *Recent Advances in the Development of HIV-1 Vaccines Using Replication-Incompetent Adenovirus Vectors*, 55 ANNUAL REVIEW OF MEDICINE 355, 357 (2004).
[31] Cann, *supra* note 28.

Upon E1A being made, the early phase of replication begins and E1B is made. E1B "cooperates" with E1A to transform the cell. The E1B gene product 19K also seems to function co-operatively with E1A and p53 in promoting oncogenesis and transformation, mainly by ensuring that the downstream consequences of cell cycle release do not induce apoptosis.[32]

At this point E3 proteins are made. There are seven E3 proteins, none of which is required for replication in cultured cells, implying anti-immune functions. E3 has therefore been called the "stealth" gene, allowing adenoviruses to evade the host immune response.[33]

Thereafter, late transcription ensues, with five cassettes of transcripts (termed L1 to L5) resulting from a complex series of splicing events. These lead to the production of the virus structural components and the encapsidation and maturation of virus particles in the nucleus. A key player in the control of transcription is the major late promoter (MLP), which is attenuated during transcription of the early genes. Late phase gene expression is primarily concerned with the synthesis of virion proteins.[34]

The adenovirus genome has inverted terminal repeats (ITRs) of about 100 bp. Located within the ITRs are the cis-acting DNA sequences which define *ori*, the origin of DNA replication. Covalently attached to each 5' end is a terminal protein (TP) which is likely to be an additional cis-acting component of *ori*. Within the terminal 51 bp of the adenovirus 2 genome, four regions have been defined that are involved in initiation of replication. The terminal 18 bp are regarded as the minimal replication origin and these sequences can direct limited initiation with just the three viral proteins involved in replication: preterminal protein (pTP), DNA polymerase (pol) and DNA binding protein (DBP). However, two cellular transcription factors, nuclear factor I (NFI) and nuclear factor III (NFIII) are required for efficient levels of replication. In contrast adenovirus 4 replicates efficiently without NFI and NFIII. A further cellular factor, a topoisomerase, is required for complete elongation.[35]

The DNA replication has multiple steps:

- First, the viral genome is coated with DBP
- This protein reacts co-operatively with the cellular transcription factor NFI which binds to a recognition site within the origin of replication, separated from the 1-18 bp core by a precisely defined spacer region.
- NFIII also binds at a specific recognition site between nucleotides 39 and 48.
- Protein-protein interactions, between NFI and pol, and pTP and NFIII help recruit the pTP-pol heterodimer into the preinitiation complex.
- Interaction between the heterodimer and specific base pairs 9 to 18 in the DNA sequence ensures correct positioning and the complex is further stabilized by interactions between the incoming pTP-pol and the genome-bound TP.

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[32] W.C. Russell, *Update on adenovirus and its vector*, 81 J. GEN. VIROLOGY 2573, 2576 (2000).
[33] MicrobiologyBytes, *supra* note 9.
[34] Russell, *supra* note 32, at 2577.
[35] MicrobiologyBytes, *supra* note 9.

- DNA replication is then initiated by a protein priming mechanism in which a covalent linkage is formed between the alpha-phosphoryl group of the terminal residue, dCMP and the beta-hydroxyl group of a serine residue in pTP, a reaction catalysed by pol. This acts as a primer for synthesis of the nascent strand.
- Base pairing with the second GTA triplet of the template strand guides the synthesis of a pTP-trinucleotide, which then jumps back 3 bases, to base pair with the first triplet (also GTA) and synthesis then proceeds by displacing the non-template strand.
- NFI dissociates as the first nucleotide binds just prior to the initiation reaction. Dissociation of pTP from pol begins as the pTP-trinucleotide is formed and is almost complete by the time 7 nucleotides have been synthesized.
- NFIII dissociates as the replication binding fork passes through the NFIII binding site.

Assembly of these virion proteins starts in the cytoplasm where the monomers become penton and hexon capsomers. The newly replicated DNA is then inserted into these hollow capsids in the nucleus.[36]

Eventually, the cell will lyse from the continuous replication of the Adenovirus, facilitated by the adenovirus protein E3-11.6K which induces apoptosis. This allows release of the virus to infect more of the host's cells.[37]

1.C. Adenovirus Infection

Adenovirus infection is widespread in nature, affecting many species including humans, monkeys, pigs, cows, horses, sheep, dogs and birds.[38] Adenovirus infects the tissue lining of the respiratory tract causing illnesses including acute upper respiratory tract infections and may also be the cause of illness such as gastroenteritis, conjunctivitis, cystitis, and rashes.[39] A particular illness may be associated with a certain type of adenovirus as illustrated in Table 1.

Disease	At Risk
Acute Respiratory Illness	Military recruits, boarding schools, etc.
Pharyngitis	Infants
Gastroenteritis	Infants
Conjunctivitis	All
Pneumonia	Infants, military recruits
Keratoconjunctivitis	All
Acute Haemorrhagic	Infants

[36] *Id.*
[37] *Id.*
[38] *Id.*; Teng Chih Yang et al., *T-cell Immunity Generated by Recombinant Adenovirus Vaccines*, 6(3) EXPERT REVIEW VACCINES 347, 348 (2007).
[39] MicrobiologyBytes, *supra* note 9; Center for Disease Control, http://www.cdc.gov/ncidod/dvrd/revb/respiratory/ eadfeat.htm (last visited Dec. 3, 2008).

Cystitis	
Hepatitis	Infants, liver transplant patients

Table 1: List of Diseases and Associated at risk person(s)[40]

Most people will have been infected with some sort of adenovirus infection by the age of fifteen due to its prevalence within the population. Because the adenovirus is only present within a few cells of the body, scientists have been unable to ascertain how long the virus can live within the body or if it is capable of re-activation resulting in illness after long periods of dormancy. However, it has been ascertained that virus re-activation occurs during times of immunosuppression (i.e. AIDS and organ transplants).[41]

In order to replicate, the adenovirus must remain hidden from the immune system until such time as the replication has completed. Adenoviruses have three main means of avoiding the host immune system. The first method of avoidance by the virus involves preventing the action of the interferons which play a crucial role in attacking the adenovirus infection. Interferons seek to stop the replication of the adenovirus and boost the body's immune response (i.e. macrophages and natural killer cells). By preventing the action of the interferons, the adenovirus survives and replicates. The second method of avoidance by the virus involves preventing cell death using the adenovirus E1b protein. Preventing a cell from "commit[ting] suicide" to spare the host from viral infection allows the virus to continue spreading. Finally, the final method of avoidance by the virus involves ensnaring the host major histocompatibility complex (MHC) within the endoplasmic reticulum. The MHC functions to signal distress to the immune system. The trapping of the MHC, thus, allows virus cells to preserve themselves by not displaying viral peptides to the immune system.[42]

Figure 6 illustrates the process of adenovirus infection. First, the adenovirus vector binds to a specific cellular receptor, coxsackievirus and adenovirus receptor (CAR) on the surface of the host cell. Next, endocytosis occurs, resulting in the virus being freed into the cytoplasm. The virus then heads to the nucleus where gene expression occurs.[43]

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[40] MicrobiologyBytes, *supra* note 9.
[41] *Id.*
[42] Immune System Evasion and Adenovirus, http://www.stanford.edu/group/virus/adeno/2004takahashi/webpage/Immune%20System%20Evasion%20and%20Adenoviruses.htm (last visited Dec. 3, 2008).
[43] Juan Contreras, *Nonhuman Primate Models in Type 1 Diabetes Research*, 45(3) INST. LABORATORY ANIMAL RESEARCH J. 334, 337.

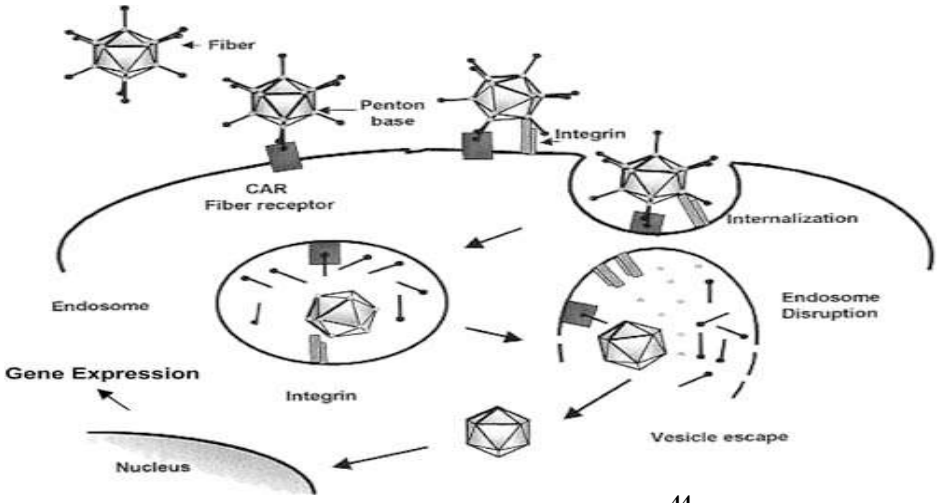

Figure 6: Adenovirus Infection[44]

At least 49 adenovirus serotypes have been identified to date, classified into six subgroups (i.e. A, B, C, D, E, and F) based on hemagglutination properties, genomic organization and ability to produce tumors in rodents.[45] Adenoviruses belonging to subgroup A including serotype 12 (Ad12) have been found to induce tumors with short latency and high frequency. Those belonging to subgroup B including serotypes 3 and 7 (Ad3 and Ad7) are weakly oncogenic. Adenoviruses belonging to subgroup C including serotypes 1, 2 and 5 (Ad1, Ad2 and Ad5) as well as the serotypes in subgroups D, E and F are non-oncogenic. Serotypes 1, 2 and 5 (Ad1, Ad2 and Ad5) are adenoviruses which most commonly infect humans and generally cause mild upper respiratory infections in children. Serious infections such as pneumonia and meningioencephalitis may be caused by adenovirus serotypes 4 and 7 (Ad4, Ad7) and serotypes 7, 12 and 32 (Ad7, Ad12 and Ad32), respectively.[46]

The serotypes most frequently used in human vaccination research are Ad5. This particular serotype is rigid, accepting only those genomes which are no bigger than 105% of the wild-type genome. This characteristic allows the insertion of only about 2 kb of exogenous DNA. Recombinant serotype 5 (rAd5) has specifically been targeted for vaccination research based on the above. Additionally, recombinant adenoviruses are highly immunogenic, have been extensively researched resulting in simple methods of introducing DNA into the genome and their characteristics are easily amplified in culture.[47]

2. Vaccine Vectors

2.A. Adenovirus Uses Other Than Cancer and HIV

[44] *Id.*
[45] *Id.*; Yang et al., *supra* note 38, at 348.
[46] MicrobiologyBytes, *supra* note 9; Tatsis et al., *supra* note 2, at 618.
[47] Yang et al., *supra* note 38, at 348.

Adenoviruses have been heavily used as vectors to deliver a vaccine primarily because of their benign history of upper respiratory tract infections and more generally, their lack of association with oncogenicity in humans.[48] The use of serotypes Ad4 and Ad7 have been particularly useful as they have been used for decades in soldiers to combat acute respiratory distress without any adverse effects.[49] In addition to the safety factors, adenoviruses are excellent candidates for use as vaccine vectors because adenoviruses have high gene-transfer potential, the ability to be propagated to high titers, a broad cell tropism, a large insert capacity, a well characterized genome and protocols for manipulation and are highly immunogenic. These characteristics make adenoviruses excellent candidates to be used as vectors not only for HIV, but also for other diseases.[50]

The majority of adenovirus vectored vaccines for infectious and non-infectious disease are based on first generation Ad5.[51] The E1 and E3 replication regions are generally removed or manipulated to carry an antigen expression cassette in place of the deleted region.[52] Several laboratories are also experimenting with vectors from other serotypes, non-human adenoviruses and chimeric or hybrid vectors.[53]

One group of viral infections that have been attacked using adenovirus vectors includes Hepatitis C, Dengue viruses, Ebola virus, Marburg giloviruses and most recently, SARS.[54] See Table 2. Replication defective rAd vectors encoding Hepatitis C virus (HCV) have been shown to elicit specific immune responses and varying degrees of protection using a mouse model.[55] Structural proteins of several different adenovirus serotypes in animals have shown encouraging results for Dengue Fever.[56] Using rAd to encode a recombinant antibody was shown to protect mice against a lethal West Nile Virus Challenge.[57] Human Ad5 expressing an Ebola envelope glycoprotein was shown to elicit immune responses in mice and fully protect monkeys from the virus. A human ebola vaccine is still needed as one of the more successful NIH ebola vaccine trials has been paused for review. Encouraging results to combat SARS (avian flu), Marburg virus, Rabies, and malaria have also been produced.[58]

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[48] Tatsis et al., *supra* note 5, at 618.
[49] Tanu Chawla et al., *Adenovirus-Vectored Vaccines*, 18(3) EXPERT OPINION ON THERAPEUTIC PATENTS 293, 293–94 (2008).
[50] Tatsis et al., *supra* note 5, at 616.
[51] *Id.*
[52] *Id.* at 619.
[53] *Id.* at 624.
[54] *Id.*
[55] Chawla, *supra* note 49, at 299.
[56] Tatsis et al., *supra* note 5, at 624.
[57] Chawla, *supra* note 49, at 299.
[58] Tatsis et al., *supra* note 5, at 624.

Pathogen	Animal Model	Insert	Immune Response
Rabies	rodent, dog	Glycoprotein	CMI and anti body
Dengue virus	Rodent	Envelope	CMI and anti body
Ebola virus	Rodent, NHP	Glycoprotein, nuceloptotein	CMI and anti body
SARS - coronaviurs	Rodent, NHP	Spike, nucelocapsid, membrane protein	CMI and anti body
Human Papillomavirus	Rodent, NHP	L1, E5, E6, E7	CMI and anti body
Hepati tus C Virus	Rodent	E1, E2, core, NS3	CMI and anti body
Hepati tus B Virus	Rodent, dog, NHP	Surface Anti gen	Anti body
Rotavirus	Rodent	VP7sc	Anti body
Measles Virus	Rodent	Nucelocapsid, hemaggluti nin, fusion protein	CMI and anti body
Respiratory syncyti al virus	Rodent, dog, NHP	Glycoprotein	Anti body
Cytomegalovirus	Rodent	Glycoprotein B	Anti body
Herpes simplex 2virus	Rodent	Glycoprotein B	CMI and anti body
Epstein-Barr Virus	Rodent	latent membrane proteins 1 + 2, envelope glycoprotein	CMI and anti body

Abbreviations: CMI, cell-mediated immunity; NHP, nonhuman primate.

Table 2[59]

2.B. Methods for Production of Adenovirus Vectors

There are a number of methods that have been used by clinicians to prepare alternative adenovirus (Ad) vectors to treat HIV.[60] The prominent methods that are currently receiving the majority of attention are ligation, deletions, alternative serotypes, and altered tropisms. These methods are all used to increase the effectiveness of gene transfer with an adenovirus vector. Prior to looking at the methods it is important to first look at the evolution of adenovirus vectors.[61]

The first attempts at creating a vector involved non replicating vectors, also commonly referred to as First Generation adenoviruses. These were based on an E1 deletion. This is followed by the insertion of foreign DNA through homologous recombination. There was also the potential to include an E3 deletion, this would allow for a larger piece of DNA to be inserted, and has shown to decrease host immune

[59] *Id.*
[60] John W. Shiver et al., *Replication-Incompetent Adenoviral Vaccine Vector Elicits Effective Anti-Immunodeficiency - Virus Immunity*, 415 NATURE 331, 332 (2002).
[61] Eric J. Kremer et al., *Canine Adenovirus Vectors: an Alternative for Adenovirus-Mediated Gene Transfer*, 74 J. VIROLOGY 505, 505 (2000).

response.[62] One of the major drawbacks of the First Generation is that the deletion of the E1 gene is not enough to totally obliterate all viral gene activation.[63]

Those limitations lead to the advent of the Second Generation vectors. At this point the vector contained additional deletions and/or mutations within E2 or E4 regions. This increased the potential package size. The E4 deletion in the viral genome offered an improvement in the stability of gene expression, with a reduction in the inflammatory response.[64] The most resent work has been done in the Last Generation or Gutless adenoviruses. These vectors are devoid of all viral coding regions.[65] It also contains only the cis-acting elements. These vectors often require a Helper Virus to produce the virus. The use of a Helper requires the use of a strategy to avoid/reduce helper contamination.[66]

One of the first methods for producing a vector was by *in vitro* ligation. This method starts with a deletion at the E-1 deleted Ad vectors.[67] After the gene of interest is inserted downstream of the viral sequence of the plasmid, the fragment containing viral sequence and the gene of interest is excised and ligated into the unique site, in this case the *Cl*aI site, replacing a portion of the viral E1 region, the ligated DNA is then transfected into cells to make recombinant virus. This method is rarely used as it is very inefficient and requires additional steps of purification for contamination and transgene null viruses related to the incomplete restrictions digestions and self-relegation.[68]

Construction of recombinant adenovirus by ligation consists of the following steps: first, introduce three unique restriction sites into the E1 deletion site of the vector plasmid, this plasmid contains a complete E1, E3-deleted adenovirus type 5 genome; second, a shuttle plasmid containing multiple cloning sites between the sites, is then constructed.[69] Once the gene of interest is inserted into the shuttle plasmid, the plasmid for E1-deleted adenovirus vector can be prepared by *in vitro* ligation using the sites. The large number and strategic location of the unique restriction sites will not only increase

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[62] Kathleen M. Hehir et al., *Molecular Characterization of Replication-Competent Variants of Adenovirus Vectors and Genome Modifications to Prevent their Occurrence*, 70 J. VIROLOGY 8459, 8466 (1996).
[63] Wolfgang Poller et al., *Stabilization of Transgene Expression by Incorporation of E3 Region Genes into an Adenoviral Factor IX Vector and by Transient Anti-CD4 Treatment of the Host*, 3 GENE THERAPY 521, 521 (1996).
[64] M. Lusky et al., *In Vitro and In Vivo Biology of Recombinant Adenovirus Vectors with E1, E1/E2A, or E1/E4 Deleted*, 72 J. VIROLOGY 2022, 2023 (1998).
[65] Gudran Schiedner et al., *Genomic DNA Transfer with a High-Capacity Adenovirus Vector Results in Improved In Vivo Gene Expression and Decreased Toxicity*, 18 NATURE GENETICS 180, 180 (1998).
[66] Dennis J. Hartigan-O'Connor et al., *Improved Production of Gutted Adenovirus in Cells Expressing Adenovirus Preterminal Protein and DNA Polymerase*, 73 J. VIROLOGY 7835, 7836 (1999).
[67] Kathleen L. Berkner & Phillip A. Sharp, *Generation of Adenovirus by Transfection of Plasmids*, 11 NUCLEIC ACIDS RESEARCH 6003, 6007–08 (1983).
[68] Hiroyuki Mizuguchi & Mark A. Kay, *Efficient Construction of a Recombinant Adenovirus Vector by an Improved In Vitro Ligation Method*, 9(17) HUMAN GENE THERAPY 2577, 2578 (1998).
[69] Guang Ping Gao et al., *A Cell Line for High-Yield Production of E1-Deleted Adenovirus Vectors without the Emergence of Replication-Competent Virus,* 11 HUMAN GENE THERAPY 213, 214 (2000).

the rapidity of production of new first generation vectors for gene transfer but will allow for rapid further improvements in the vector DNA backbone.[70]

The adenovirus capsid allows for some latitude regarding the length of the genome that can be inserted. This variability comes into play through the amount of the adenovirus sequence can be deleted. With the deletion of E3, which encodes gene products that are nonessential for virus replication, there is room to accommodate an additional 3.5 kb of foreign sequence.[71]

Deletion of adenovirus is done to facilitate the insertion of the desired gene of interest. The steps to achieve the deletion are: first, generate knockout point mutations into the unassigned adenovirus open reading frames (ORFs) to determine if they were essential for virus replication; second, construct genomes with various deletions in the regions of these nonessential ORFs; third, an expression cassette coding for the enhanced green fluorescent protein (eGFP) is inserted in place of the deletions to follow expression of the transgene and propagation of the vector in cell monolayers; fourth, retain the vector backbone that has the largest deletion, this can then be used for the construction of vectors carrying infectious virus proteins.[72] These vectors can then be used for vaccinations.[73]

Another area of research has been in alternative serotypes, most currently used adenovirus vectors are based upon serotypes 2 and 5 (Ad2 and Ad5), but these vectors are limited in their application due to anti-immunity in the population.[74] There are 51 identified serotypes of human adenovirus, divided into six species (A-F), each with a different tropism. Adenoviruses of different species have different tropisms, indicating that serotypes other than Ad2 or Ad5 could be evaluated for their potential as a vector. It stands within reason that these other serotypes can alleviate the limited tissue tropism and immunity problems of Ad2 and Ad5.[75]

Altered tropisms have also been used to increase the viability of adenovirus vectors. Gene delivery to cells by adenovirus is initiated by the binding of the adenovirus fiber knob to a cellular receptor.[76] Of the 6 species, A and C-F have the same coxsackievirus and adenovirus receptor (CAR), species B uses a receptor different from CAR. Studies have shown that the fiber of the subtype C can be replaced with that of

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[70] *Id.* at 215–16.
[71] I. Saito et al., *Construction of Nondefective Adenovirus Type 5 Bearing a 2.8-kilobase Hepatitis B Virus DNA near the Right End of the Genome*, 54 J. VIROLOGY 711, 714 (1985).
[72] Janice M. Boyd et al., *Adenovirus E1A N-Terminal Amino Acid Sequence Requirements for Repression of Transcription In Vitro and in Vivo Correlate with those Required for E1A Interference with TBP-TATA Complex Formation*, 76 J. VIROLOGY 1461, 1461-1466 (2002).
[73] Gao, *supra* note 69, at 213.
[74] Stefan Kostense et al., *Adenovirus Types 5 and 35 Seroprevalence in AIDS risk Groups Supports Type 35 as a Vaccine Vector*, 18 AIDS 1213, 1213 (2004).
[75] Dan Barouch et al., *Immunogenicity of Recombinant Adenovirus Serotype 35 Vaccine in the Presence of Pre-existing Anti-Ad5 Immunity*. 172 J. IMMUNOLOGY 6290, 6297–98 (2004).
[76] Jeffery Bergelson et al., *Isolation of a Common Receptor for Coxsackie B Viruses and Adenoviruses 2 and 5*, 28 SCIENCE 1320, 1321. (1997).

subtype B. This ability to genetically engineer the tropisms allows for a variety of potential vaccines.[77]

2.C. Strategies to Attack Pre-existing Immunity

2.C.1. From Drawbacks to Merits

Recombinant adenovirus vectors have been recognized as a favorable candidate for gene therapy because of their high transduction efficiency. However, transgene expression from adenovirus gene therapy vectors was significantly limited by the rapid emergence of potent cellular and humoral immune responses against both the vector and the insert.[78] Ironically, however, it is a desirable feature for vector-based vaccine.

2.C.2. Adenovirus Immunogenecity Mechanism

The mechanism of the adenovirus immunogenicity can be divided into four steps. First, adenovirus vectors attach to cells by a specific interaction between the adenovirus fiber proteins and its cell receptors. The receptors vary according to the adenovirus serotypes. For example, Ad5 attaches to the coxsackievirus and adenovirus receptor (CAR) on the surface of the host cell, and Ad35 attaches to CD46 rather than CAR as the receptor. Second, once an adenovirus vector attaches to the receptor of the host cell, it enters into the cell by an endocytosis mechanism between RGD motif of penton base and cellular intergrins. Third, the acidification of endosomes allows the vector to escape into the cytoplasm and traffic to the nucleus. Finally, antigens are synthesized intracellularly, and these antigens are efficiently processed and presented in association with MHC class I molecules on the cell surface.[79]

[77] Thomas J. Wickham, *Targeting Adenovirus,* 17 GENE THERAPY 110, 111 (2000).
[78] Barouch et al., *supra* note 5, at 150.
[79] *Id.*

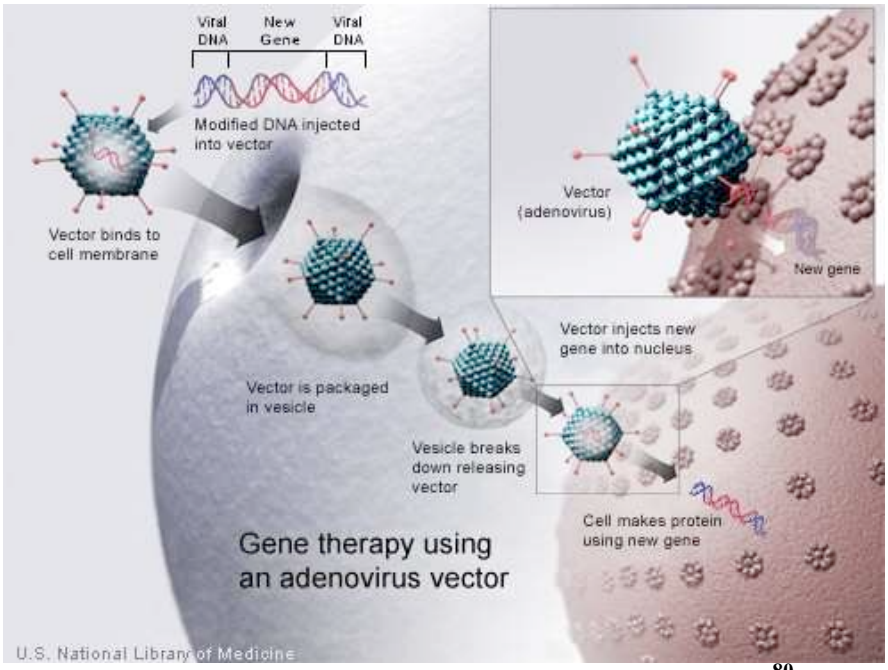


Figure 7: Transduction of adenovirus into the cell[80]

2.C.3. Problems of Pre-existing Antivector Immunity

Pre-existing anti-vector immunity could neutralize the vaccine and eliminate transduced cells before immune priming; thereby, suppressing vaccine-elicited immune responses. For example, in certain regions in developing countries, Ad5 sero-prevalence is more than 90%, with remarkably high neutralizing antibody (Nab) titers.[81] Not only are Ad5 neutralizing antibodies a major reason for anti-Ad5 immunity, but also Ad5 specific humoral and cellular immune response (CD4+ or CD8+ T Lymphocytes) contribute to the suppression of the immunogenicity of adenovirus vaccine.[82]

2.C.4. Strategies to Attack Pre-existing Immunity

Scientists have been studying the effects of fulfilling pre-existing antivector immunity. Currently, there are at least three categories being considered. The first category includes the use of novel methods to deliver existing rAd5 vectors, molecular engineering of rAd5 vectors, and developing novel rAd vectors from alternative serotypes or different species. It also includes an administration of higher doses of rAd5 vectors, rAd5 boosting after DNA priming, or mucosal delivery of rAd5 vectors, etc. The second category includes the use of specific engineering of rAd5 vectors including chimeric rAd5 vectors with regions of the Ad5 fiber proteins or hexon proteins which have been exchanged for the corresponding regions of different Ad serotypes. The third category

[80] U.S. National Library of Medicine, *Genetic Therapy Using an Adenovirus Vector*, http://ghr.nlm.nih.gov/handbook/ illustrations/therapyvector (last visited Dec. 4, 2008).
[81] R. Vogels et al., *Replication –Deficient Human Adenovirus Type 35 Vectors for Gene Transfer and Vaccination; Effiecient Human Cell Infection and Bypass of Preexisting Adenovirus Immunity*, 77(15) J. VIROLOGY 8263, 8263–71 (2003).
[82] Barouch et al., *supra* note 5, at 152.

includes the use of novel rAd vectors from alternative Ad serotypes, including non-human adenovirus (Ovine, porcine, bovine, and chimpanzee Ads, etc.) or rare human adenovirus (Ad35, Ad11, etc.).[83] See Figure 8 and Table 3.

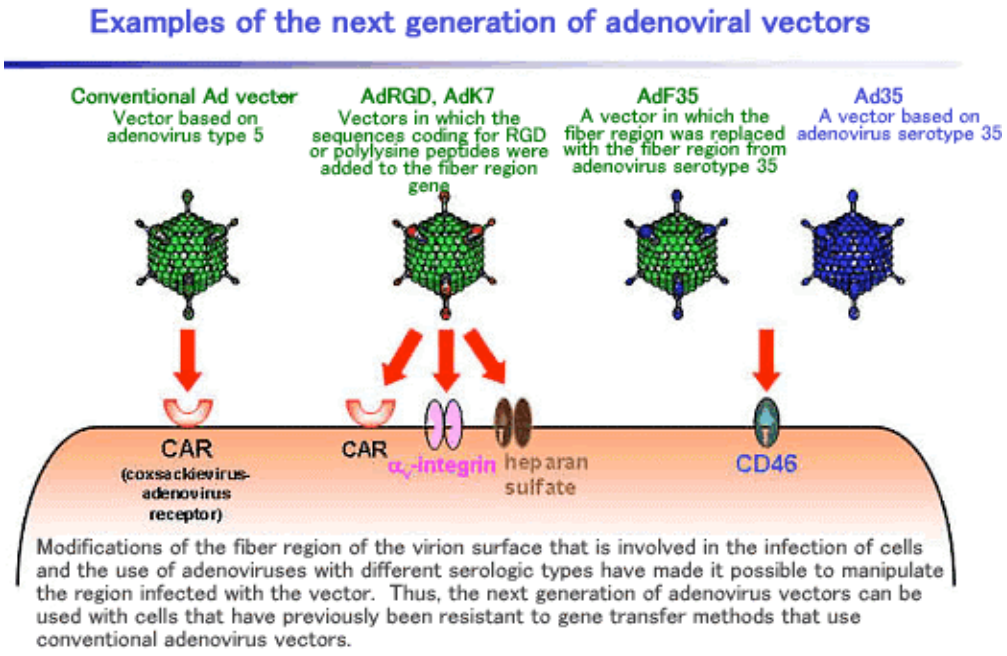


Figure 8: Strategies to attack pre-existing antivector immunity[84]

Strategy	Potential pitfalls
Dose escalation	Marginal effect Dose toxicity
Mucosal site vaccination	Nasal delivery may not be safe
Prime-boost vaccination	Marginal effect when AdV Nab titers are high
Rare HAdV serotypes	Low immunogenicity Possibility of cross-recognition by HAdV5-specific CTLs
Non-HAdV vectors	Safety unknown Possibility of recombination with HAdV Possibility of cross-recognition by HAdV-5-specific CTLs
Hexon chimeric vectors	Partially effective Technically challenging
Masked or shielded vectors	Induction of antibodies to new epitopes could preclude re-dosing

Table 3: Explanation of each the three strategies and their potential pitfalls[85]

[83] *Id.*
[84] National Institute of Biomedical Innovation, http://www.nibio.go.jp/english/part/fundamental/detail6.html (last visited Dec. 4, 2008).
[85] Chawla, *supra* note 49, at 301 (2008).

3. HIV Vaccines

3.A. Using the Adenovirus Vector as an HIV Vaccine

CD8+ cytotoxic T lymphocytes (CTL) play a critical role in control of both acute and chronic HIV-1 infections. Further, experiments in rhesus monkeys demonstrate that CD8+ T-cells are absolutely required for control of the persistent viremia established by the related simian immunodeficiency virus (SIV). Several studies also suggest that the elicitation in monkeys of virus-specific CTL can influence the outcome. Experiments also show that recombinant viral vectors, particularly those based on replication-defective adenoviruses were most effective in eliciting specific CTL responses.[86]

An optimal HIV-1 vaccine vector produces the vaccine antigen in excess of its own proteins. This will allow the immune response to focus on the target antigen and would be produced in cells that can serve as antigen-presenting cells for induction of CTL responses. Adenovirus vectors have a broad cell tropism, and they can enter and replicate in cells from most animal species.[87] See Figure 9.

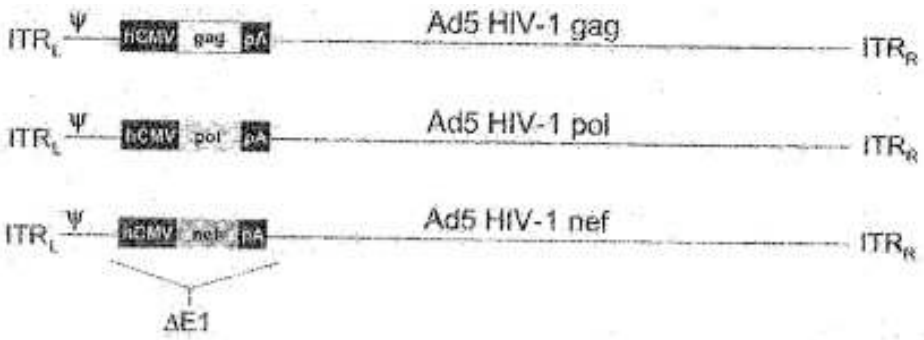


Fig. 9 – Schematic diagrams of replication-incompetent Ad5 HIV-1 gag, pol and nef vaccine vectors.[88]

An adenovirus vector is commonly based on a replication-defective adenovirus type 5 (Ad5). Recombinant Ad5 vaccine vectors are highly immunogenic and elicit the highest antigen-specific CTL responses.[89] The viral vector is rendered replication-defective by removing the E1 gene, which is required for both adenovirus replication and downstream viral gene expression. Genes encoding vaccine antigens may be inserted in

[86] Shiver, *supra* note 30, at 356.
[87] *Id.* at 357.
[88] *Id.* at 358.
[89] Barouch et al., *supra* note 5, at 150.

place of the E1 gene with expression driven by heterologous regulatory elements. Some experiments use the cytomegalovirus (CMV) promoter and bovine growth hormone transcription regulatory elements to drive expression of the vaccine antigen.[90] See Figure 10.

Advantages	*Disadvantages*
Readily manipulated in the laboratory	High levels of preexisting immunity in humans
Grows to high titers in suspension cell cultures	Requires complementing cell lines for growth
Efficient transduction of mammalian cells	Vaccine induces antivector immunity
Highly immunogenic in animals and humans	Reduced immunogenicity with repeat administration
Prime–boost strategies can augment responses	Increased complexity of prime–boost regimens
Vector appears safe and does not persist *in vivo*	Limited long-term safety data in humans available
Scale-up feasibility and manufacturing capacity	Limited experience with large-scale production

Fig. 10: Advantages and disadvantages of rAd5 Vector-Based Vaccines for HIV-1.[91]

Adenovirus vectors retain the ability to efficiently bind cells, become internalized and deliver their genome to the nucleus for subsequent expression of encoded antigen genes. E1-deleted adenoviruses can be produced in large quantities in human cell lines designed to provide the E1 gene product in trans. The most typical cell lines used for E1-deleted adenovirus propagation are 293 and PER.C6™ cells.[92] See Figure 11.

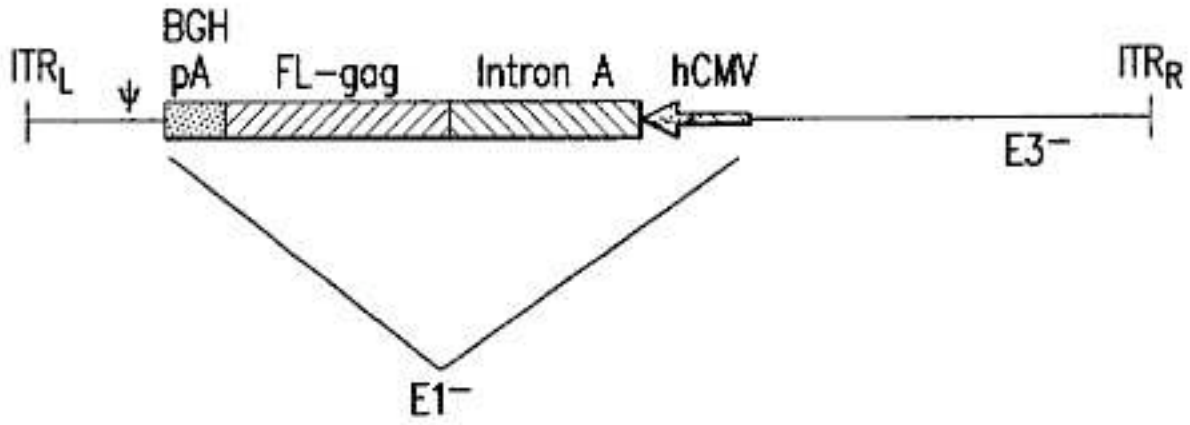


Fig. 11: The Original HIV-1 gag Adenovector (Ad5HIV-1gag) disclosed in U.S. Patent No. 6,733,993.[93]

3.B. Measuring Cellular Immune Responses Against HIV-1 Antigens

Since the objective of the HIV-1 vaccine is to elicit anti-HIV-1 cytotoxic and helper T-cell immune responses, a proper method must be used to measure the CTL

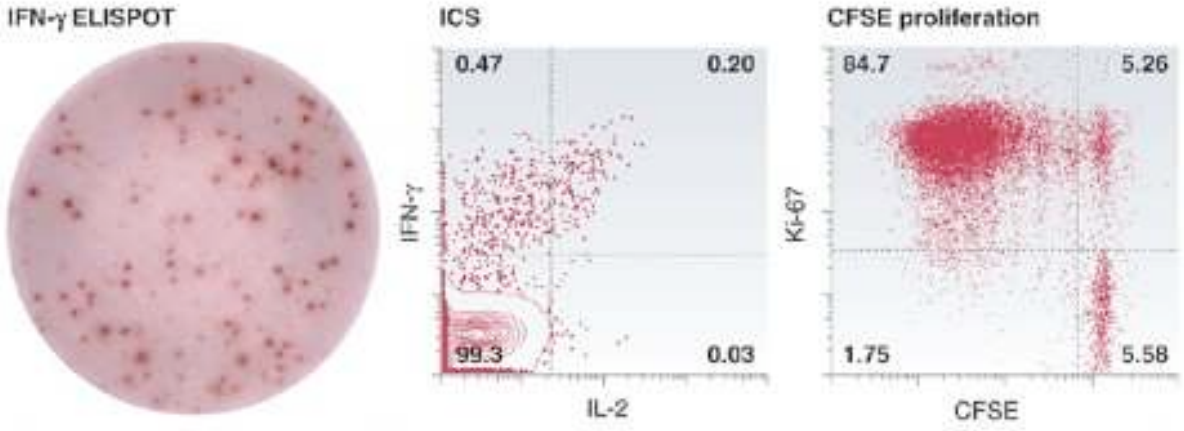
[90] Shiver et al., *supra* note 30, at 357.
[91] Barouch et al., *supra* note 5, at 150.
[92] Shiver et al., supra note 30, at 358.
[93] U.S. Patent No. 6,733,993 (filed Sept. 14, 2001).

responses. Traditionally, CTL responses were measured by the in vitro capacity of CD8+ T cells to kill autologous cells presenting appropriate cytotoxicity assays. These assays are not quantitative and are extremely tedious to perform. However new methods have emerged that enable a more accurate measurement of the antigen-specific population for CD8+ and CD4+ T cells.[94]

The ELISPOT assay is an efficient and sensitive means of assessing the total T-cell response to a given antigen and detects a much larger fraction of the actual responding T-cell population than previously used assays. The ELISPOT is performed in 96-well plates coated with anticytokine antibodies into which peripheral-blood mononuclear cells (PBMCs) are added along with peptides representing a processed form of the target antigen. When activated by the processed antigen, cells produce and secrete cytokines that are captured by the anticytokine antibodies. The cells are washed away after overnight stimulation with the antigen and a second anticytokine antibody is added. The second antibody is conjugated to an enzyme that leaves a colorimetric substrate that becomes insoluble. Spots representing individual cytokine-secreting cells may be visualized, counted and normalized with respect to the number of cells added to each well.[95]

The ICS assay is similar to the ELISPOT assay except that the induced cytokines are trapped within the cells by brefeldin A treatment. These cytokines accumulate within cells that are identified using anticytokine antibodies but are visualized by flow cytometry. The ICS is a little less sensitive than the ELISPOT but provides additional information regarding the T-cell population responding to the antigen. T-cells can be phenotyped as either CD8+ or CD4+ so that the total and relative contributions of each T-cell can be quantified.[96]

[94] Shiver et al., *supra* note 30, at 358.
[95] *Id.* at 359.
[96] *Id.* at 359–60.



Assay	Substrate	Time for assay	Need for HLA typing	Read out	Information on functionality
Tetramer	Whole blood or PBMC	2 h	Yes	Epitope-specific CD8 and CD4	None
ELISPOT	PBMC	24–36 h	No	Total response unless subsets depleted	Single parameter
ICS	Whole blood or PBMC	10 h	No	CD8 and CD4	Multiple parameter
[^{3}H]-thymidine proliferation	PBMC	5 d	No	Total response unless subsets depleted	Single parameter
CFSE proliferation	PBMC	5 d	No	CD8 and CD4	Multiple parameter
Killing	PBMC	5 d	No	Chromium release	Single parameter

Fig. 12: Examples of an IFN-gamma ELISPOT assay, an ICS and a CFSE proliferation assay are shown. All assays test for responses to peptide stimulations. For the ELISPOT assay, the spots represent IFN-gamma, which has been secreted by an individual cell in response to stimulation. For the ICS assay, each dot represents a CD8 T cell and the position in the FACScan represents the cytokines produced in response to peptide stimulation. Cells in the upper left quadrant are IFN-gamma−producing cells, cells in the upper right quadrant are IFN-gamma− and IL-2−producing cells and cells in the lower right quadrant are cells that produce only IL-2 (this cell type is rare among CD8 cells). The strength of cytokine production by individual cells is reflected by the positions of cells in their respective quadrants. For the CFSE assay, cells were pre-stained with CFSE and then stimulated with peptide for 6 days. Following the stimulation, CD8 cells were analyzed for CFSE and staining with Ki-67 (a marker for dividing cells). Cells with the least intense staining for CFSE (furthest to the left in the FACScan) and positive for Ki-67 (upper quadrants) are the ones that have undergone the most division. h, hours; d, days.[97]

3.C. Selecting Vaccine Antigens and Potential for Cross-Clade Immune Responses

HIV-1 contains many genetically diverse groups that have been separated into at least 10 defined families or clades of viruses. These clades have been alphabetically designated. Clade C, the most prevalent worldwide, is found predominantly in southern Africa and southern Asia. Clade A, the second most prevalent, predominates in central Africa and eastern Asia. Clade B, the third most prevalent, is found mostly in the western hemisphere and Europe. Together, Clades A, B and C comprise about 85% of all

[97] Harriet L. Robinson & Rama Rao Amara, 11 NATURE MEDICINE S25, S30 (2005).

infections worldwide. The best T-cell based vaccine for covering this diverse range of genetic groups requires a T-cell response against multiple epitopes to ensure a sufficient match between vaccine antigen and infecting virus to trigger an effective immune response.[98]

Consequently, the leading vaccine candidate for initial efficacy studies is a trivalent mixture of Ad5 vectors, each encoding either HIV-1 gag, pol or nef as vaccine antigens. The antigens are among the most conserved and largest gene products of HIV-1 that serve as targets for CTL responses in HIV-1 infected humans. The highest level of T-cell responses was observed against gag, pol and nef.[99]

3.D. Current Progress for HIV Vaccines Using Adenovirus Vector- Clinic Trials

3.D.1. Clinical Trial Overview[100]

Clinical trials for vaccines are divided into three phases: Phase I, Phase II, and Phase III.

A phase I trial is the first test on human for a vaccine. The trial is usually tests a small number (ten to thirty) of healthy volunteers. The main goal is to evaluate the safety of the vaccine. The trial also collects data for the immune responses evoked by the vaccine, and dosage and immunization schedule of the vaccine. A Phase I trial takes about eight to twelve months to complete.

A phase II trial usually tests a mixture of low-risk and higher-risk volunteers. The number of volunteers is usually increased in a range of fifty to five hundred. These volunteers are chose from people where the corresponding phase III will be conducted. In this stage, the researchers collect additional safety data and additional information for refining the dosage and immunization schedule. Sometimes, this information is enough to indicate the efficacy of the tested vaccine.

A phase III trial increases the number of volunteers to thousands. These volunteers are high-risk people from the area that the HIV is circulating. A phase III trial of HIV vaccine is generally expected to require a minimum of three years for enrollment, immunizations, and assessments of efficacy.

3.D.2. Current Clinical Trial for HIV Vaccine Using Human Adenovirus Ad5 Vector

There are more than 30 clinic trials studying different approaches for HIV vaccine candidates. Some related to adenovirus vectors are listed below.[101]

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[98] Shiver et al., *supra* note 30, at 361.
[99] Shiver et al., *supra* note 30, at 361–62.
[100] International AIDS Vaccine Institute, *Vaccine Science: Clinical Trials for a Candidate Vaccine are Divided into Three Distinct Phases* (2008), http://www.iavi.org/viewpage.cfm?aid=27 (last visited Dec. 4, 2008.)

Phase	Vector	Antigen (clade)	Organizer, Sponsor, manufacturer*
I	DNA prime/ Ad boost	Gag, Pol, Env (B); Gag, Pol, Env (A,B,C); Gag/Pol Polyprotein, Env (A,B,C)	WRAIR, VRC, NIAID, VRC HVTN, NIAID, VRC
I	DNA prime/ Ad boost or Ad alone	Gag, Pol, Nef (B), Nnv (ABC); Gag, Pol (B), Env (ABC)	IAVI, NIAID, VRC
I	DNA prime/ Ad boost or Ad prime/ Ad boost	Gag, Pol, Env (B); Gag, Pol, Env (A, B, C)	HVTN, VRC
I	Ad	Gag, Pol (B), Env (A,B, C)	HVTN, NIAID, VRC
II	DNA prime/ Ad boost	Gag, Pol, Nef (B), Env (A,B,C); Gag, Pol (B), Env (A, B, C)	NIAID, VRC, HVTN, Vical, GenVec
II	Ad	Gag, Pol, Nef (B)	HTVN, NIAID, Merck

* HVTN: HIV Vaccine Trials Network;
IAVI: International AIDS Vaccine Initiative;
NIAID: US National Institute of Allergy and Infectious Diseases;
VRC: Vaccine Research Center at the US National Institutes of Health;
WRAIR: Walter Reed Army Institute of Research

Table 4[102]

Among these trials, two demonstrate the highest level of immunogenicity by two different approaches: (1) recombinant Ad5 adenovirus vector, or (2) in combination with plasmid DNA in a heterologous DNA/Ad5 prime-boost regimen.[103] The two trials are performed by Merck and VRC (Vaccine Research Center of NIH).

3.D.2.a. Merck Research

The vector used in Merck's research is a modified human adenovirus vector Ad5. The vector is called MRKAd5.[104] It is an Ad5-gag recombinant vector or an Ad5-gag/pol/nef vector.[105] The Ad5-gag recombinant vector generated CD8+ CTL response

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[101] David A. Hokey et al., *DNA Vaccines for HIV: Challenges and Opportunities*, 28 Springer Seminars in Immunopathology 267, 275 (2006).
[102] *Id.*
[103] *Id.*
[104] Kristen J. Kresge, *Understanding the Science of AIDS Vaccine for Preexisting Immunity*, DECIPHERING AIDS VACCINES 11, 13 (2008), *available at* http://www.iavi.org/viewfile.cfm?fid=43103.
[105] Marc P. Girard et al., *A Review of Vaccine Research and Development: The Human Immunodeficiency Virus (HIV)*, 24 VACCINE 4069 (2006)

of high magnitude and prolong duration in Macaques.[106] The CTL response were capable of protecting macaques from challenge with SHIV 89.6P.[107] When used in a DNA/Ad5 prime-boost strategy, a study showed the vaccine has an ability to reduce viral loads by up to 7-fold in monkeys; however it did not last more than 6 months.[108]

3.D.2.a.i. Merck's Phase II Trial [109]

A Phase II trial is formed for Ad5-gag/pol/nef trivalent recombinant Ad5 vaccine by Merck, HVTN (HIV Vaccine Trial Network) and NIAID (US National Institute of Allergy and Infectious Diseases) at several centers in North America, Peru, Brazil, Caribbean Island, and Australia. Originally, the vaccine is tested on 1500 volunteers in eight countries. This project only enrolls people with a low level of pre-existing immunity to Ad5 so the researches can fairly assess how effective the vaccine would be. The result will come out by the end year 2009.

3.D.2.a.ii. Merck's Phase IIb Trial [110]

The project later progressed into a Phase IIb "test of concept" trial. This kind of trial enrolls only 2000-5000 volunteers, which is much less than what a Phase III trials usually requires (more than 10,000 volunteers). The trial is not designed to establish the efficacy of this vaccine; it is to help researches decide if this vaccine candidate is worth testing in larger Phase III trials. More diverse population of volunteers enrolled in this phase; that is, not only people with a low level pre-existing immunity were enrolled. The vaccine candidate is tested on approximately 3,000 volunteers.

3.D.2.b. VRC Research[111]

This vaccine candidate uses another non-replicative adenovirus vector. The VRC vector expresses Env glycoprotein from clades A/B/C and gag/pol/nef proteins from Clade B.[112] On the other hand, the Merck vector only encodes conserved genes gag/pol/nef from clade B. By using a DNA prime/Adenovirus boost strategy, the study shows the vaccine candidate enhanced CD4+T lymphocyte count in macaques. DNA prime is one method dealing with pre-existing immunity issue. DNA prime may allow the levels of boosted CD8 responses in seropositive individual to approach those of seronegatives who receive Ad5 vectors alone.

3.D.2.b.i. VRC Phase I Trial[113]

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[106] Paul Spearman, *Current Progress in the Development of HIV Vaccines*, 12 CURRENT PHARMACEUTICAL DESIGN 1149, 1157 (2006)
[107] *Id.*
[108] Hokey et al., *supra* note 101, at 274.
[109] Kresge, *supra* note 104, at 13.
[110] *Id.* at 36–37.
[111] Spearman, *supra* note 107, at 1157.
[112] Girard et al., *supra* note 105, at 4069.
[113] *Id.*

A DNA based vaccine was tested in Phase I trials in USA and showed good immunogenicity. A Phase I DNA-Ad5 prime-boost trial test is further tested in US, Brazil and South Africa and extended to East Africa in collaboration with IAVI (International AIDS Vaccine Initiative). In 2006, a trial begun at IAVI's sites in Kenya and Rwanda and IAVI's core laboratory at Imperial College in UK. IAVI and NIH planned to do an additional 500-person trial in high-risk population in Africa.[114] IAVI also proposed enrolling approximately 600 participants to do a Phase IIb efficacy trial; however, this project is on hold in light of Merck Ad5 trial results (which might yield efficacy data in late 2008 or early 2009). [115]

3.D.3 Other Clinical Trials Using Vectors Other than Human Ad5 Vector

The pre-existing immunity problem is the major issue affecting the efficacy of these HIV vaccine candidates using adenovirus vectors. There are numerous strategies are underway to circumvent this issue, including (1) the use of higher doses of virus, (2) using different less common adenoviral serotypes, and (3) using different viruses in a prime-boost regimen.[116] One study examines the use of an Ad prime/MVA or canarypox boost that resulted in enhance immune responses in macaques; however, a use of a poxvirus prime/ Ad boost failed to elicit impressive immune responses.[117] The data indicate that the immunization order is critical to ability to generate immune response.[118] In addition, less common adenoviral serotypes such as Ad6, Ad35, Ad11, or Ad24 are studied to replace Ad5 vector in future HIV vaccine trials conducted by Merck, Crucell, Transgene and IAVI.[119]

There are two more ways researches tried to solve the pre-existing immunity issue- use nonhuman adenovirus vectors such as nonreplicative chimpanzee adenoviruses AdC68, AdC6, or AdC7; or use chimeric adenoviruses such as Ad5/Ad11 or Ad5/Ad35.[120] By replacing the fiber gene of an Ad5 vector by that from a rare Ad subtype to achieve the goal to escape the anti-Ad5 pre-existing immunity.[121]

3.D.3.a. Clinical trial Using Human Adenovirus Vector Other than Ad5 by IAVI [122]

The trial has been conducted by IAVI, Crucell, a Dutch biotech firm and Harvard Medical School since 2004. Replication-defective Ad35 and Ad11 are used as vectors.

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[114] International AIDS Vaccine Institute, *2006 Annual Progress Report* (2006), *available at* http://www.iavi.org/viewfile.cfm?fid=46170
[115] *Id.*
[116] Hokey et al., *supra* note 101, at 274–76
[117] *Id.*
[118] *Id.*
[119] Girard et al., *supra* note 105, at 4069.
[120] *Id.*
[121] *Id.*
[122] International AIDS Vaccine Institute, *2007 Annual Progress Report* (2007), *available at* http://www.iavi.org/viewfile.cfm?fid=49059; International AIDS Vaccine Institute, *2005 Annual Progress Report* (2005), *available at* http://www.iavi.org/viewfile.cfm?fid=40735; *see also* International AIDS Vaccine Institute, *2006 Annual Progress Report*, *supra* note 31.

In year 2006, IAVI completed characterization of a cell line licensed from Crucell and received favorable regulatory feedback from FDA. IAVI further provided a non-exclusive license to Beth Israel Deaconess medical center, which a major teaching hospital of Harvard Medical School to manufacture Ad vector for clinical trials. IAVI also ready to initiate a Phase I trial in US and Ease Africa in Q3 of 2008.

3.D.3.b Clinical trial using Nonhuman Primate Adenovirus by IAVI [123]

In June 2005, IAVI contracted GSK (GlaxoSmithKline) for this project. The main focus is to evaluate replication-defective chimpanzee adenovirus vectors including AdC68, AdC6, or AdC7, as human vaccine for HIV. However, this project was terminated in year 2007.

3.E. Future Approaches Towards Developing an Adenovirus-based Vaccine

After the clinical trials for the promising Merck rAd5 vaccine were terminated due to its failure to show efficacy and to the problem of pre-existing Ad5-specific immunity, scientists began to search for a way to circumvent pre-existing vector immunity and for a reason why the vaccine was actually increasing the risk of HIV-1 acquisition among some volunteers.[124] This unexpected discovery that prior immunity against the adenovirus would increase susceptibility to HIV infection in volunteers has shifted many scientists back to basic research for a better understanding about the relationship between infection and immunity and to search for alternative approaches towards developing effective vector-based vaccines, including the use of novel animal models for testing immune responses to the vaccines.[125]

3.E.1. Major Alternative Approaches

There are currently two major alternative approaches involving adenovirus vectors to circumvent the problem of pre-existing immunity.[126] The first approach involves DNA prime-boost in combination with Ad5; the second approach explores other types of adenoviral vectors, such as Ad26 and Ad35, that may be more effective than Ad5 due to lower pre-existing immunity to these alternative adenoviral vectors and because they do have the same receptor as Ad5.[127] Other alternative approaches include using non-human adenoviral vectors such as those from a chimpanzee origin, novel rAd chimeric vectors combining different characteristics of different adenoviral vectors, and masked adenoviral vectors.[128]

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[123] *Id.*
[124] Rafick-Pierre Sekaly, *The failed HIV Merck vaccine study: a step back or a launching point for future vaccine development?*, 205(1) J. EXPERIMENTAL MEDICINE 7, 7 (2008).
[125] *Id.* at 10.
[126] Shan Lu, *Human versus HIV: Round 2 Defeat in AIDS Vaccine Development*, 7 EXPERT REVIEW OF VACCINES 151, 152 (2008).
[127] *Id.*
[128] Chawla et al., *supra* note 49, at 301–02.

3.E.2. Prime-Boosting Regimens

One alternative approach is to develop a DNA prime plus adenoviral vector boost approach. DNA priming is important for inducing strong HIV-specific CD4+ and CD8+ T-cell responses in monkeys; the DNA prime boost regimen has led to strong env-specific responses and the Merck rAd5 vaccine, focusing on the gag/pol/nef genes, did not involve env constructs.[129] Since many people in developing countries have already developed a pre-existing immunity to Ad5 in its naturally circulating form, this suggests that the use of Ad5 alone may not be the best choice as a carrier virus in a vaccine. However, DNA priming can be used in combination with Ad5 or with other adenovirus serotypes to circumvent pre-existing immunity because the level of CD8+ responses is higher with the boost than the level of responses with Ad5 alone.[130] The NIH Vaccine Research Center has developed a vaccine regimen using this DNA prime-boost approach and early studies has shown the vaccine to be immunogenic, especially to env-antigens.[131]

3.E.3. Adenoviral Vectors from Rare Human Serotypes

Since Ad5 may not be the ideal carrier virus, alternative adenoviral vectors derived from less common serotypes are being studied for use in vaccines; in particular, alternative adenoviral vectors that can provide a level of immunogenicity at a similar level as Ad5 are needed.[132] There are 51 known human Ad serotypes, divided into six subgroups, from A-F. A past study found Ad35 and Ad11 from subgroup B as promising alternatives to Ad5, but it noted that there are disadvantages for using less common serotypes, such as "lack of knowledge regarding the biology of these viruses including tropism on human cells, potential difficulties in manufacturing, and the possibility of in vivo recombination with human types leading to unknown disease."[133] A more recent study has compared the seroprevalence and immunogenicity of six rare serotype recombinant adenovirus vaccine vectors and has identified the Ad serotypes that are highly immunogenic and that best circumvent anti-Ad5 immunity.[134] The study compared Ad5 from group C with Ad11, Ad35, and Ad50 from group B and Ad26, Ad48, and Ad49 from group D; the seroprevalence of all six serotypes were lower than that of Ad5.[135] The results showed that in the absence of anti-Ad5 immunity, Ad5 vectors were consistently the most immunogenic; the reason for Ad5's potency is unclear, but possible reasons are efficient entry into cells or efficient triggering of innate immunity that amplifies adaptive immune responses.[136] With anti-Ad5 immunity, all six rare serotype Ad vectors were significantly more immunogenic than the Ad5 vectors; and among the

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[129] Spearman, *supra* note 106, at 1157.
[130] *Id.*
[131] Dan H. Barouch, *Challenges in the Development of an HIV-1 Vaccine*, 455 NATURE 613, 617 (2008).
[132] Chawla et al., *supra* note 49, at 301.
[133] Vogels et al., *supra* note 81, at 8263.
[134] Peter Abbink et al., *Comparative Seroprevalence and Immunogenicity of Six Rare Serotype Recombinant Adenovirus Vaccine Vectors from Subgroups B and D*, 81 J. VIROLOGY 4654, 4654 (2007).
[135] *Id.* at 4662.
[136] *Id.*

six serotypes, Ad26 vectors were the most immunogenic.[137] The comparison study shows that the most promising rare serotype, such as Ad26, for use in vaccines would have characteristics such as having low seroprevalence, high immunogenicity as a vector alone and as a part of a heterologous prime-boost regimen, and the ability of the vectors to grow such that large-scale manufacturing of the vectors would be possible.[138]

Based on these studies, future vaccines may utilize Ad26, Ad35, or Ad11 vectors, in combination with the DNA prime-boost approach. Priming with a rare Ad26 vector followed by boosting with Ad5 has proved to be a very potent combination.[139] A clinical trial has showed that rAd26 elicited strong immune responses in rhesus macaques at levels similar to those observed with rAd5, and a rAd26 prime/rAd5 boost combination elicited cellular responses that were ten times that observed with a homologous rAd5 immunization.[140]

3.E.4. Nonhuman Primate Studies

A current method used to understand the interaction between infection and vaccination in order to develop an effective HIV vaccine is to develop better animal models for studying HIV infection and find clues about virus control from nonhuman primates.[141] Scientists believe that although nonhuman primates are excellent animal models currently available for studies, they still need to be improved for studying HIV infection in humans. In this regard, mice have been genetically altered to express human immune cells and these humanized mice are presently used to study HIV pathogenesis in the gut, the area where virus replication and CD4+ T-cell depletion occurs early when humans are infected with HIV.[142]

The humanized mouse model is still under development; thus, for the time being, primates are still the best available model for studying HIV infection. Scientists are currently experimenting with sooty mangabeys, which are natural hosts of SIV and can be infected with the virus without harming them.[143] These monkeys showed a lack of immune activation during infection, despite chronic high levels of viral replication, and showed low CCR5 expression on CD4+ T-cells. Scientists are searching for connections between this absence of immune activation, the low CCR5 expression on CD4+ T-cells, and the lack of disease progression to AIDS.[144]

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[137] *Id.*
[138] *Id.*
[139] *Id.*
[140] Kimberly A. Schoenly & David B. Weiner, *Human Immunodeficiency Virus Type 1 Vaccine Development: Recent Advances in the Cytotoxic T-Lymphocyte Platform "Spotty Business,"* 82 J. VIROLOGY 3166, 3169 (2008).
[141] Regina McEnery, *HIV Prevention Research: The Relay Race Continues*, IAVI REP., July-Aug. 2008, at 1, 3.
[142] *Id.*
[143] *Id.*
[144] *Id.*

3.E.5. Adenoviral Vectors from Nonhuman Serotypes

The pre-existing immunity problem can also be addressed by using non-human adenoviral vectors, such as chimpanzee or porcine adenovirus vectors, as vaccine carriers.[145] Chimpanzee adenovirus vectors have been shown to be the most immunogenic, inducing good CD8+ T-cell responses in the presence of preexisting antibodies against Ad5.[146] Chimpanzee vectors C6, C7, and C68 have been identified as favorable carriers, and neutralizing antibodies to Ad5 do not impair transgene product-specific T-cell responses to these chimpanzee adenovirus vectors.[147] However, CD8+ T cells to antigens of Ad5 reduce induction of transgene product-specific CD8+ cells elicited by those chimpanzee vectors, affecting the efficacy of these vaccine carriers in humans.[148] In addition, there is however a safety concern regarding the use of nonhuman serotypes instead of human serotypes that the nonhuman serotype adenoviral vectors "may have the potential to recombine with their human counterparts and/or cause disease."[149]

3.E.6. Chimeric Adenoviral Vectors and Masking Adenoviral Vectors

Novel rAd chimeric vectors that combine different characteristics of different adenoviral vectors may be used to circumvent the pre-existing immunity problem.[150] The rAd5 vectors can be modified to circumvent anti-Ad5 immunity and to construct a novel rAd5/rAd48 chimeric vector by replacing the seven short hypervariable regions on the surface of the Ad5 hexon protein with the corresponding HVRs from a rare adenovirus serotype Ad48.[151] Other chimeric vectors that have developed include combining Ad5 fiber with Ad35.[152] A chimeric vector based on a nonhuman serotype has recently been developed, combining chimpanzee adenovirus vector C1 with another chimpanzee adenovirus vector C5; the T-cell responses from this combination can then be enhanced by using a prime-boost regimen.[153]

Finally, masking adenoviral vectors from the immune system is another alternative approach to escape pre-existing immunity.[154] Adenoviral vectors can become "hidden" by being coated with polymers such as polyethylene glycol; the polymer-coating would mask the capsid surface and thus block the neutralizing antibodies.[155]

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[145] Chawla et al., *supra* note 49, at 301.
[146] Julie C. Fitzgerald et al., *A Simian Replication-Defective Adenoviral Recombinant Vaccine to HIV-1 Gag*, 170 J. IMMUNOLOGY 1416, 1421 (2003).
[147] Nia Tatsis et al., *A CD46-Binding Chimpanzee Adenovirus Vector as a Vaccine Carrier*, 15 MOLECULAR THERAPY 608, 608 (2007).
[148] *Id.*
[149] Chawla et al., *supra* note 49, at 301.
[150] Schoenly & Weiner, *supra* note 140, at 3169.
[151] *Id.*
[152] Chawla et al., *supra* note 49, at 302.
[153] Tatsis et al., *supra* note 65, at 608.
[154] Chawla et al., *supra* note 49, at 302.
[155] *Id.*

Present research on rare human serotype adenovirus vectors, nonhuman adenovirus vectors, and chimeric adenoviral vectors as suitable vaccine carriers are showing promising results. In the future, the ideal adenovirus vector should be able to circumvent pre-existing adenoviral vector immunity, elicit strong immune responses against HIV, and be effective after a single dosage.[156]

[156] *Id.* at 303.

II. Patent Search Methodology and Results

1. Patent Search Methodology

The International Intellectual Technology Institute Patent Landscape Analysis Clinic began on August 28, 2008 with a conference call between the Clinic members, Professor Jon Cavicchi, Dr. Stanley Kowalski, and Dr. Kerri Clark at PIPRA. The scope of the project was defined as conducting a patent landscape analysis of technologies pertaining to adenovirus vector vaccines having applicability to HIV. The team began the project reviewing past and recent literature relating to HIV vaccines and adenovirus vectors. The nine-member team was divided into three groups, and each group was assigned to research and present on a different aspect of adenovirus vector vaccines. The three groups presented on the general biology of adenoviruses, adenoviral vectors, and HIV vaccines; one team also researched on past and current clinical trials on HIV vaccines, which gave team members initial exposure to some of the major inventors and assignees. The first team researched the three generations of adenovirus vectors and the critical components necessary for final vaccines. The second team researched production methods of assembling HIV vaccines, including purification, packaging cell lines, screening methods, and cell lines specific for virus production. The third team researched chimeric adenovirus vector chimeras, nonhuman adenovirus vectors, and clinical trials looking at alternative adenovirus serotypes. All teams jointly researched on HIV adenovirus vector vaccines in general.

The team then commenced an intense four-month journey of patent searching and coding. Delphion was the primary patent searching database that the team used. In addition to a general HIV adenovirus vector vaccine search, each group was assigned to search for patents relating to the aspect of adenovirus vector vaccine technology that the group researched and presented on. The search methodology was devised to initially generate a broad set of patents and then to narrow down the results using the "Iterative Search Approach," as promoted by Professor Cavicchi. The searches utilized keywords derived from the literature reviewed and initial searches to generate useful search strings; the searches also used United States Patent Classifications, International Patent Classifications, and Derwent Classifications that were identified through subsequent searches and team meetings. Top inventor and assignee names were also identified from clinical trial data. The combination of keywords, inventor/assignee names, and classifications in search strings was useful for parsing the technology into compartments and allowing each team group to generate a different set of search results that keywords alone could not provide.

The initial round of searching involved a search string ("Adenovirus + Vector + HIV + Vaccine") that generated a broad set of patents. Keywords and classifications were then used in subsequent rounds of searching. Later correspondences with Dr. Clark led to modifications in the team search strategy, taking into account of the future possibilities of using different types of adenovirus or vectors that have been used so far in HIV vaccines. After each round of searching, team meetings were held to identify the most important keywords, inventor names, assignee names, and classifications for use in

subsequent search strings that became more defined and effective. The main keywords used by the three groups in the searches were:

- All Teams (search for HIV adenovirus vector vaccine patents in general):
Adenovir! or Ad?? or Ad? or HuAd?? or HuAd? or AdHu?? or AdHu? or rAd?? or rAd? or AdC? or AdC?? or CAd? or CAd?? or rAdC?? or rAdC? or AdPan? Or AdPan?? or PanAd? or PanAd??, Vacc! and immu!, AIDS or HIV or "human immunodeficiency virus"

- Team 1 (assigned to search for patents relating to adenovirus vectors):
Adenovirus, Ad??, Ad?, HuAd??, HuAd?, AdHu??, AdHu?, rAd??, rAd?, AdC?, AdC??, CAd?, CAd??, rAdC??, rAdC?, AdPan?, AdPan??, PanAd?, PanAd??, AdHu5, Ad5, HuAd5, rAd5, AdHu6, Ad6, HuAd6, rAd6, AdHu35, Ad35, HuAd35, rAd35, AdHu11, Ad11, HuAd11, rAd11, AdHu24, Ad24, HuAd24, rAd24, Ad26, AdHu26, HuAd26, rAd26, AdC6, Cad6, rAdC6, AdC7, Cad7, rAdC7, AdHu2, Ad2, HuAd2, rAd2, AdHu4, Ad4, HuAd4, rAd4, AdHu7, Ad7, HuAd7, rAd7, AdHu48, Ad48, HuAd48, rAd48, AdHu49, Ad49, HuAd49, rAd49, AdHu50, Ad50, HuAd50, rAd50, AdC68, CAd68, rAdC68, AdHu34, Ad34, HuAd34, rAd34, AdPan6, PanAd6, rAdPan6, AdPan7, PanAd7, rAdPan7, AdPan68, PanAd68, rAdPan68, First, 1st, 2nd, second, third, 3rd, gutless, generation, vector, plasmid, vehicle, virion, E1, E2, E3, E4, AIDS, HIV, and "human immunodeficiency virus"

- Team 2 (assigned to search for patents relating to production methods):
"cell line" or "cell lines" or "cell types" or "cell culture", purification, purify, purif*, cut, transfect, transf*, "gene expression," packaging, method, production, produc*, assembly, adenovirus, or Ad?? or Ad? or HuAd?? or HuAd? or AdHu?? or AdHu? or rAd?? or rAd? or AdC? or AdC?? or Cad? or CAd?? or rAdC?? or rAdC? or AdPan? Or AdPan?? or PanAd? or PanAd??, vaccine, HIV, and "human immunodeficiency virus"

- Team 3 (assigned to search for patents relating to chimeric proteins and alternative serotypes):
gag or pol or nef, hexon or penton or fib**, heterologous or chim! or hybrid, E1 or E2 or E3 or E4 or gutless, Adenovir? or Ad?? or Ad? or HuAd?? or HuAd? or AdHu?? or AdHu? or rAd?? or rAd? or AdC? or AdC?? or Cad? or CAd?? or rAdC?? or rAdC? or AdPan? Or AdPan?? or PanAd? or PanAd??, hybrid <near> protein? or prime boost or chimer! or fusion <near> Protein or "cell binding," vaccine, HIV, and "human immunodeficiency virus"

Most of these keywords were searched under the search field of "Title, Abstract, Claims, " since searches under the field of "Description" or "Specification" led to too many irrelevant results. It was useful to limit the most important keywords under the search field of "Claims." The keywords above were then combined with inventor names, assignee names, U.S. classifications and subclasses, International classifications

and subclasses, and Derwent classes to generate different sets of search results. Some of the most common classifications used were US Classifications 435/456, 435/320.1, and 435/235.1, IPC Codes A61K, C12N, and C07K, and Derwent classes B04, D16, and C06. The top inventors used in searches were Emilio Emini, John Shiver, Ronald Vogels, and Danilo Casimiro; the top assignees used in searches were Merck, Crucell Holland, GenVec, the United States Government, University of Saskatchewan, Glaxo Group, and the Trustees of the University of Pennsylvania.

The search strings gave the team an outcome of more than 1000 patents, which was deduplicated using the family option of MicroPatent® into 690 patents (for the meaning of 'deduplication', see the Appendix B). Each team member saved their own search results and created their own work files in Delphion. The search results were assembled together and extracted into PDF files for coding and into Excel spreadsheets for data analysis. The subsequent data analyzed were placed into a Master Sheet. The 690 patent documents were divided into the three groups for coding; the claims in the documents were analyzed and the document was then coded under one of the seven categories:

1. Vectors
2. Production Methods
3. Adenovirus Serotypes
4. Chimeric Protein
5. Final Vaccine Product
6. Prime-Boost
7. Adjuvant

Each patent was initially coded by individual team members and emphasis was placed on claim language in order to determine whether the patent was relevant to adenovirus vector vaccine technology for HIV. When coding, team members also took consideration of the patent's title, abstract, and specification. Each patent was then reviewed by the entire team and Dr. Kowalski, and each patent was coded according to their relevancy. Of the 690 patents, 267 patents were found to be relevant. The coding results were inserted into a Master Sheet containing all of the information on each of the patent documents.

2. Patent Search Tables

(Note : The following search tables are a part of the whole search tables for this project which is included in the Attached DVD)

2.1 Search #1

Preliminary Search (Week 3)

Database	Delphion (US & EP applications and patents, WIPO PCT publications)
Keywords	Vaccine, HIV, human immunodeficiency virus, adenovirus, Ad, AdHu5, AdHu, Ad5, HuAd, HuAd5
US Classification/ Sub-classification	Not in use
Search Strings	((vaccine) <in> AB) AND ((HIV or Human immunodeficiency virus or AIDS) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((adenovirus or Ad or AdHu5 or AdHu or HuAd or HuAd5 or Ad5) <in> AB) AND ((adenovirus or Ad or AdHu5 or AdHu or HuAd or HuAd5 or Ad5) <in> CLAIMS)
Result	Very narrow results of 27

Search Round 1 (Week 4)

Database	Delphion (US & EP applications and patents, WIPO PCT publications)
Keywords	Vaccine, Ad, AdHu5, AdHu, Ad5, HuAd, HuAd5, generation, bett, chen and youil
US Classification/ Sub-classification	Not in use
Search Strings	((vaccine) <in> AB) AND ((HIV) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((adenovirus or Ad or AdHu5 or HuAd5 or Ad5 or AdHu or HuAd) <in> AB) AND ((generation) <in> AB) ((bett or chen or youil) <in> IN) AND ((vaccine) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((adenovirus or Ad or AdHu or HuAd or Ad5 or AdHu5 or HuAd5) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((HIV or human immunodeficiency virus or AIDS) <in> (TITLE,ABSTRACT,CLAIMS))
Result	Total narrow results: 18 + 23= 41

Search Round 2 (Week 5)

Database	Delphion (US & EP applications and patents, WIPO PCT publications)
Keywords	Adenovirus, Ad, AdHu5, HuAd5, Ad5, AdHu, HuAd, rAd, rAd5, HIV, AIDS, Human immunodeficiency virus, E1, E2, E3, E4, gutless, vacc*, first generation, 1st generation, 2nd generation, second generation, third generation, and 3rd generation
US Classification/ Sub-classification	Not in use
Search Strings	((adenovirus or Ad or AdHu5 or HuAd5 or Ad5 or AdHu or HuAd or rAd or rAd5) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((vaccine) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((HIV or AIDS or Human immunodeficiency virus) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((E1 or E2 or E3 or E4 or gutless) <in> (TITLE,ABSTRACT,CLAIMS)) ((E1 or E2 or E3 or E4 or gutless) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((vacc*) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((HIV or AIDS or Human immunodeficiency virus) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((adenovirus or Ad or Ad5 or AdHu or AdHu5 or HuAd or HuAd5 or rAd or rAd5) <in> (TITLE,ABSTRACT,CLAIMS)) ((E1 or E2 or E3 or E4 or gutless) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((vaccine and HIV or AIDS or Human immunodeficiency virus) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((first generation or 1st generation or 2nd generation or second generation or third generation or 3rd generation) <in>

	(TITLE,ABSTRACT,CLAIMS)) AND ((adenovirus or Ad or AdHu or HuAd or Ad5 or AdHu5 or HuAd5 or rAd or rAd5) <in> (TITLE,ABSTRACT,CLAIMS))
Result	Total results: 73 + 86 + 13= 172 Total results considered= 100

Search Round 3 (Week 6)

Database	Delphion (US & EP applications and patents, WIPO PCT publications)
Keywords	Vaccine, vaccination, gene therapy, HIV, Human immunodeficiency virus, AIDS, adenovirus, Ad, AdHu, HuAd, rAd, AdHu5, Ad5, HuAd5, rAd5, AdHu6, Ad6, HuAd6, rAd6, AdHu35, Ad35, HuAd35, rAd35, AdHu11, Ad11, HuAd11, rAd11, AdHu24, Ad24, HuAd24, rAd24, Ertl, Emini, Wang, Chen, Bett, Casmiro, and Shiver
US Classification/ Sub-classification	424/199, 424/233.1, 435/320.1 and 424/208.1
Search Strings	((vaccine) <in> AB) AND ((HIV or Human immunodeficiency virus or AIDS) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((adenovirus or Ad or AdHu5 or AdHu or HuAd or HuAd5 or Ad5) <in> AB) AND ((adenovirus or Ad or AdHu5 or AdHu or HuAd or HuAd5 or Ad5) <in> CLAIMS) (((vaccine or vaccination or "gene therapy") <in> (TITLE,ABSTRACT,CLAIMS)) AND ((HIV or AIDS or "human immunodeficiency virus") <in> (TITLE,ABSTRACT,CLAIMS)) AND ((adenovirus or Ad) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((Ertl or Emini or Wang or Chen or Bett or Casmiro or Shiver) <in> IN)) (((adenovirus or • AdHu or Ad or HuAd or rAd or AdHu5 or Ad5 or HuAd5 or rAd5 or AdHu6 or Ad6 or HuAd6 or rAd6 or AdHu35 or Ad35 or HuAd35 or rAd35 or AdHu11 or Ad11 or HuAd11 or rAd11 or AdHu24 or Ad24 or HuAd24 or rAd24) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((vaccine or vaccination) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((HIV or AIDS or "human immunodeficiency virus") <in> (TITLE,ABSTRACT,CLAIMS)) AND ((424/199 or 424/233.1 or 435/320.1 or 424/208.1) <in> NC))
Result	Total results: 63 + 61 + 45= 169 Total results considered: 73

Search Round 4 (Week 7)

Database	Delphion (US & EP applications and patents, WIPO PCT publications)
Keywords	Adenovirus, Ad??, Ad?, HuAd??, HuAd?, AdHu??, AdHu?, rAd??, rAd?, AdC?, AdC??, CAd?, CAd??, rAdC??, rAdC?, AdPan?, AdPan??, PanAd?, PanAd??, AdHu5, Ad5, HuAd5, rAd5, AdHu6, Ad6, HuAd6, rAd6, AdHu35, Ad35, HuAd35, rAd35, AdHu11, Ad11, HuAd11, rAd11, AdHu24, Ad24, HuAd24, rAd24, Ad26, AdHu26, HuAd26, rAd26, AdC6, Cad6, rAdC6, AdC7, Cad7, rAdC7, AdHu2, Ad2, HuAd2, rAd2, AdHu4, Ad4, HuAd4, rAd4, AdHu7, Ad7, HuAd7, rAd7, AdHu48, Ad48, HuAd48, rAd48, AdHu49, Ad49, HuAd49, rAd49, AdHu50, Ad50, HuAd50, rAd50, AdC68, CAd68, rAdC68, AdHu34, Ad34, HuAd34, rAd34, AdPan6, PanAd6, rAdPan6, AdPan7, PanAd7, rAdPan7, AdPan68, PanAd68, rAdPan68, vaccine, immune, immunogenic, vector, plasmid, vehicle, virion, first, second, third, gutless, generation, Merck, Crucell, Betagene, UAB, Pennsylvania, Wyeth, Lexicon, Rhone-Poulenc Rorer, Connaught, Genstar, Baylor, Transgene, Genphar, Wistar, Glaxo, AIDS, HIV and “human immunodeficiency virus”
US Classification/ Sub-classification	Not in use
Search Strings	(((Adenovirus or Ad?? or Ad? or HuAd?? or HuAd? or AdHu?? or AdHu? or rAd?? or rAd? or AdC? or AdC?? or CAd? or CAd?? or rAdC?? or rAdC? or AdPan? Or AdPan?? or PanAd? or PanAd??) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((Vaccine or immune or immunogenic) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((Vector or plasmid or vehicle or virion) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((AIDS or HIV or “human immunodeficiency virus”) <in> DESCRIPTION) AND ((First or second or third or gutless and generation) <in> (TITLE,ABSTRACT,CLAIMS)))

	((((Adenovirus or AdHu5 or Ad5 or HuAd5 or rAd5 or AdHu6 or Ad6 or HuAd6 or rAd6 or AdHu35 or Ad35 or HuAd35 or rAd35 or AdHu11 or Ad11 or HuAd11 or rAd11 or AdHu24 or Ad24 or HuAd24 or rAd24 or Ad26 or AdHu26 or HuAd26 or rAd26 or AdC6 or Cad6 or rAdC6 or AdC7 or Cad7 or rAdC7 or AdHu2 or Ad2 or HuAd2 or rAd2 or AdHu4 or Ad4 or HuAd4 or rAd4 or AdHu7 or Ad7 or HuAd7 or rAd7 or AdHu48 or Ad48 or HuAd48 or rAd48 or AdHu49 or Ad49 or HuAd49 or rAd49 or AdHu50 or Ad50 or HuAd50 or rAd50 or AdC68 or CAd68 or rAdC68 or AdHu34 or Ad34 or HuAd34 or rAd34 or AdPan6 or PanAd6 or rAdPan6 or AdPan7 or PanAd7 or rAdPan7 or AdPan68 or PanAd68 or rAdPan68) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((Vaccine or immune or immunogenic) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((Vector or plasmid or vehicle or virion) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((First or second or third or gutless and generation) <in> (TITLE,ABSTRACT,CLAIMS))) AND ((merck or crucell or betagene or uab or pennsylvania or wyeth or lexicon or Rhone-Poulenc Rorer or Connaught or Genstar or Baylor or Transgene or Genphar or Wistar or Glaxo) <in> PA)) (((((Adenovirus or Ad?? or Ad? or HuAd?? or HuAd? or AdHu?? or AdHu? or rAd?? or rAd? or AdC? or AdC?? or CAd? or CAd?? or rAdC?? or rAdC? or AdPan? Or AdPan?? or PanAd? or PanAd??) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((Vaccine or immune or immunogenic) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((Vector or plasmid or vehicle or virion) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((First or second or third or gutless and generation) <in> (TITLE,ABSTRACT,CLAIMS))) AND ((merck or crucell or betagene or uab or pennsylvania or wyeth or lexicon or Rhone-Poulenc Rorer or Connaught or Genstar or Baylor or Transgene or Genphar or Wistar or Glaxo) <in> PA))) ((((Vaccine or immune or immunogenic) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((AIDS or HIV or "human immunodeficiency virus") <in> DESCRIPTION) AND ((Adenovirus or AdHu or Ad or HuAd or rAd or AdHu5 or Ad5 or HuAd5 or rAd5 or AdHu6 or Ad6 or HuAd6 or rAd6 or AdHu35 or Ad35 or HuAd35 or rAd35 or AdHu11 or Ad11 or HuAd11 or rAd11 or AdHu24 or Ad24 or HuAd24 or rAd24 or Ad26 or AdHu26 or HuAd26 or rAd26 or AdC6 or Cad6 or rAdC6 or AdC7 or Cad7 or rAdC7 or AdHu2 or Ad2 or HuAd2 or rAd2 or AdHu4 or Ad4 or HuAd4 or rAd4 or AdHu7 or Ad7 or HuAd7 or rAd7 or AdHu48 or Ad48 or HuAd48 or rAd48 or AdHu49 or Ad49 or HuAd49 or rAd49 or AdHu50 or Ad50 or HuAd50 or rAd50 or AdC68 or CAd68 or rAdC68 or AdHu34 or Ad34 or HuAd34 or rAd34 or AdPan or PanAd or rAdPan or AdPan6 or PanAd6 or rAdPan6 or AdPan7 or PanAd7 or rAdPan7 or AdPan68 or PanAd68 or rAdPan68) <in> (TITLE,ABSTRACT,CLAIMS))) AND ((merck or crucell or betagene or uab or pennsylvania or wyeth or lexicon or Rhone-Poulenc Rorer or Connaught or Genstar or Baylor or Transgene or Genphar or Wistar or Glaxo) <in> PA))
Result	Total results: 700 + 120 + 31= 851 Total results considered: 377

Search Round 5 (Week 8)

Database	Delphion (US & EP applications and patents, WIPO PCT publications)
Keywords	Adenovirus, Ad??, Ad?, HuAd??, HuAd?, AdHu??, AdHu?, rAd??, rAd?, AdC?, AdC??, CAd?, CAd??, rAdC??, rAdC?, AdPan?, AdPan??, PanAd?, PanAd??, AdHu5, Ad5, HuAd5, rAd5, AdHu6, Ad6, HuAd6, rAd6, AdHu35, Ad35, HuAd35, rAd35, AdHu11, Ad11, HuAd11, rAd11, AdHu24, Ad24, HuAd24, rAd24, Ad26, AdHu26, HuAd26, rAd26, AdC6, Cad6, rAdC6, AdC7, Cad7, rAdC7, AdHu2, Ad2, HuAd2, rAd2, AdHu4, Ad4, HuAd4, rAd4, AdHu7, Ad7, HuAd7, rAd7, AdHu48, Ad48, HuAd48, rAd48, AdHu49, Ad49, HuAd49, rAd49, AdHu50, Ad50, HuAd50, rAd50, AdC68, CAd68, rAdC68, AdHu34, Ad34, HuAd34, rAd34, AdPan6, PanAd6, rAdPan6, AdPan7, PanAd7, rAdPan7, AdPan68, PanAd68, rAdPan68, First, 1st, 2nd, second, third, 3rd, gutless, generation, Vector, plasmid, vehicle, virion, E1, E2, E3, E4, AIDS, HIV and "human immunodeficiency virus"
US Classification/ Sub-classification	435/456, 424/199.1, 435/006, 424/208.1 and 424/232.1
Search Strings	((((Adenovirus or Ad?? or Ad? or HuAd?? or HuAd? or AdHu?? or AdHu? or rAd?? or rAd? or AdC? or AdC?? or CAd? or CAd?? or rAdC?? or rAdC? or AdPan? Or AdPan??

	or PanAd? or PanAd??)) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((435/456 or 424/199.1 or 435/006 or 424/208.1 or 424/232.1) <in> NC) AND ((Vector or plasmid or vehicle or virion) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((First or 1st or 2nd or second or third or 3rd or gutless and generation) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((E1 or E2 or E3 or E4) <in> (TITLE,ABSTRACT,CLAIMS))) ((((Adenovirus or Ad?? or Ad? or HuAd?? or HuAd? or AdHu?? or AdHu? or rAd?? or rAd? or AdC? or AdC?? or CAd? or CAd?? or rAdC?? or rAdC? or AdPan? Or AdPan?? or PanAd? or PanAd??)) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((435/456 or 424/199.1 or 435/006 or 424/208.1 or 424/232.1) <in> NC) AND ((Vector or plasmid or vehicle or virion) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((First or 1st or 2nd or second or third or 3rd or gutless and generation) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((E1 or E2 or E3 or E4) <in> (TITLE,ABSTRACT,CLAIMS))) AND ((AIDS or HIV or "human immunodeficiency virus") <in> DESCRIPTION) (((Adenovirus or AdHu5 or Ad5 or HuAd5 or rAd5 or AdHu6 or Ad6 or HuAd6 or rAd6 or AdHu35 or Ad35 or HuAd35 or rAd35 or AdHu11 or Ad11 or HuAd11 or rAd11 or AdHu24 or Ad24 or HuAd24 or rAd24 or Ad26 or AdHu26 or HuAd26 or rAd26 or AdC6 or Cad6 or rAdC6 or AdC7 or Cad7 or rAdC7 or AdHu2 or Ad2 or HuAd2 or rAd2 or AdHu4 or Ad4 or HuAd4 or rAd4 or AdHu7 or Ad7 or HuAd7 or rAd7 or AdHu48 or Ad48 or HuAd48 or rAd48 or AdHu49 or Ad49 or HuAd49 or rAd49 or AdHu50 or Ad50 or HuAd50 or rAd50 or AdC68 or CAd68 or rAdC68 or AdHu34 or Ad34 or HuAd34 or rAd34 or AdPan6 or PanAd6 or rAdPan6 or AdPan7 or PanAd7 or rAdPan7 or AdPan68 or PanAd68 or rAdPan68) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((first or 1st or second or 2nd or third or 3rd or gutless and generation) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((Vector or plasmid or vehicle or virion) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((435/456 or 424/199.1 or 435/006 or 424/208.1 or 424/232.1) <in> NC) AND ((AIDS or HIV or "human immunodeficiency virus") <in> DESCRIPTION))
Result	Total results: 132 + 56 + 153= 341 Total results considered: 200

Search Round 6 (Week 9)

Database	Delphion (US & EP applications and patents, WIPO PCT publications)
Keywords	Refer to Search Round 3, 4 & 5 keywords
US Classification/ Sub-classification	435/456, 424/199.1, 435/006, 424/208.1 and 424/232.1
Search Strings	Search Round 3, 4 & 5 results limited by US Classification
Result	Total results: 650 Total results considered: 250

2.2 Search #2

1. Preliminary Search (Round 1)

Database	Delphion
Keywords	1. Core Keywords (Abstract>Claim>Title) a. Adenovirus i. General : Adeno*vir* (it covers adenovirus, adeno virus, adenoviral, adenoviruses, etc.) (we didn't use the term adeno* → too much 'adenosine' or 'adenose') ('Serotype' → too broad) ii. Human : Ad*(1-18, 19a, 19p, 20-51), AdHu*(no need to add numbers, b/c enough specific), rHuAd*, HuAd*, rAd*(1-18, 19a, 19p, 20-51), rAdHu*, HAd*(1-51, 19a, 19p), AdV, rAdV, Adgp, Adt, rAdg, rAdN 1. There are several patents having 'Ad(number)' without mentioning 'Adenovirus' 2. We didn't use the term 'Ad?' → too much 'add' or 'ADC' or other similar abbreviations. 3. 'Ad??' also the same problem.

	4. '?Ad' or '??Ad' didn't work iii. Chimpanzee : AdC(1, 2, 5, 6, 7, 68), CAdV, Pan(6,7), AdPan*, PanAd* iv. Canine : CAV*2 b. Vector i. Vector, Vehicle, Plasmid 2. Optional Keywords a. Veccine : Vaccin* ('immu*' is too broad) b. Adenovirus gene : E1*, E2*, E3, E4, gutless, gutted, oncolytic ('generation' is too broad) c. Adenovirus type : Mastadenovir*, Atadenovir*, Aviadenovir*, Siadenovir*, Ichtadenovir*, Porcine, Bovine, Chimpanzee d. Adenovirus structure : Fibre, Fiber, Penton, Hexon, Virion e. Mechanism : APC(Ag-presenting cells), CAR(coxsackie adenovirus receptor), CD46, CD80, CD86, PentAd41, MHC, CD4, CD8 f. Cell line : CHO, HeLa, A549, HEK*293, PER, 293*C2, 293*E2T, IGRP2 g. HIV : HIV, AIDS, immunodeficien*, SIV, SHIV, FIV, BIV h. Assay : Assay, ELIspot i. Administration : Prime <near> boost, combi* j. Chimera : Chimer*, Hybrid*, Heterolog* k. Exceptions : not (AAV, adeno*associated*virus, rep, parvovirus, VLP, virus*like*particle*) l. Current Clinical Trials : Baden, Barouch, Fuchs, Koblin, Casapia, De Rosa, Kalams, Gray, Duerr, Keeefer, Dolin, Kaleebu, Hammer, Bwayo, Karita, Churchyard, Peiperi, Robb, Schooley, McElrath
Classification / Sub-Classification	Not in use
Search String	(((Adenovir*) and (Vector* or vehicle* or plasmid*)) <in> (TITLE,ABSTRACT,CLAIMS)
Number of results	3514 hits (US patent / publication)

2. Hybrid Search (Round 2)

Database	Delphion
Keywords	Claim, Abstract, Title : (Adeno* or Ad?? or Ad? or HuAd?? or HuAd? or AdHu?? or AdHu? or rAd?? or rAd? or AdC? or AdC?? or CAd? or CAd?? or rAdC?? or rAdC? or AdPan? Or AdPan?? or PanAd? or PanAd??) and (AIDS or HIV or "human immunodeficiency virus") and (Vacc* and immu*) Description : (Hexon or Fiber or Fusion or Hybrid) <near> protein*) or chimer! or "cell binding"
Classification / Sub-Classification	IPC : C07K or A61K or C12N or A61P US Class : 436/456 or 435/320.1 or 435/235.1 or 424/199.1 or 435/325 or 435/069.1 or 424/093.2 or 435/456.000 or 536/023.72 or 424/208.1
Search String	(((Adeno*vir* and (vector or vehicle or plasmid)) <in> (TITLE,ABSTRACT,CLAIMS)) AND (((435 or 424 or 514 or 536 or 530 or 800 or 935 or 977 or 604 or 436) <in> CNC) OR ((A61K or C12N or C07K or A61P or C12Q or C07H or C12P or G01N or A01K or C12R) <in> (ICINV,MC))))
Number of results	3491 Hits (US Patent and Publication)

Database	Delphion

Keywords	Claim, Abstract, Title : (Adeno* or Ad?? or Ad? or HuAd?? or HuAd? or AdHu?? or AdHu? or rAd?? or rAd? or AdC? or AdC?? or CAd? or CAd?? or rAdC?? or rAdC? or AdPan? Or AdPan?? or PanAd? or PanAd??) and (AIDS or HIV or "human immunodeficiency virus") and (Vacc* and immu*) Description : (Hexon or Fiber or Fusion or Hybrid) <near> protein*) or chimer! or "cell binding"
Classification / Sub-Classification	IPC : C07K or A61K or C12N or A61P US Class : 436/456 or 435/320.1 or 435/235.1 or 424/199.1 or 435/325 or 435/069.1 or 424/093.2 or 435/456.000 or 536/023.72 or 424/208.1
Search String	(((Adenovir* or adeno* or Ad?? or Ad? or HuAd?? or HuAd? or AdHu?? or AdHu? or rAd?? or rAd? or AdC? or AdC?? or CAd? or CAd?? or rAdC?? or rAdC? or AdPan? Or AdPan?? or PanAd? or PanAd??)) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((((Hexon or Fiber or Fusion or Hybrid) <near> protein*) or chimer! or "cell binding") <in> DESCRIPTION) AND (((Vacc* and immu*) and (AIDS or HIV or "human immunodeficiency virus")) <in> (TITLE,ABSTRACT,CLAIMS))
Number of results	195 hits

Database	Delphion
Keywords	Claim, Abstract, Title : (Adeno* or Ad?? or Ad? or HuAd?? or HuAd? or AdHu?? or AdHu? or rAd?? or rAd? or AdC? or AdC?? or CAd? or CAd?? or rAdC?? or rAdC? or AdPan? Or AdPan?? or PanAd? or PanAd??) and (AIDS or HIV or "human immunodeficiency virus") and (Vacc* and immu*) Description : (Hexon or Fiber or Fusion or Hybrid) <near> protein*) or chimer! or "cell binding"
Classification / Sub-Classification	IPC : C07K or A61K or C12N or A61P US Class : 436/456 or 435/320.1 or 435/235.1 or 424/199.1 or 435/325 or 435/069.1 or 424/093.2 or 435/456.000 or 536/023.72 or 424/208.1
Search String	((((((Adeno*vir* <in> (Abstract)) and (vector or vehicle or plasmid)) <in> (TITLE,ABSTRACT,CLAIMS)) AND (((435 or 424 or 514 or 536 or 530 or 800 or 935 or 977 or 604 or 436) <in> CNC) OR ((A61K or C12N or C07K or A61P or C12Q or C07H or C12P or G01N or A01K or C12R) <in> (ICINV,MC)))) AND ((vaccin* and (HIV or AIDS or immunodeficien* or SIV or SHIV or FIV or BIV)) <in> DESCRIPTION)) AND NOT ((AAV or Adeno*associated*virus or parvovirus or VLP or virus*like*particle) <in> (TITLE,ABSTRACT,CLAIMS)
Number of results	197 Hits (US Patent and Publication)

2.3 Search #3

I. Preliminary search (Week 1, Sep. 8 ~ Sep. 12)
(i)

Database	Delphion (US & EP applications and patents, WIPO PCT publications)
Keywords	Adenovirus, HIV, Human Immunodeficiency Virus, vaccine
US Classification	Not in use
Search strings	((adeno* and adenovirus*) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((hiv or (human and immun* and virus)) <in> (TITLE,ABSTRACT, CLAIMS)) AND ((vaccin*) <in> (TITLE,ABSTRACT,CLAIMS))
Result	927 hits

(ii)

Database	Delphion

	(US granted patent and US patent applications)
Keywords	Vaccine, Adenovirus, HIV, Human Immunodeficiency Virus
US Classification	Not in use
Search strings	(1) (((vaccin*) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((adeno*) <in> DESCRIPTION) AND ((Hiv or (human and immun* and virus)) <in> (TITLE,ABSTRACT, CLAIMS))) : 1,195 hits (2) (((vaccin*) <in> (description)) AND ((adeno* or adenovirus*) <in> DESCRIPTION) AND ((Hiv or (human and immun* and virus*)) <in> (TITLE, ABSTRACT,CLAIMS))) : 2,800 hits
Result	(1) Briefly reviews patents might relate to HIV vaccine using adenovirus vector; (2) Top 5 classes of patents of these searches are 534, 424, 514, 530, 536

(iii)

Database	Delphion (US granted patent and US patent applications)
Keywords	Adenovirus, HIV, Human Immunodeficiency Virus, Caccine
US Classification	424
Search strings	(((vaccin*) <in> (description)) AND ((adeno* or adenovirus*) <in> DESCRIPTION) AND ((Hiv or (human and immun* and virus*)) <in> (TITLE, ABSTRACT, CLAIMS))) : 1566 hits
Result	Top 5 assignees of this search are: Duke university, University of Pennsylvania, Connaught Lab. Limited, NIH and Genentech.

II. Round II search (Week 2, 3, 4-- Sep. 15~ Oct. 3)
After a conference call with Dr. Kerri, each team is responsible to search patents for different topic of HIV vaccine patents. Round II search is to locate these patents covering these topic. The Round II search contain two parts; the first part is to use different keyword to do searches in Delphion, and the second part is to locate could-be-relevant patents from every search by reviewing Derwent title and abstract.

Part 1
(i)

Database	Delphion (US granted patent and US patent applications)
Keywords	Vaccine, HIV, Cell line, Adenovirus
US Classification	Not in use
Search strings	(1) ((vaccine and HIV) <in> DESCRIPTION) AND ((hiv or (human immun* and virus*)) <in> CLAIMS) AND ((cell and line) <in> (TITLE,ABSTRACT,CLAIMS)) AND (adenovirus*): 155 hits (2) ((vaccine and HIV) <in> DESCRIPTION) AND ((hiv or (human immun* and virus*)) <in> CLAIMS) AND (((cell and line) or screen* or purif* or pack*) <in> (TITLE, ABSTRACT, CLAIMS)) AND (adenovirus*) : 436 hits
Result	Get a sense what the result would be if use “cell line” as a keyword to search US patents

(ii)

Database	Delphion (US & EP applications and patents, WIPO PCT publications)
Keywords	Vaccine, HIV, Cell line, Adenovirus

US Classification	Not in use
Search strings	(1) ((vaccine and HIV) <in> DESCRIPTION) AND ((hiv or (human immun* and virus*)) <in> CLAIMS) AND (((cell and line) or screen* or purif* or pack*) <in> (TITLE, ABSTRACT,CLAIMS)) AND (adenovirus*) : 877 hits (2) ((vaccine and HIV) <in> DESCRIPTION) AND ((hiv or (human immun* and virus*)) <in> CLAIMS) AND ((cell and line) <in> (TITLE,ABSTRACT,CLAIMS)) AND (adenovirus*): 298 hits
Result	Get a sense what the result would be if use "cell line" as a keyword to search US & WIPO patents

(iii)

Database	Delphion for US granted, US application, EP granted, EP application & WIPO PCT Publication
Keywords	Adenovirus, HIV, Vaccine, Cell line, Production, Package, Purification, Purify, Screen
US Classification	Not in use
Search strings	(1) ((hiv or (human and immun* and virus)) <in> CLAIMS) AND ((adeno* or adenovirus* or ad5 or ad35 or ad11 or ad6 or ad24 or adc6* or adc7) <in> CLAIMS) AND ((vaccin*) <in> CLAIMS): 1,152 hits (2) ((hiv or (human and immun* and virus)) <in> CLAIMS) AND ((adeno* or adenovirus* or ad5 or ad35 or ad11 or ad6 or ad24 or adc6* or adc7) <in> CLAIMS) AND ((vaccin*) <in> CLAIMS) AND (((cell and line) and produc*) <in> CLAIMS): 206 hits (3) ((hiv or (human and immun* and virus)) <in> CLAIMS) AND ((adeno* or adenovirus* or ad5 or ad35 or ad11 or ad6 or ad24 or adc6* or adc7) <in> CLAIMS) AND ((vaccin*) <in> CLAIMS) AND (((cell and line) and pack*) <in> CLAIMS): 93 hits (4) (((hiv or (human and immun* and virus)) <in> CLAIMS) AND ((adeno* or adenovirus* or ad5 or ad35 or ad11 or ad6 or ad24 or adc6* or adc7) <in> CLAIMS) AND ((vaccin*) <in> CLAIMS) AND ((purification or purify or purif* or screen*) <in> CLAIMS)): 325 hits
Result	Get a sense what the result would be if use more keywords to search US, EP & WIPO patents

(iv)

Database	Delphion for US granted, US application, EP granted, EP application & WIPO PCT Publication
Keywords	Last name of researchers listed in Clinic trials
US Classification	Not in use
Search strings	((hiv*) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((baden or fuchs or koblin or casapia or rosa or kalams or gray or kublin or duerr of keefer or dolin or kaleebu or hammer or bwayo or karita or churchyard or peiperl or robb or schooley or mcelrath) <in> IN): 127 hits
Result	All are HIV treatment patents; None is related to HIV vaccine

Part II

(i)

Database	Delphion for US granted, US application, EP granted, EP application & WIPO PCT Publication
Keywords	HIV, Adenovirus,Vaccine, Cell line, Production
US Classification	Not in use
Search strings	((hiv or (human and immun* and virus)) <in> CLAIMS) AND ((adeno* or adenovirus* or ad5 or ad35 or ad11 or ad6 or ad24 or adc6* or adc7) <in> CLAIMS) AND ((vaccin*) <in> CLAIMS) AND (((cell and line) and produc*) <in> CLAIMS) : 206 hits
Result	Locate 11 relevant patents from the 206 hits: EP495811B1, EP1433851A2, EP1535995A1, US2003044421A1, US2004101957A1, US2005070017A1, US2005123511A1, WO0063403A2, WO0222080A2, WO09516048A2, WO08056179A1

(ii)

Database	Delphion for US granted, US application, EP granted, EP application & WIPO PCT Publication
Keywords	HIV, Adenovirus, Vaccine, Cell line, package
US Classification	Not in use
Search strings	((hiv or (human and immun* and virus)) <in> CLAIMS) AND ((adeno* or adenovirus* or ad5 or ad35 or ad11 or ad6 or ad24 or adc6* or adc7) <in> CLAIMS) AND ((vaccin*) <in> CLAIMS) AND (((cell and line) and pack*) <in> CLAIMS): 93 hits
Result	Locate 12 patents from the 93 hits: EP1433851A2, EP1535995A1, US2003044421A1, US2003064054A1, US2003099615A1, US2003143200A1, US2004101957A1, US2005070017A1, US2007077257A1, WO0222080A2, WO03040305A2, WO9516048A2

(iii)

Database	Delphion for US granted, US application, EP granted, EP application & WIPO PCT Publication
Keywords	HIV, Adenovirus, Vaccine, Cell, Purification, Screen
US Classification	Not in use
Search strings	(((hiv or (human and immun* and virus)) <in> CLAIMS) AND ((adeno* or adenovirus* or ad5 or ad35 or ad11 or ad6 or ad24 or adc6* or adc7) <in> CLAIMS) AND ((vaccin* and cell*) <in> CLAIMS) AND ((purif* or screen*) <in> CLAIMS)): 392 hits
Result	Locate 8 patents from the 392 hits: EP1000628A1, EP1433851A2, US2003044421A1, US2004101957A1, US2005070017A1, US2005196384A1, US2007077257A1, WO0222080A2

(iv)

Database	Delphion for US granted, US application, EP granted, EP application & WIPO PCT Publication
Keywords	Merck, Adenovirus, HIV, Vaccine
US Classification	Not in use
Search strings	((merck) <in> PA) AND ((adeno* or adenovirus* or ad5 or ad35 or ad11 or ad6 or ad24 or adc6* or adc7) <in> CLAIMS) AND ((hiv*) <in> CLAIMS) AND ((vaccin*) <in> DESCRIPTION) : 22 hits
Result	Locate 16 patents from the 22 hits: WO05071093A2, WO06086357A2, WO06086284A2, WO06020480A2, WO05027835A2, WO04097016A1, WO04083418A1, US6787351, US6733993, WO04018627A2, US20030228329A1, WO03077859A2, WO03076598A2, WO0222080A2, WO0102607A1, WO09748370A2

(v)

Database	Delphion for US granted, US application, EP granted, EP application & WIPO PCT Publication
Keywords	HIV, Adenovirus, Vaccine, Vector, Viral, Recombinant
US Classification	Not in use
Search strings	(1) (((hiv or (human and immun* and virus)) <in> CLAIMS) AND ((adeno* or adenovirus* or ad5 or ad35 or ad11 or ad6 or ad24 or adc6* or adc7) <in> CLAIMS) AND ((vaccin*) <in> CLAIMS) AND ((vector* and viral*) <in> CLAIMS)) : 516 hits (2) (((hiv or (human and immun* and virus)) <in> CLAIMS) AND ((adeno* or adenovirus* or ad5 or ad35 or ad11 or ad6 or ad24 or adc6* or adc7) <in> CLAIMS) AND ((vaccin*) <in> CLAIMS) AND ((vector* and viral* and recombin*) <in> CLAIMS)) : 326 hits
Result	Locate 11 patents from the 326 hits: EP1000628A1, US2003099615A1, US2004197770A1, US2004214162A1, US2006088909A1, US2006216702A1, WO0029561A2, WO0066179A1, WO03040305A2, WO04108939A2, WO09516048A2

III. Round III search (Week 5-- Oct. 6~ Oct. 10)
(i)

Database	Delphion for US granted, US application, EP granted, EP application & WIPO PCT Publication
Keywords	HIV, Adenovirus, Vaccine, Cell line, Vector
US Classification	Not in use
Search strings	(1) (((hiv* or (human and immun* and virus)) <in> CLAIMS) AND ((adeno* or adenovirus* or ad5 or ad35 or ad11 or ad6 or ad24 or adc6* or adc7) <in> CLAIMS) AND ((vaccin*) <in> CLAIMS) AND ((cell and line) <in> CLAIMS)) : 243 hits (2) ((((hiv* or (human and immun* and virus)) <in> CLAIMS) AND ((adeno* or adenovirus* or ad5 or ad35 or ad11 or ad6 or ad24 or adc6* or adc7) <in> CLAIMS) AND ((vaccin*) <in> CLAIMS) AND ((cell and line) <in> CLAIMS)) and vector*) : 215 hits (3) ((((hiv* or (human and immun* and virus)) <in> CLAIMS) AND ((adeno* or adenovirus* or ad5 or ad35 or ad11 or ad6 or ad24 or adc6* or adc7) <in> CLAIMS) AND ((vaccin*) <in> CLAIMS) AND (((cell and line) and vector*) <in> CLAIMS))) : 170 hits (4) ((((hiv* or (human and immun* and virus)) <in> CLAIMS) AND ((adeno* or adenovirus* or ad5 or ad35 or ad11 or ad6 or ad24 or adc6* or adc7) <in> CLAIMS) AND ((vector*) <in> CLAIMS) AND (((cell and line)) <in> CLAIMS))) : 399 hits (5) ((((hiv* or (human and immun* and virus)) <in> CLAIMS) AND ((adeno* or adenovirus* or ad5 or ad35 or ad11 or ad6 or ad24 or adc6* or adc7) <in> CLAIMS) AND ((cell*) <in> CLAIMS) AND (((line)) <in> CLAIMS))) : 622 hits

	(6) ((((hiv* or (human and immun* and virus)) <in> CLAIMS) AND ((adeno* or adenovirus* or ad5 or ad35 or ad11 or ad6 or ad24 or adc6* or adc7) <in> CLAIMS) AND ((cell*) <in> CLAIMS) AND (((line)) <in> CLAIMS)) and vector*) : 489 hits (7) ((((hiv* or (human and immun* and virus)) <in> CLAIMS) AND ((adeno* or adenovirus* or ad5 or ad35 or ad11 or ad6 or ad24 or adc6* or adc7) <in> CLAIMS) AND ((cell* and line) <in> CLAIMS) AND ((vector*) <in> (TITLE,ABSTRACT,CLAIMS))) : 407 hits

(ii)

Database	Delphion for US granted, US application, EP granted, EP application & WIPO PCT Publication
Keywords	HIV, Adenovirus, Cell-line, Vector, Viral, Prophylatic
US Classification	Not in use
Search strings	(1) ((hiv* or (human and immun* and virus)) <in> DESCRIPTION) AND (adeno! or ad? or ad??) <in> (TITLE,ABSTRACT,CLAIMS) : 12,112 hits (2) ((hiv* or (human and immun* and virus)) <in> DESCRIPTION) AND ((adeno* or ad? or ad??) <in> (TITLE,ABSTRACT,CLAIMS)) : 21,250 hits (3) ((hiv* or (human and immun* and virus)) <in> DESCRIPTION) AND ((adeno* or ad? or ad??) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((cell-line) <in> (TITLE,ABSTRACT,CLAIMS)) : 2,117 hits (4) ((hiv* or (human and immunodefici* and virus*)) <in> DESCRIPTION) AND ((adeno* or ad? or ad??) : 11,825 hits (5) ((hiv* or (human and immunodefici* and virus*)) <in> CLAIMS) AND ((adeno* or ad? or ad??) <in> (TITLE,ABSTRACT,CLAIMS)) : 3,768 hits (6) ((hiv* or (human and immunodefici* and virus*)) <in> CLAIMS) AND ((adeno* or ad? or ad??) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((vector*) <in> (TITLE,ABSTRACT,CLAIMS)) : 1,263 hits (7) ((hiv* or (human and immunodefici* and virus*)) <in> CLAIMS) AND ((adeno* or ad? or ad??) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((vector* or viral) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((vaccin* or prophyla*) <in> DESCRIPTION) : 1,653 hits

(iii)

Database	Delphion for US granted, US application, EP granted, EP application & WIPO PCT Publication
Keywords	Virus, Viral, Purification, Preparation, Production, Preservation, Package, Gene expression, Transfection, Transcription, HIV, Method, Cell line, Purification, Adeno
US Classification	Not in use
Search strings	(1) ((virus or viral) <in> (TITLE,ABSTRACT,CLAIMS))

	AND ((purifi* or prepar* or product* or perserv* or packag* or (gene and express*) or transc* or transf*) <in> (TITLE, ABSTRACT, CLAIMS)) AND (("cell line" or "cell-line") <in> (TITLE, ABSTRACT, CLAIMS)) : 4,516 hits (2) ((virus or viral) <in> (TITLE,ABSTRACT,CLAIMS)) AND (("cell line" or "cell-line") <in> (TITLE,ABSTRACT,CLAIMS)) AND ((hiv or (human and immunodeficiency and virus)) <in> DESCRIPTION) : 2,223 hits (3) ((virus or viral) <in> (TITLE,ABSTRACT,CLAIMS)) AND (("cell line" or "cell-line") <in> (TITLE,ABSTRACT,CLAIMS)) AND ((hiv* or (human and immunodeficiency and virus)) <in> DESCRIPTION) AND ((method or packag*) <in> (TITLE,ABSTRACT,CLAIMS)) : 2,072 hits (4) ((virus or viral) <in> (TITLE,ABSTRACT,CLAIMS)) AND (("cell line" or "cell-line") <in> (TITLE,ABSTRACT,CLAIMS)) AND ((hiv* or (human and immunodeficiency and virus)) <in> DESCRIPTION) AND ((method and (packag* or purif*)) <in> (TITLE,ABSTRACT, CLAIMS)) : 813 hits (5) ((virus or viral) <in> (TITLE,ABSTRACT,CLAIMS)) AND (("cell line" or "cell-line") <in> (TITLE,ABSTRACT,CLAIMS)) AND ((hiv* or (human and immunodeficiency and virus)) <in> DESCRIPTION) AND ((method and (packag* or purif* or prepar*)) <in> (TITLE, ABSTRACT,CLAIMS)) : 1,131 hits (6) ((((virus or viral) <in> (TITLE,ABSTRACT,CLAIMS)) AND (("cell line" or "cell-line") <in> (TITLE,ABSTRACT,CLAIMS)) AND ((hiv or ("human immunodeficiency virus")) <in> DESCRIPTION) AND (method <in> CLAIMS) AND ((packag* or purif* or prepar* or preserva* or produc*) <in> CLAIMS) AND ((molecular and clon*) <in> DESCRIPTION) AND ((adeno* or ad? or ad?? or adc? or adc??) <in> CLAIMS))) : 329 hits (7) (((((virus or viral) <in> (TITLE,ABSTRACT,CLAIMS)) AND (("cell line" or "cell-line") <in> (TITLE,ABSTRACT,CLAIMS)) AND ((packag* or purif* or prepar* or preserva* or produc*) <in> CLAIMS) AND ((molecular and clon*) <in> DESCRIPTION) AND ((adeno* or ad? or ad?? or adc? or adc??) <in> CLAIMS)))) : 911 hits (8) (((((virus or viral) <in> (TITLE,ABSTRACT,CLAIMS)) AND (("cell line" or "cell-line") <in> (TITLE,ABSTRACT,CLAIMS)) AND ((packag* or purif* or prepar* or preserva* or produc*) <in> CLAIMS)

	AND ((molecular and clon*) <in> DESCRIPTION) AND ((adeno* or ad? or ad?? or adc? or adc??) <in> CLAIMS) AND ((vaccin* or prophyla* or prevent*))))) : 835 hits

(iv)

Database	Derwent database for US granted, US application, EP granted, EP application & WIPO PCT Publication
Keywords	Cell line, HIV, package, Purification, Preparation, preservation, Production, Propagation, Adeno, Cloning, Viral, Virus, Transfection
US Classification	Not in use
Search strings	(1) (((cell* and line) or "cell-line") <in> AB) AND ((hiv or "human immunodeficiency virus") <in> TEXT) AND ((packag* or purif* or prepar* or preserva* or produc* or propaga*) <in> AB) AND ((adeno* or ad? or ad?? or adc? or adc??) <in> TEXT) : 73 hits (2) (((cell* and line) or "cell-line") <in> TEXT) AND ((packag* or purif* or prepar* or preserva* or produc* or propaga*) <in> TEXT) AND ((adeno* or ad? or ad?? or adc? or adc??) <in> TEXT) : 983 hits (3) (((cell* and line) or "cell-line" or "cell line") <in> TEXT) AND ((clon* or viral or virus) <in> TEXT) AND ((packag* or purif* or prepar* or preserva* or produc* or propaga* or transf*) <in> TEXT) AND ((adeno* or ad? or ad?? or adc? or adc??) <in> TEXT) : 522 hits (4) (("cell-line" or "cell line") <in> TEXT) AND ((clon* or viral or virus) <in> TEXT) AND ((packag* or purif* or prepar* or preserva* or produc* or propaga* or transf*) <in> TEXT) AND ((adeno* or ad? or ad?? or adc? or adc??) <in> TEXT) : 376 hits

(v)

Database	Derwent database for US granted, US application, EP granted, EP application & WIPO PCT Publication
Keywords	
US Classification	Not in use
Search strings	(1) (((((hiv or (human and immunodeficiency and virus)) <in> AB) AND ((adeno* or ad? or ad?? or adc? or adc??) <in> AB) AND ((vector or viral) <in> AB)))) : 864 hits (2) (((hiv or (human and immunodeficiency and virus)) <in> AB) AND ((adeno* or ad? or ad?? or adc? or adc??) <in> AB) AND ((vector or viral) <in> AB) AND ((vaccin* or prophyla*) <in> text)) : 323 hits (3) (((hiv or ("human immunodeficiency virus")) <in> AB) AND ((adeno* or ad? or ad?? or adc? or adc??) <in> AB) AND ((vector or viral or virus) <in> AB) AND ((vaccin* or prophyla* or prevent*) <in> AB) ANDNOT (("adeno-associated" or "aav") <in> AB)) : 545 hits

	(4) (((hiv or ("human immunodeficiency virus")) <in> claims) AND ((adeno* or ad? or ad?? or adc? or adc??) <in> AB) AND ((vector or viral or virus) <in> AB) AND ((vaccin* or prophyla* or prevent*) <in> AB) ANDNOT (("adeno-associated" or "aav") <in> AB)) : 13 hits (5) (((hiv or ("human immunodeficiency virus")) <in> TITLE) AND ((adeno* or ad? or ad?? or adc? or adc??) <in> AB) AND ((vector or viral or virus) <in> AB) AND ((vaccin* or prophyla* or prevent*) <in> AB) ANDNOT (("adeno-associated" or "aav") <in> AB)) : 119 hits (6) (((packag* or purif* or prepar* or preserva* or produc* or propag* or transf*) <in> AB) AND ((adeno or adenovirus or adenoviral or ad? or ad?? or adc? or adc?? or rad? or rad?? or radc? or radc??) <in> AB)) : 86,982 hits (7) (((packag* or purif* or prepar* or preserva* or produc* or propag* or transf*) <in> AB) AND ((adeno or adenovirus or adenoviral or ad? or ad?? or adc? or adc?? or rad? or rad?? or radc? or radc??) <in> AB) AND (cell and line)) : 1,025 hits

(vi)

Database	Delphion for US granted, US application, EP granted, EP application & WIPO PCT Publication Or Derwent database for US granted, US application, EP granted, EP application & WIPO PCT Publication
Keywords	HIV, Adeno, Vector, Viral, Vaccine, Prophylatic, Cell line, Package, Purification, Preparation, Preservation, Production, Molecular, Cloning,
US Classification	Not in use
Search strings	Delphion (1) ((hiv* or (human and immunodefici* and virus*)) <in> CLAIMS) AND ((adeno* or ad? or ad??) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((vector* or viral) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((vaccin* or prophyla*) <in> (TITLE,ABSTRACT,CLAIMS)) : 1,026 hits (2) ((((virus or viral) <in> (TITLE,ABSTRACT,CLAIMS)) AND (("cell line" or "cell-line") <in> (TITLE,ABSTRACT,CLAIMS)) AND ((hiv or ("human immunodeficiency virus")) <in> DESCRIPTION) AND ((packag* or purif* or prepar* or preserva* or produc*) <in> CLAIMS) AND ((molecular and clon*) <in> DESCRIPTION) AND ((adeno* or ad? or ad?? or adc? or adc??) <in> CLAIMS))) : 354 hits (3) (((((virus or viral) <in> (TITLE,ABSTRACT,CLAIMS)) AND (("cell line" or "cell-line") <in> (TITLE,ABSTRACT,CLAIMS)) AND ((packag* or purif* or prepar* or preserva* or produc*) <in> CLAIMS) AND ((molecular and clon* and transf*) <in> DESCRIPTION)

	AND ((adeno* or ad? or ad?? or adc? or adc??) <in> CLAIMS) AND ((vaccin* or prophyla* or prevent*) <in> TEXT)))) : 817 hits Derwent: (1) ((hiv or (human and immunodefici* and virus*)) <in> AB) AND ((adeno* or ad? or ad??) <in> AB) AND ((vector or viral) <in> AB) AND ((vaccin* or prophyla*) <in> AB) : 321 hits (2) (("cell-line" or "cell line") <in> TEXT) AND ((clon* or virual or virus) <in> TEXT) AND ((packag* or purif* or prepar* or preserva* or produc* or propaga* or transf* or screen*) <in> TEXT) AND ((adeno* or ad? or ad?? or adc? or adc??) <in> TEXT) : 421 hits
Result	From these search results, locate (1) Top Three Derwent class: B04, D16, C06; (2) Top Ten US class-subclass: 435/235.1, 435/320.1, 435/456, 435/235.100, 435/320.1, 435/239, 435/006, 435/069.1, 435/366, 435/455; (3) Top Ten IPC class: C12N 15/861, A61K 48/00, C12N 5/10, C12N 7/00, C12N 7/01, C12N 15/86, C12N 7/02, C12 15/09, A61P 35/00, A61K 39/00

IV. Round IV search (Week 6-- Oct. 11~ Oct. 17)
(i)

Database	Delphion (US granted patent and US patent applications)
Keywords	Adenovirus, Cell line, HIV, Package, Purification, Preparation, Preservation, Production, Propagation, transfection
US Classification	435/235.1, 435/320.1, 435/456, 435/235.100, 435/320.1, 435/239, 435/006, 435/069.1, 435/366, 435/455
Search strings	(1) (((435/235.1 or 435/320.1 or 435/456 or 435/235.100 or 435/320.1 or 435/239 or 435/006 or 435/069.1 or 435/366 or 435/455) <in> NC)) : 46,378 hits (2) (((435/235.1 or 435/320.1 or 435/456 or 435/235.100 or 435/320.1 or 435/239 or 435/006 or 435/069.1 or 435/366 or 435/455) <in> NC) AND ((adeno or adenovirus or ad? or ad?? or adc? or adc??) <in> (TITLE, ABSTRACT, CLAIMS))) : 3,489 hits (3) (((435/235.1 or 435/320.1 or 435/456 or 435/235.100 or 435/320.1 or 435/239 or 435/006 or 435/069.1 or 435/366 or 435/455) <in> NC) AND ((adeno or adenovirus or ad? or ad?? or adc? or adc??) <in> (TITLE, ABSTRACT, CLAIMS)) AND (("cell line" or "cell lines" or "cell-line" or "cell-lines") <in> (TITLE, ABSTRACT, CLAIMS))) : 511 hits (4) (((((435/235.1 or 435/320.1 or 435/456 or 435/235.100 or 435/320.1 or 435/239 or 435/006 or 435/069.1 or 435/366 or 435/455) <in> NC) AND ((adeno or adenovirus or ad? or ad?? or adc? or adc??) <in> (TITLE, ABSTRACT, CLAIMS)) AND (hiv or (human and immunodeficiency and virus)) <in> DESCRIPTION))) : 1,173 hits (5) ((((435/235.1 or 435/320.1 or 435/456 or 435/235.100 or 435/320.1 or 435/239 or 435/006 or 435/069.1 or 435/366 or 435/455) <in> NC) AND

	((adeno or adenovirus or ad? or ad?? or adc? or adc??) <in> (TITLE, ABSTRACT, CLAIMS)) AND (("cell line" or "cell lines" or "cell-line" or "cell-lines") <in> (TITLE, ABSTRACT, CLAIMS)) AND ((packag* or purif* or prepar* or preserva* or produc* or propag* or transf*) <in> (TITLE, ABSTRACT, CLAIMS)))) : 485 hits

(ii)

Database	Delphion (US granted patent and US patent applications)
Keywords	Adenovirus, Cell line, HIV
US Classification	435/235.1, 435/320.1, 435/456, 435/235.100, 435/320.1, 435/239, 435/006, 435/069.1, 435/366, 435/455
Search strings	((435/235.1 or 435/320.1 or 435/456 or 435/235.100 or 435/320.1 or 435/239 or 435/006 or 435/069.1 or 435/366 or 435/455) <in> NC) AND ((adeno or adenovirus or ad? or ad?? or adc? or adc??) <in> (TITLE, ABSTRANCT, CLAIMS)) AND (("cell line" or "cell lines" or "cell-line" or "cell-lines") <in> (TITLE, ABSTRANCT, CLAIMS)) AND (hiv or (human and immunodeficiency and virus)) <in> DESCRIPTION))) : 167 hits
Result	Locate 41 patents from the 167 hits: US25069866A1, US23008390A1, US7247472, US25070017A1, US23166140A1, US23099615A1, US7232899, US25158278A1, US24096426A1, US23143200A1, US6723558, US28206837A1, US23157688A1, US26211115A1, US24253210A1, US7285265, US25163753A1, US27231303A1, US6867022, US25170463A1, US6458586, US7291498, US28176218A1, US23092160A1, US6319716, US24136963A1, US25123511A1, US5994108, US22187128A1, US6083716, US22088014A1, US24106194A1, US7267824, US28090281A1, US23044421A1, US26233756A1 US7005277, US27172949A9, US24101957A1, US27054395A1, US26270041A1

(iii)

Database	Delphion (US granted patent and US patent applications)
Keywords	Adenovirus, Cell line, Package, Purification, Preparation, Preservation, Production, Propagation, Transfection, Vaccine, Prophylatic, prevantation
US Classification	435/235.1, 435/320.1, 435/456, 435/235.100, 435/320.1, 435/239, 435/006, 435/069.1, 435/366, 435/455
Search strings	(((((435/235.1 or 435/320.1 or 435/456 or 435/235.100 or 435/320.1 or 435/239 or 435/006 or 435/069.1 or 435/366 or 435/455) <in> NC) AND ((adeno or adenovirus or ad? or ad?? or adc? or adc??) <in> (TITLE, ABSTRACT, CLAIMS)) AND (("cell line" or "cell lines" or "cell-line" or "cell-lines") <in> (TITLE, ABSTRACT, CLAIMS)) AND ((packag* or purif* or prepar* or preserva* or produc* or propag* or transf*) <in> (TITLE, ABSTRACT, CLAIMS)) AND (((vaccin* or prophyla* or prevent*) <in> DESCRIPTION)))) : 370 hits
Result	Locate 83 patents from the 370 hits: US25069866A1, US26211115A1, US6867022, US23044421A1, US23157688A1, US27231303A1, US22192185A1, US24101957A1, US23119192A1, US7291498, US6730507, US25070017A1, US23171336A1, US23040101A1, US6379943, US6492169, US23185801A1, US24136963A1, US25123511A1, US6869794, US25163753A1, US6083716, US21026938A1, US7182759, US22119942A1, US6261551, US22019051A1, US25158278A1, US25074885A1, US6270996, US22072120A1, US6670188,

	US5820868, US6475769, US25003545A1, US7037716, US6086890, US7238526, US23100116A1, US6974695, US7025967, US28090281A1, US21043922A1, US28199433A1, US6379944, US25112103A1, US6033908, US7344883, US6492343, US7306794, US25123898A1, US28206837A1, US6458586, US7247472, US6113913, US7285265, US6319716, US7247472, US22004040A1, US7250293, US22187128A1, US6063622, US22031831A1, US5872005, US24038205A1, US6723558, US22110545A1, US5994108, US22064859A1, US24253210A1, US5851806, US24106194A1, US23099615A1, US6451596, US5994106, US25277194A1, US23143200A1, US6057158, US7195896, US27054395A1, US6083750, US23104626A1, US22164802A1

3. Patent Search Results Spreadsheet Summery

3.1 Categorization Summary

Adenovirus patents generally fall into 5 categories: **(1) HIV-specific adenovirus vectors, (2) Methods of producing an adenovirus HIV vaccine, (3) Adenovirus Serotypes, (4) Chimeras, (5) Adjuvants, and (6) HIV Vaccines using Adenovirus**.

There are three generations of adenovirus vectors. First generation adenovirus vectors have been developed by the deletion of E1 genes necessary for expression of E2 and late genes required for adenovirus DNA synthesis, capsid protein expression and viral replication. First generation adenovirus vectors often also include deletion of the E3 gene.[157] Second generation adenovirus vectors also removed the E2 and E4 genes to provide increased packaging capacity.[158] Third generation adenoviruses are gutless and require a helper virus to produce the adenovirus.[159] The spreadsheet will indicate all patents that discuss any of these generations of adenovirus vectors in the category labeled "**vector**."

Patents also claim methods of producing and constructing the adenovirus vector for HIV vaccines. Original adenovirus vectors are constructed by homologous recombination. These vectors are ligated with the purified shuttle vector. The vector is then purified and used to transfect E-1 transcomplementing cells. When plaques develop, the vector is purified and tested for replication competent virus.[160] Cell lines for the propagation of adenoviruses are created for transcomplementation.[161] Patents generally claim methods of large-scale production and efficient purification techniques including chromatography

[157] Barry, Michael A., *Current Advances and Future Challenges in Adenovirus Vector Biology and Targeting*, 7 CURRENT GENE THERAPY 189, 189–190 (2007); Wu, et al., Cancer Gene Therapy by Adenovirus-Mediated Gene Transfer, 1 Current Gene Therapy 101, 103 (2001).
[158] Kochanek, Stefan, Division of Gene Therapy, Adenovirus: Biology and Vectors at the University of Ulm (Nov. 9, 2006); Wu et al. *supra* note 157 at 104.
[159] *Id.*
[160] Tatsis, Nia and Ertl, Hildegund C.J., *Adenoviruses as Vaccine Vectors*, 10 MOLECULAR THERAPY, 616, 620 (2004).
[161] Chawla, et al., *Adenovirus-Vectored Vaccines*, 18 EXPERT OPINION ON THERAPEUTIC PATENTS 293, 295 (2008).

and of the adenovirus vector. Patents also claim packaging of complementing cell-lines for adenovirus production. These patents are categorized under "**method**."

There are at least 49 different human adenovirus serotypes.[162] Adenovirus serotypes are distinguishable strains of adenovirus that vary in cross-reactivity with antibodies. These patents have been appropriately labeled "**serotype**." Most patents in this category will fall under multiple categories.

Another strategy is to incorporate desirable serological and immunological attributes of different adenovirus vectors into one chimeric protein.[163] Chimeras are formed from a heterology of genetically distinct cells. To retain inherent immunogenicity of Ad5 while at the same time evading Ad5 neutralizing antibodies, domains of Ad5 capsid proteins are replaced with corresponding domains from other adenovirus serotypes.[164] Ad35 can also carry an Ad5 fiber shaft in a different construct.[165] Patents of this kind are labeled "**chimeric protein**" and possibly fall under multiple categories as well.

Adjuvants are modulatory agents that help boost the effect of the vaccine without having any specific antigenic effect in itself in order to increase the immunity to a particular disease, in this case, HIV.[166] Patents that claim adjuvants have been labeled "**adjuvants**."

The final category of patents contains HIV vaccine using adenoviruses. These patents claim the innoculation and the eliciting of immune responses. Vaccine patents are labeled "**final product**" in the patent search results summary.

[162] MicrobiologyBytes, *Adenoviruses*, http://www.microbiologybytes.com/virology/Adenoviruses.html (last visited Dec. 4, 2007).
[163] Chawla, et al., *supra* note 161, at 302.
[164] *Id.*
[165] *Id.*
[166] U.S. National Institutes of Health, Dictionary of Cancer Terms, http://www.cancer.gov/templates/db_alpha.aspx?CdrID=43987.

3.2 Master Spreadsheet

Publication Number	Vectors	Production methods	Ad Serotype	Chimeric Protein	Final Vaccine Product	Prime Boost	Adjuvant	COMMENT	Title	Assignee/Applicant Name	Inventor Name
US5106965	N	N	Y	N	N	N	N		Detection of human adenovirus	Research Corporation Technologies, Inc.	Pieniazek; Norman J.|Slemenda; Susan B.|Pieniazek; Danuta|Velarde, Jr.; Jorge|Luftig; Ronald B.
US5559099	Y	N	N	Y	N	N	N		Penton base protein and methods of using same	GenVec, Inc.	Wickham; Thomas J.|Kovesdi; Imre|Brough; Douglas E.|McVey; Duncan L.|Brader; Joseph T.
US5707618	Y	N	Y	N	N	N	N		Adenovirus vectors for gene therapy	Genzyme Corporation	Armentano; Donna|Romanczuk; Helen|Wadsworth; Samuel Charles
US5731172	Y	Y	N	N	N	N	N		Recombinant adenovirus and process for producing the same	Sumitomo Pharmaceuticals Company, Ltd.	Saito; Izumu|Kanegae; Yumi
US5770442	Y	N	Y	Y	N	N	N		Chimeric adenoviral fiber protein and methods of using same	Cornell Research Foundation, Inc.; GenVec, Inc.	Wickham; Thomas J.|Falck-Pedersen; Erik|Roelvink; Petrus W.|Bruder; Joseph T.|Gall; Jason|Kovesdi; Imre
US5820868	Y	N	N	N	Y	N	N		Recombinant protein production in bovine adenovirus expression vector system	Veterinary Infectious Disease Organization	Mittal; Suresh K.|Graham; Frank L.|Prevec; Ludvik|Babiuk; Lorne A.
US5837511	Y	Y	Y	N	N	N	N		Non-group C adenoviral vectors	Cornell Research Foundation, Inc.	Falck-Pedersen; Erik S.|Crystal; Ronald G.|Mastrangeli; Andrea|Abrahamson; Karil
US5851806	Y	Y	N	N	Y	N	N		Complementary adenoviral systems and cell lines	GenVec, Inc.	Kovesdi; Imre|Brough; Douglas E.|McVey; Duncan L.|Bruder; Joseph T.|Lizonova; Alena

US5866136	N	N	N	N	Y	N	Y		Recombinant vaccine	Commonwealth Scientific and Industrial Organisation|The Australian National University	Ramshaw; Ian Allister|Boyle; David Bernard|Coupar; Barbara Elizabeth Howieson|Andrew; Marion Elizabeth
US5882877	Y	Y	N	N	N	N	N		Adenoviral vectors for gene therapy containing deletions in the adenoviral genome	Genzyme Corporation	Gregory; Richard J.|Armentano; Donna|Couture; Larry A.|Smith; Alan E.
US5891690	N	Y	N	N	N	N	N		Adenovirus E1-complementing cell lines	MASSIE; BERNARD	Massie; Bernard
US5989805	N	Y	N	N	N	N	N		Immortal avian cell line to grow avian and animal viruses to produce vaccines	Michigan State University	Reilly; John David|Taylor; Daniel C.|Maes; Roger|Coussens; Paul M.
US5994134	N	Y	N	N	N	N	N		Viral production process	Canji, Inc.	Giroux; Daniel D.|Goudreau; Ann M.|Ramachandra; Muralidhara|Shabram; Paul W.
US6001557	Y	Y	Y	N	N	N	N		Adenovirus and methods of use thereof	University of Pennsylvania	Wilson; James M.|Fisher; Krishna J.|Chen; Shu-Jen|Weitzman; Matthew
US6033908	N	Y	N	N	N	N	N		Packaging systems for human recombinant adenovirus to be used in gene therapy	IntroGene, b.v.	Bout; Abraham|Hoeben; Robert Cornelis
US6057158	Y	Y	N	N	N	N	N		Adenovirus vectors	University of Michigan	Chamberlain; Jeffrey S.|Hartigan-O'Connor; Dennis J.
US6080569	Y	Y	N	N	N	N	N		Adenovirus vectors generated from helper viruses and helper-dependent vectors	Merck & Co., Inc.	Graham; Frank L.|Parks; Robin|Chen; Liane
US6083716	Y	Y	N	N	N	N	N		Chimpanzee adenovirus vectors	University of Pennsylvania	Wilson; James M.|Farina; Steven F.|Fisher; Krishna J.
US6090393	Y	Y	N	N	Y	N	N		Recombinant canine adenoviruses, method for making and uses thereof	MERIAL LIMITED	Fischer; Laurent

US6261807	Y	Y	Y	N	N	N	N		Method for preparing a recombinant adenovirus genome	Rhone-Poulenc Rorer S.A.	Crouzet; Joel|Naudin; Laurent|Yeh; Patrice|Orsini; Cecile|Vigne; Emmanuelle
US6287571	Y	N	N	N	Y	N	N		Replication-defective adenovirus human type 5 recombinant as a vaccine carrier	The Wistar Institute of Anatomy and Biology; University of Pennsylvania	Ertl; Hildegund C. J.|Wilson; James M.
US6287814	N	N	N	N	N	N	Y		RNA export element and methods of use	Salk Institute	Hope; Thomas J.|Zufferey; Romain|Trono; Didier|Donello; John Edward
US6291214	Y	Y	Y	N	N	N	N		System for generating recombinant viruses	Glaxo Wellcome Inc.	Richards; Cynthia Ann|Weiner; Michael Phillip
US6296852	Y	Y	Y	N	Y	N	N		Recombinant avian adenovirus vector	Commonwealth Scientific and Industrial Research Organisation	Johnson; Michael A.|Prideaux; Christopher T.|McCoy; Richard J.|Lowenthal; John W.
US6319716	Y	Y	N	N	N	N	N		Bovine adenovirus type 3 genome and vector systems derived therefrom	University of Saskatchewan	Tikoo; Suresh Kumar|Babiuk; Lorne A.|Reddy; Police Seshidhar|Zakhartchouk; Alexandre|Baxi; Mohit
US6322969	Y	Y	N	Y	N	N	N		Method for preparing permuted, chimeric nucleic acid libraries	University of California	Stull; Robert A.|Pallavicini; Maria|Green; Gary
US6335016	Y	Y	Y	N	N	N	N		Chicken embryo lethal orphan (CELO) virus	Boehringer Ingelheim International GmbH	Baker; Adam|Cotten; Matthew|Chiocca; Susanna|Kurzbauer; Robert|Schaffner; Gotthold
US6365394	N	Y	Y	N	N	N	N		Cell lines and constructs useful in production of E1-deleted adenoviruses in absence of replication competent adenovirus	University of Pennsylvania	Gao; Guangping|Wilson; James M.

US6399587	Y	N	N	N	N	N	N		Recombinant adenoviral vectors comprising a splicing sequence	Transgene S.A.	Mehtali; Majid|Leroy; Pierre|Michou; Anne-Isabelle
US6410013	Y	N	N	N	N	N	N		Viral vectors for use in monitoring HIV drug resistance	Musc Foundation for Research Development	Dong; Jian-yun
US6458586	Y	Y	N	N	N	N	N		Bovine cells expressing adenovirus essential functions for propagation of recombinant adenoviral vectors	University of Saskatchewan	Tikoo; Suresh Kumar|Babiuk; Lorne A.|Reddy; Police Seshidhar
US6489142	Y	Y	N	N	N	N	N		Methods and compositions for producing viral particles	Aventis Pharma S.A.; Genopoietic	Torrent; Christophe|Yeh; Patrice|Perricaudet; Michel|Klatzmann; David|Salzmann; Jean-Loup
US6492169	N	Y	Y	N	N	N	N		Complementing cell lines	Crucell Holland, B.V.	Vogels; Ronald|Havenga; Menzo|Mehtali; Majid
US6511845	N	N	Y	N	Y	Y	N		Methods for producing an immune response against HIV-1	Wyeth	Davis; Alan R.|Hung; Paul P.|Lubeck; Michael D.|Natuk; Robert J.|Chanda; Pranab K.|Murthy; Shridhara C. S.|Lee; Shaw-Guang L.
US6558948	N	Y	N	N	N	N	N		Permanent amniocytic cell line, its production and use for the production of gene transfer vectors	KOCHANEK STEFAN; SCHIEDNER GUDRUN	Kochanek; Stefan|Schiedner; Gudrun
US6569677	Y	Y	N	N	N	N	N		Modified adenoviral fiber and target adenoviruses	Transgene S.A.; Centre National de la Recherche Scientifique (CNRS)	Legrand; Valerie|Mehtali; Majid|Boulanger; Pierre
US6576463	Y	N	Y	N	N	N	N		Hybrid vectors for gene therapy	University of California	Kasahara; Noriyuki|Higo; Collin|Soifer; Harris|Mitani; Kohnosuke

US6686200	Y	Y	N	N	N	N	N	AAV	Methods and compositions for the large scale production of recombinant adeno-associated virus	UAB Research Foundation	Dong; Jianyun|Frizzell; Raymond A.
US6692956	Y	Y	Y	N	N	N	N		Recombinant adenoviral vectors	Transgene S.A.	Rooke; Ronald
US6723558	N	N	N	N	Y	Y	N		Preparation and use of viral vectors for mixed envelope protein vaccines against human immunodeficiency viruses	St. Jude Children's Research Hospital	Hurwitz; Julia|Coleclough; Christopher|Owens; Randall|Slobod; Karen
US6844192	Y	Y	N	N	N	N	N		Adenovirus E4 protein variants for virus production	Wake Forest University	Orlando; Joseph S.|Ornelles; David A.
US6852528	Y	N	N	Y	N	N	N		Human and mouse uroplakin II gene transcriptional regulatory elements	Cell Genesys, Inc.	Yu; De-Chao|Zhang; Hong|Henderson; Daniel R.
US6869936	N	Y	Y	N	N	N	N		Means and methods for fibroblast-like or macrophage-like cell transduction	Crucell Holland B.V.	Vogels; Ronald|Schouten; Govert J.|Bout; Abraham|Havenga; Menzo Jans Emco
US7094398	Y	N	Y	Y	N	N	N		Recombinant adenoviral vectors expressing chimeric fiber proteins for cell specific infection and genome integration	University of Washington	Lieber; André|Shayakhmetov; Dmitry M|Farrer; Denise R|Papayannopoulou; Thalia|Stamatoyannopoulos; George
US7109025	Y	N	Y	N	N	N	N		Viral vectors and viral vaccines based on recombinant porcine adenoviruses	Merial|Ecole Nationale Veterinaire de Maison Alfort	Eloit; Marc|Klonjkowski; Bernard Georges
US7323177	Y	N	Y	N	N	Y	N		Recombinant porcine adenovirus vector	Vectogen Pty Ltd.	Johnson; Michael Anthony|Hammond; Jeffrey Michael|McCoy; Richard J.|Sheppard; Michael G.
US7326692	Y	N	N	N	N	N	N		Induction of immunity using inhibitors of granzymes	University of Chicago	Ashton-Rickardt; Philip G.|Opferman; Joseph T.

US7344873	N	Y	N	N	N	N	N		Methods of adenovirus production	Merck & Co., Inc.	Xie; Liangzhi|Goochee; Charles F.
US2001010933A1	Y	Y	N	N	N	N	N		Use of trans-activation and CIS-activation to modulate the persistence of expression of a transgene in an at least E4-deficient adenovirus	GenVec, Inc.	Brough, Douglas E.|Kovesdi, Imre
US2001026938A1	Y	Y	N	N	N	N	N		Adenovirus mutants with deleted protease gene, complementing cell lines, and corresponding vectors for gene transfer and positive selection of recombinant adenoviral vectors	MASSIE BERNARD|QUALIKENE WAHIBA	Massie, Bernard|Qualikene, Wahiba
US2001046965A1	N	Y	N	N	N	N	N		Adenovirus E1-complementing cell lines	GENSTAR THERAPEUTICS	Ayares, David|Alemany, Ramon|Zhang, Wei-Wei
US2001049136A1	Y	Y	Y	N	N	N	N		Defective adenoviruses and corresponding complementation lines	Transgene S.A.	Imler, Jean-Luc|Mehtali, Majid|Pavirani, Andrea
US2002006395A1	Y	N	Y	N	N	N	N		DEFECTIVE ADENOVIRUSES INCLUDING A THERAPEUTIC GENE AND AN IMMUNOPROTECTIVE GENE	Aventis Pharma S.A	PERRICAUDET, MICHEL|LEE, MARTIN
US2002019051A1	Y	Y	Y	Y	Y	N	N		Chimeric adenoviral vectors	Transgene S. A	Lusky, Monika|Winter, Arend Jan
US2002028497A1	Y	Y	N	N	Y	N	N		METHOD FOR PRODUCING RECOMBINANT ADENOVIRUS	Centelion	BLANCHE, FRANCIS|GUILLAUME, JEAN-MARC
US2002034519A1	Y	N	Y	N	Y	N	N		Modified bovine adenovirus having altered tropism	University of Saskatchewan	Tikoo, Suresh K.|Babiuk, Lorne A.|Zhang, Linong|Wu, Qiaohua

US2002061517A1	Y	Y	Y	N	Y	Y	N		Adenovirus carrying gag gene HIV vaccine	Merck & Co., Inc.	Chen, Ling|Shiver, John W.|Bett, Andrew J.|Casimiro, Danilo R.|Caulfield, Michael J.|Chastain, Michael A.|Emini, Emilio A.
US2002064859A1	Y	Y	Y	N	Y	N	N		Adenovirus vectors comprising introns	University of Saskatchewan	Tikoo, Suresh K.
US2002072120A1	Y	Y	N	N	N	N	N		Helper viruses for the preparation of recombinant viral vectors	Transgene S.A.	Lusky, Monika|Mehtali, Majid
US2002085999A1	Y	N	N	N	N	N	N		Marek's disease virus genes and their use in vaccines for protection against marek's disease	The USA, Secretary of Agriculture and Nippon Zeon Co., Ltd.	Lee, Lucy F.|Nazerian, Keyvan|Witter, Richard L.|Wu, Ping|Yanagida, Noboru|Yoshida, Shigeto
US2002086837A1	Y	N	N	N	Y	N	Y		Acne vaccine	ARKAGEN, INC	Gauldie, Jack|Braciak, Todd
US2002102731A1	Y	Y	N	N	N	N	N		Hybrid adenovirus/adeno-associated virus vectors and methods of use thereof	University of New York	Hearing, Patrick|Bahou, Wadie F.|Sandalon, Ziv|Gnatenko, Dmitri V.
US2002119942A1	Y	Y	Y	N	N	N	N		Packaging systems for human recombinant adenovirus to be used in gene therapy	Crucell Holland B.V.	Vogels, Ronald|Bout, Abraham
US2002123057A1	Y	N	N	N	N	N	N		In vitro methods of producing and identifying immunoglobulin molecules in eukaryotic cells	University of Rochester	Zauderer, Maurice|Smith, Ernest S.
US2002127690A1	Y	N	N	N	N	N	N		Methods and compositions for stabilizing microtubules and intermediate filaments in striated muscle cells	University of Texas System	Olson, Eric N.|Spencer, Jeffrey A.
US2002136707A1	Y	Y	N	N	N	N	N		Human glandular kallikrein enhancer, vectors comprising the enhancer and methods of use thereof	Cell Genesys, Inc.,	Yu, De Chao|Henderson, Daniel R.|Schuur, Eric R.

US2002137678A1	Y	Y	N	N	N	N	N		Treatment of ocular neovascularization and related diseases	Children's Hospital Research Foundation	Gendron, Robert L.|Paradis, Helene
US2002146828A1	Y	Y	N	N	Y	N	Y		Microparticles and methods for delivery of recombinant viral vaccines	CORIXA CORPORATION	Hural, John|Johnson, Mark E.|Spies, A. Gregory
US2002155127A1	Y	Y	N	N	Y	Y	Y		Genetic vaccine against human immunodeficiency virus	Genphar, Inc.	Wang, Danher
US2002187128A1	Y	Y	Y	Y	N	N	N		Novel replication deficient adenovirus vectors and methods for making and using them	University of Michigan	Imperiale, Michael J.
US2003017138A1	Y	Y	Y	Y	N	N	N		CHIMERIC ADENOVIRUSES	Crucell Holland B.V.	HAVENGA, MENZO|VOGELS, RONALD|BOUT, ABRAHAM
US2003044421A1	Y	Y	N	N	Y	N	N		Enhanced first generation adenovirus vaccines expressing codon optimized HIV1-Gag, Pol, Nef and modifications	Merck & Co., Inc.	Emini, Emilio A.|Youil, Rima|Bett, Andrew J.|Chen, Ling|Kaslow, David C.|Shiver, John W.|Toner, Timothy J.|Casimiro, Danilo R.
US2003092160A1	N	Y	N	N	N	N	N	CRUCELL	Recombinant protein production in a human cell	Crucell Holland, B.V.	Bout, Abraham|Hateboer, Guus|Verhulst, Karina Cornelia|Uytdehaag, Alphonsus Gerardus|Schouten, Govert Johan
US2003096415A1	Y	N	Y	Y	N	N	N		Infection with chimaeric adenoviruses of cells negative for the adenovirus serotype 5 Coxsacki adenovirus receptor (CAR)	CRUCELL HOLLAND B.V.	Havenga, Menzo|Vogels, Ronald
US2003099615A1	Y	Y	Y	N	N	N	N		Porcine adenovirus E1 and E4 regions	UNIVERSITY OF SASKATCHEWAN	Tikoo, Suresh K.

US2003099619A1	Y	Y	N	Y	N	N	N		Method and composition for targeting an adenoviral vector	GenVec, Inc.	Wickham, Thomas J.|Kovesdi, Imre|Roelvink, Petrus W.|Einfeld, David|Brough, Douglas E.|Lizonova, Alena
US2003100116A1	Y	N	N	N	N	N	N		Canine adenovirus vectors for the transfer of genes in targeted cells	GENETHON; INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE	Kremer, Eric|Chillon Rodriguez, Miguel|Soudais, Claire|Boutin, Sylvie|Peltekian, Elise|Garcia, Luis|Vincent, Nathalie|Danos, Olivier
US2003104625A1	Y	N	Y	N	N	N	N		Novel oncolytic adenoviral vectors	NOVARTIS PHARMA AG	Cheng, Cheng|Clarke, Lori|Connelly, Sheila|Ennist, David Leonard|Forry-Schaudies, Suzanne|Gorziglia, Mario|Hallenbeck, Paul L.|Hay, Carl M.|Jakubczak, John Leonard|Kaleko, Michael|Phipps, Sandrina|Police, Seshidhar Reddy|Ryan, Patricia Clare|Stewart, David A.|Xie, Yuefeng
US2003108521A1	Y	Y	N	Y	N	N	N		Adenovirus protein IX, its domains involved in capsid assembly, transcriptional activity and nuclear reorganization	UNITED THERAPEUTICS CORPORATION	Calatrava, Manuel Rosa
US2003133912A1	Y	N	N	Y	N	N	N		Receptor-targeted adenoviral vectors	UNIVERSITY OF IOWA RESEARCH FOUNDATION	Davidson, Beverly L.|Xia, Haibin|Law, Lane K.
US2003152914A1	N	Y	N	N	N	N	N		Method for generating replication defective viral vectors that are helper free	ROCKEFELLER UNIVERSITY	Kaplitt, Michael G.|Moussatov, Sergei

US2003157688A1	Y	Y	Y	Y	N	N	N		Adenovirus vectors, packaging cell lines, compositions, and methods for preparation and use	Scripps Research Institute	Von Seggern, Daniel J.|Nemerow, Glen R.|Hallenbeck, Paul|Stevenson, Susan|Skripchenko, Yelena
US2003215948A1	Y	Y	Y	Y	N	N	N		Fiber shaft modifications for efficient targeting	Scripps Research Institute|Novartis AG	Kaleko, Michael|Nemerow, Glen R.|Smith, Theodore|Stevenson, Susan C.
US2003219460A1	N	Y	N	N	N	N	N		Cotton rat lung cells for virus culture	MERIAL LIMITED	David, Frederic R.|Reddy, Sudhir K.|Tanner, Michael E.
US2003228327A1	Y	N	N	N	Y	Y	N	PRIME BOOST IS SIMULTANEOUS ADMINISTRATION	DNA-based plasmid formulations and vaccines and prophylactics containing the same	PICOSCRIPT LTD, LLP	Lasher, Alfred W.|Kittle, Joseph D.|Widen, Steven G.
US2004023389A1	Y	N	N	N	N	N	Y		Adenoviral vectors having nucleic acids encoding immunomodulatory molecules	GENZYME CORPORATION	Scaria, Abraham|Wadsworth, Samuel
US2004038205A1	N	N	N	Y	N	N	N		Modified adenoviral fiber and uses	TRANSGENE, S.A.	Van Raaij, Mark Johan|Cusack, Stephen|Legrand, Valerie|Leissner, Philippe|Mehtali, Majid
US2004106184A1	N	Y	N	N	N	N	N		Chromatographic methods for adenovirus purification	INTROGEN THERAPEUTICS INC.	Senesac, Joseph
US2004106194A1	Y	Y	Y	Y	Y	N	N		Methods for propagating adenovirus and virus produced thereby	Merck & Co., Inc.	Bett, Andrew J.|Chastain, Michael|Sandig, Volker|Emini, Emilio A.|Shiver, John W.|Casimiro, Danilo R.|Kaslow, David C.|Morsy, Manal

US2004136963A1	Y	Y	Y	N	N	N	N		Simian adenovirus vectors and methods of use	University of Pennsylvania	Wilson, James M.|Gao, Guangping|Roy, Soumitra
US2004191761A1	N	N	N	Y	Y	N	N		Modified adenoviral E1A constructs and methods of use thereof	NATIONAL JEWISH MEDICAL AND RESEARCH CENTER	Routes, John M.
US2004214162A1	Y	Y	N	N	Y	N	N		PAV regions for encapsidation and E1 transcriptional control	UNIVERSITY OF SASKATCHEWAN	Tikoo, Suresh K.
US2004219516A1	N	Y	N	N	N	N	N		Viral vectors containing recombination sites	Invitrogen Corporation	Bennett, Robert P.|Welch, Peter J.|Harwood, Steven|Madden, Knut|Frimpong, Kenneth|Franke, Kenneth E.
US2004229335A1	N	Y	N	N	N	N	N		Methods and compositions for the production of adenoviral vectors	Introgen Therapeutics, Inc.	Zhang, Shuyuan|Pham, Hai
US2004248827A1	Y	N	N	Y	Y	N	N		Hybrid adenoviral vector	National Institutes Of Health	Zheng, Changyu|Baum, Bruce J.
US2004253210A1	Y	Y	Y	N	Y	N	N		Adenovirus type7 vectors	National Institutes of Health	Robert-Guroff, Marjorie|Nan, Xinli|Peng, Bo|Hahn, Tae-Wook
US2005003545A1	N	Y	N	N	N	N	N		Adenovirus packaging cell lines	CELL GENESYS, INC.	Li, Yuanhao|Farson, Deborah|Tao, Luqun|Yu, DeChao
US2005019752A1	N	N	N	Y	Y	N	N		Novel chimeric rev, tat, and nef antigens	National Institutes of Health; AVENTIS PASTEUR	Franchini, Genoveffa|Hel, Zdenek|Tartaglia, James
US2005032039A1	N	N	N	N	Y	N	N		HIV-specific T-cell induction	UNIVERSITY OF TEXAS SYSTEM	Sastry, K. Jagannadha|Arlinghaus, Ralph B.|Nehete, Pramod N.

US2005106123A1	Y	N	N	N	Y	Y	N		Method of inducing an enhanced immune response against hiv	Merck & Co., Inc.	Emini; Emilio A|Shiver; John W|Chastain; Michael|Casimiro; Danilo R|Fu; Tong-Ming|Liang; Xiaoping
US2005123511A1	Y	Y	N	N	Y	N	N		Dna vaccine	UNIVERSITY OF LIVERPOOL	McCreavy; David Thomas|Fraser; William Duncan|Gallagher; James Anthony
US2005123898A1	N	Y	N	N	N	N	N		System for producing clonal or complex populations of recombinant adenoviruses, and the application of the same	DEVELOGEN AKTIENGESELLSCHAFT FÜR ENTWICKLUNGSBIOLOGISCHE FORSCHUNG	Hillgenberg; Moritz
US2005129713A1	Y	Y	N	N	Y	N	N		BAV packaging regions and E1 transcriptional control regions	UNIVERSITY OF SASKATCHEWAN	Tikoo; Suresh K.|Xing; Li
US2005153420A1	N	Y	N	N	N	N	N		Methods of adenovirus purification	MERCK AND CO., INC	Konz Jr.; John O.|Lee; Ann L|To; Chin Shung Brian|Goerke; Aaron R
US2005163753A1	Y	Y	Y	N	Y	N	N		Stable adenoviral vectors and methods for propagation thereof	Crucell Holland B.V.	Vogels; Ronald|Havenga; Menzo Jans Emco|Zuijdgeest; David Adrianus Theodorus Maria
US2005175627A1	Y	N	N	N	N	N	N		HIV pharmaccines	Oxxon Therapeutics Ltd.	Schneider; Joerg
US2005176129A1	Y	Y	Y	N	N	N	N		Adenovirus vector	Fuso Pharmaceutical Industries Ltd.; Hiroyuki Mizuguchi; Takao Hayakawa; Fuminori Sakurai	Mizuguchi; Hiroyuki|Hayakawa; Takao|Sakurai; Fuminori

US2005196384A1	Y	N	Y	N	Y	Y	N		Settings for recombinant adenoviral-based vaccines	Crucell Holland B.V.	Vogels; Ronald|Pau; Maria Grazia|Holterman; Lennart|Kostense; Stefan|Havenga; Menzo Jans Emco|Sprangers; Mieke Caroline
US2006051747A1	N	Y	N	N	N	N	N		Production of vaccines	Crucell Holland B.V.	Pau; Maria Grazia|Uytdehaag; Alphonsus Gerardus Cornelis Maria|Schouten; Govert Johan
US2006073123A1	Y	N	Y	N	N	N	N		Adenovirus vectors for immunotherapy	AVIOR THERAPEUTICS, INC.	Mi; Jie|Lieber; Andre
US2006115456A1	Y	Y	Y	N	Y	N	N		Replication-competent adenoviral vectors	The Government of the USA as represented by the Secretary of the Department of Health and Human|Istituto Superiore de Sanita	Peng; Bo|Voltan; Rebecca|Ensoli; Barbara|Robert-Guroff; Marjorie
US2006120995A1	N	N	N	N	N	N	Y		Neoadjuvant genetic compositions and methods	SAINT LOUIS UNIVERSITY	Shah; Maulik R.
US2006140908A1	Y	Y	N	N	Y	N	Y		Methods for inducing an immune response via oral administration of an adenovirus	WISTAR INSTITUTE	Ertl; Hildegund C. J.
US2006140920A1	Y	N	Y	N	N	N	N	AB VACCINE	Adenoviral vectors encoding an antibody fused to a CD4 extracellular domain	TRANSGENE S.A.	Leroy; Pierre|Mehtali; Majid
US2006142221A1	Y	N	N	Y	Y	Y	Y		Vaccine	GLAXO GROUP LIMITED	Ertl; Peter Franz
US2006153805A1	Y	N	N	N	Y	N	Y	TREATMENT	Viral vectors and the use of the same for gene therapy	UNIVERSITÄTSKLINIKUM HAMBURG-EPPENDORF	Walhler; Reinhard|Schnieders; Frank

US2006165664A1	Y	Y	Y	N	Y	Y	N		Method of inducing an enhanced immune response against hiv	MERCK & CO., INC.	Emini; Emilio A.|Shiver; John W|Casimiro; Danilo R|Bett; Andrew J|Liang; Xiaoping|Fu; Tong-Ming
US2006183232A1	N	Y	N	N	N	N	N		Packaging cells for recombinant adenovirus	CRUCELL HOLLAND B.V.	Vogels; Ronald|Havenga; Menzo Jans Emco|Zuijdgeest; David Adrianus Theodorus Maria
US2006211115A1	Y	Y	Y	Y	Y	Y	N		Methods of generating chimeric adenoviruses and uses for such chimeric aden oviruses	University of Pennsylvania	Roy; Soumitra|Wilson; James M.
US2006228334A1	N	Y	N	Y	N	N	N	CANCER	Modified adenoviral fiber with ablated to cellular receptors	TRANSGENE S.A.	Rosa-Calatrava; Manuel|Leissner; Philippe|Legrand; Valerie
US2006233756A1	Y	Y	Y	N	N	N	N		Recombinant adenoviral vectors and applications thereof	INSTITUT NATIONAL DE LA RECHERCHE AGRONOMIQUE; ECOLE NATIONALE VETERINAIRE D'ALFORT,	Eloit; Marc|Klonjkowski; Bernard
US2006270041A1	N	Y	N	N	N	N	N		Cell lines for production of replication-defective adenovirus	CANJI, INC.	Howe; John A.|Wills; Ken N.|Ralston II; Robert Orville|Sherrill; Scott Joseph
US2006275781A1	Y	Y	N	N	N	N	N		Novel method for the protection and purification of adenoviral vectors	INTROGEN THERAPEUTICS INC.	Pham; Hai|Zhang; Shuyuan|Clarke; Peter
US2006281073A1	Y	Y	Y	Y	N	N	N		Broadening adenovirus tropism	MERCK AND CO., INC	Monaci; Paolo|Fontana; Laura

US2006286121A1	Y	Y	Y	Y	Y	N	N		Adenoviral vector-based vaccines	GENVEC, INC.	Gall; Jason G. D.|Wickham; Thomas J.|Enright; William J.|Brough; Douglas E.|Zuber; Mohammed|King; C. Richter|Nabel; Gary J.|Cheng; Cheng
US2007003923A1	Y	Y	Y	Y	N	N	N		Modified fiber proteins for efficient receptor binding	SCRIPPS RESEARCH INSTITUTE; UNIVERSITY OF CALIFORNIA	Nemerow; Glen R.|Wu; Eugene|Stewart; Phoebe
US2007042977A1	Y	N	N	Y	Y	N	N		Vaccine	GLAXO GROUP LIMITED	Ertl; Peter Franz
US2007077226A1	Y	N	N	N	N	N	N		Gutless adenovirus vector and the construction method thereof	SHANGHAI INSTITUTES FOR BIOLOGICAL SCIENCES CHINESE ACADEMY OF SCIENCES	Liu; Xinyuan|Pei; Zifel|Li; Binghua|Gu; Jinfa|Zou; Weiguo|Sun; Lanying
US2007104732A1	Y	Y	Y	Y	Y	N	N		Ligand-pseudoreceptor system for generation of adenoviral vectors with altered tropism	NATIONAL RESEARCH COUNCIL OF CANADA	Massie; Bernard|Zeng; Yue|O'Connnor-McCourt; Maureen
US2007172949A9	Y	Y	N	N	N	N	N		Vectors and viral vectors, and packaging cell lines for propagating same	Enzo Therapeutics, Inc.,	Liu; Dakai|Rabbani; Elazar
US2007207461A1	N	Y	N	N	N	N	N		Virus Purification Methods	Crucell Holland B.V.	Weggeman; Miranda|Van Corven; Emile Joannes Josephus Maria
US2007249043A1	Y	N	N	N	N	N	N		Adenoviral expression vectors	CANJI, INC	Mayall; Timothy P.
US2007269410A1	Y	N	N	Y	Y	N	Y		Chimeric adenoviral vectors	West Coast Biologicals	Tucker; Sean N.

US2007298498A1	Y	Y	N	N	N	N	N		Adenoviral Amplicon and Producer Cells for the Production of Replication-Defective Adenoviral Vectors, Methods of Preparation and Use Thereof	MERCK AND CO., INC	Colloca; Stefano|Catalucci; Daniele
US2008003236A1	Y	Y	Y	Y	Y	N	N		ADENOVIRUS FIBER SHAFT COMPOSITION AND METHODS OF USE	GenVec, Inc.; National Institute of Health	King; C. Richter|Gall; Jason G. D.|Nabel; Gary J.|Cheng; Cheng
US2008063656A1	Y	N	Y	Y	Y	N	N		Adenoviral Vector Compositions	MERCK AND CO., INC	Emini; Emilio A.|Shiver; John W.|Casimiro; Danilo R.|Bett; Andrew J.
US2008069836A1	Y	N	Y	Y	Y	N	Y		METHOD OF USING ADENOVIRAL VECTORS WITH INCREASED IMMUNOGENICITY IN VIVO	GenVec, Inc.; National Institute of Health	Nabel; Gary J.|Cheng; Cheng|Gall; Jason G.D.|Wickham; Thomas J.
US2008089909A1	N	N	N	Y	N	N	N	CLADE	HIV-1 CLADE A CONSENSUS SEQUENCES, ANTIGENS, AND TRANSGENES	INTERNATIONAL AIDS VACCINE INITIATIVE	Gupta; Kalpana|Jackson; Nicholas
US2008112929A1	Y	N	N	Y	N	N	N		SHIELDED ADENOVIRAL VECTORS AND METHODS OF USE	VECTORLOGICS, INC.	Kovesdi; Imre|Hedley; Susan J.|Korokhov; Nikolay
US2008124322A1	Y	N	N	N	N	N	Y		Activation and inhibition of the immune system	THE MATHILDA AND TERENCE KENNEDY INSTITUTE OF RHEUMATOLOGY TRUST	Foxwell; Brian|Feldmann; Marc
US2008138362A1	N	Y	N	N	N	N	N		Cell Strain Capable of Being Cultured Without Ingredients Derived From Animals, Method of Producing the Same, Method of Producing Virus Using the Same, and Method of Producing Vaccine	NA	Mochizuki; Masami

US2008187557A1	Y	Y	N	N	N	N	N		Vaccine Against Pandemic Strains Of Influenza Viruses	US GOVERNMENT; PURDUE RESEARCH FOUNDATION	Sambhara; Suryaprakash|Katz; Jacqueline|Hoelscher; Mary|Mittal; Suresh K.|Bangari; Dinesh S.
US2008193484A1	Y	Y	N	N	Y	N	N		Novel Methods for Producing Adenoviral Vector Preparations with Reduced Replication-Competent Adenovirus Contamination and Novel Adenoviral Vectors and Preparations	Biogen Idec MA Inc.	Wang; Xinzhong|Kaynor; George C.|Barsoum; James
US2001006947A1	N	N	N	N	Y	N	N		METHODS OF ADMINISTERING ADENOVIRAL VECTORS	GENVEC, INC.	BRUDER, JOSEPH T.|KOVESDI, IMRE
US2002037280A1	Y	Y	N	N	N	N	N		Recombinant, modified adenoviral vectors for tumor specific gene expression and uses thereof	UNIVERSITY OF WASHINGTON	Lieber, Andre|Steinwaerder, Dirk S.|Carlson, Cheryl A.|Mi, Jie
US2002051966A1	Y	Y	N	N	N	N	N		Efficient generation of adenovirus-based libraries by positive selection of adenoviral recombinants through ectopic expression of the adenovirus protease	National Research Council of Canada	Massie, Bernard|Elahi, Seyyed Mehdy|Qualikene, Wahiba
US2002058045A1	Y	Y	N	Y	N	N	N		Adenovirus vector	National Institute of Health Sciences, JP	Mizuguchi, Hiroyuki|Hayakawa, Takao
US2002090717A1	Y	Y	N	N	N	N	N		Cell lines and constructs useful in production of E1-deleted adenoviruses in absence of replication competent adenovirus	University of Pennsylvania	Gao, Guangping|Wilson, James M.

US2002098165A1	Y	N	N	N	N	N	N		RECOMBINANT ADENOVIRUSES CONTAINING AN INDUCIBLE PROMOTER CONTROLLING A GENE OF VIRAL ORIGIN	Rhone-Poulenc S.A.	PERRICAUDET, MICHEL|LATTA, MARTINE|PROST, EDOUARD|YEH, PATRICE|ORSINI, CECILE|VIGNE, EMMANUELLE
US2002106746A1	Y	Y	N	N	N	N	N		Anti-inflammatory vectors	Transgene S.A.	Rooke, Ronald
US2002164353A1	Y	Y	Y	N	Y	N	N		Replication-defective adenovirus human type 5 recombinant as a vaccine carrier	University of Pennsylvania	Ertl, Hildegund C. J.|Wilson, James M.
US2002188103A1	Y	Y	N	Y	N	N	N		CHIMERIC DNA-BINDING/DNA METHYLTRANSFERASE NUCLEIC ACID AND POLYPEPTIDE AND USES THEREOF	BESTOR TIMOTHY H.	BESTOR, TIMOTHY H.
US2003118555A1	Y	Y	N	N	N	N	N		Target cell-specific adenoviral vectors containing E3 and methods of use thereof	CALYDON, INC.	Henderson, Daniel R.|Yu, De Chao
US2003130187A1	Y	Y	N	N	Y	N	N		Porcine adenovirus type 3 genome	UNIVERSITY OF SASKATCHEWAN	Reddy, Police Seshidhar|Tikoo, Suresh Kumar|Babiuk, Lorne A.
US2003175243A1	Y	Y	Y	N	Y	N	N		Modified adenoviral fiber and target adenoviruses	TRANSGENE S.A.	Legrand, Valerie|Mehtali, Majid|Boulanger, Pierre
US2003180258A1	Y	Y	Y	Y	N	N	N		Viral vectors having tissue tropism for T-lymphocytes, B- and mast cells	GALAPAGOS GENOMICS N.V.; CRUCELL HOLLAND B.V.,	van Es, Helmuth Hendrikus Gerardus|van Zutphen, Marlijn|Ma, Libin|Havenga, Menzo Jans Emko
US2003185801A1	N	Y	Y	N	N	N	N		Complementing cell lines	CRUCELL HOLLAND B.V.	Vogels, Ronald|Havenga, Menzo Jans Emco|Mehtali, Majid

US2003192066A1	Y	Y	N	N	Y	N	N		Minimal adenoviral vector	GenStar Therapeutics Corp.	Zhang, Wei-Wei|Alemany, Ramon|Dai, Yifan|Josephs, Steven|Balague, Cristina|Ayares, David|Schneiderman, Richard
US2003219410A1	Y	N	N	N	Y	N	N		Adenoviral vectors for modulating the cellular activities associated to PODs	TRANSGENE S.A.	Calatrava, Manuel Rosa
US2003228329A1	Y	Y	N	N	Y	Y	N		Adenovirus carrying gag gene HIV vaccine	Merck & Co., Inc.	Chen, Ling|Shiver, John W.|Bett, Andrew J.|Casimiro, Danilo R.|Caulfield, Michael J.|Chastain, Michael A.|Emini, Emilio A.
US2004002060A1	Y	N	Y	Y	N	N	N		Fiber shaft modifications for efficient targeting	Novartis AG; Scripps Research Institute	Kaleko, Michael|Nemerow, Glen R.|Smith, Theodore|Stevenson, Susan C.
US2004028653A1	Y	Y	N	N	N	N	N		Self-rearranging DNA vectors	General Hospital Corporation	Seed, Brian|Freeman, Mason Wright|Kovtun, Alexander|Murakawa, Masahiro|Park, Eun-Chung|Wang, Xinzhong
US2004038405A1	Y	Y	N	N	N	N	N		Vectors and viral vectors, and packaging cell lines for propagating same	Enzo Therapeutics, Inc.	Liu, Dakai|Rabbani, Elazar
US2004101957A1	Y	Y	N	N	Y	N	Y		Enhanced first generation adenovirus vaccines expressing codon optimized hiv1-gag, pol.nef and modifications	MERCK AND CO INC	Emini, Emilio A.|Youil, Rima|Bett, Andrew J.|Chen, Ling|Kaslow, David C.|Shiver, John W.|Toner, Timothy J.|Casimiro, Danilo R.

US2004106193A1	Y	Y	N	N	N	N	N		Novel adenoviral vector and methods for making and using the same	The Board of Trustees of the Leland Stanford Junior University; University of Washington	Kay, Mark A.|Mizuguchi, Hiroyuki
EP1000628A1	N	N	N	N	Y	N	Y		Use of antigenic complexes of HIV envelope and HLA class I antigens as HIV vaccine	Fondation Mondiale Recherche et Prevention SIDA	The designation of the inventor has not yet been filed
EP1054064A1	Y	Y	Y	Y	Y	N	N		Adenovirus derived gene delivery vehicles comprising at least one element of adenovirus type 35	Introgene B.V.	Bout, Abraham|Vogels, Ronald|Havenga, Menzo Jans Emco
EP1201761A1	Y	Y	N	N	N	N	N		METHOD OF CONSTRUCTING RECOMBINANT ADENOVIRUS VECTOR	Japan Science and Technology Corporation	MIYAZAKI, Junichi|TASHIRO, Fumi
EP1224310B1	N	Y	N	N	N	N	N		RECOMBINANT ADENOVIRUSES PREPARATION AND ADENOVIRUS BANKS	Aventis Pharma S.A.	Robert, Jean-Jacques
EP1785488A1	Y	N	Y	N	Y	N	N		Adenoviral vectors with two separate expression cassettes	Crucell Holland B.V.	Vogels, Ronald|Zuijdgeest, David A.T.M.
WO0004185A1	N	Y	N	N	N	N	N		ADENOVIRAL BASED PROMOTER ASSAY	MERCK & CO., INC.	RICHARDS, Karen|RUSHMORE, Thomas, H.|MORSY, Manal, A.
WO0011140A1	N	N	N	N	N	Y	Y		METHODS OF AUGMENTING MUCOSAL IMMUNITY THROUGH SYSTEMIC PRIMING AND MUCOSAL BOOSTING	THE WISTAR INSTITUTE OF ANATOMY AND BIOLOGY	ERTL, Hildegund, C., J.
WO0034494A1	Y	Y	N	N	N	N	Y		A RECOMBINANT VECTOR EXPRESSING MULTIPLE COSTIMULATORY MOLECULES AND USES THEREOF	THERION BIOLOGICS CORPORATION	SCHLOM, Jeffrey|HODGE, James|PANICALI, Dennis

WO0042208A1	Y	Y	N	N	N	N	N		ADENOVIRUS VECTORS, PACKAGING CELL LINES, COMPOSITIONS, AND METHODS FOR PREPARATION AND USE	SCRIPPS RESEARCH INSTITUTE; NOVARTIS AG|NOVARTIS-ERFINDUNGEN VERWALTUNGSGESELLSCHAFT M.B.H.	NEMEROW, Glen, Robert|VON SEGGERN, Daniel, J.|HALLENBECK, Paul, L.|STEVENSON, Susan, C.|SKRIPCHENKO, Yelena
WO0046360A1	Y	Y	Y	N	N	N	N		IMPROVED HELPER DEPENDENT VECTOR SYSTEM FOR GENE THERAPY	MERCK & CO., INC.	BETT, Andrew|SANDIG, Volker|YOUIL, Rima
WO0063403A2	N	Y	N	N	N	N	N		RECOMBINANT PROTEIN PRODUCTION IN A HUMAN CELL	INTROGENE B.V.	HATEBOER, Guus|VERHULST, Karina, Cornelia|SCHOUTEN, Govert, Johan|UYTDEHAAG, Alphonsus, Gerardus, Cornelis, Maria|BOUT, Abraham
WO0072887A1	Y	Y	N	N	N	N	N		A NOVEL PACKAGING CELL LINE FOR THE RESCUE, PRODUCTION AND TITRATION OF HIGH-CAPACITY ADENOVIRUS AMPLICON VECTORS	MOUNT SINAI SCHOOL OF MEDICINE	KROUGLIAK, Valeri, A.|EISENSMITH, Randy, C.
WO0073480A1	Y	Y	N	N	N	N	N		COMPOSITIONS AND METHODS FOR PRODUCTION OF RECOMBINANT VIRUS USING A CARRIER VECTOR DERIVED FROM A NONMAMMALIAN VIRUS	GENOVO, INCORPORATED	RASTY, Siyamak|GONDA, Matthew, A.|CHEN, Haifeng

WO0075353A1	Y	Y	N	N	N	N	N		COMPOSITIONS AND METHODS USEFUL FOR PRODUCTION OF RECOMBINANT VIRUSES WHICH REQUIRE HELPER VIRUSES	UNIVERSITY OF PENNSYLVANIA	XIAO, Weidong|WILSON, James, M.
WO0102548A2	N	Y	N	N	N	N	N		PROPAGATION METHOD	GLAXO GROUP LIMITED	FORD, Martin, James|HISSEY, Paul, Henry|PATEMAN, Tony, James
WO0115511A2	N	Y	N	N	N	N	N		IDENTIFICATION OF PEPTIDES THAT FACILITATE UPTAKE AND CYTOPLASMIC AND/OR NUCLEAR TRANSPORT OF PROTEINS, DNA AND VIRUSES	UNIVERSITY OF PITTSBURGH	ROBBINS, Paul, D.|MI, Zhibao|FRIZZELL, Raymond|GLORIOSO, Joseph, C.|GAMBOTTO, Andrea
WO0144280A2	Y	Y	N	N	N	N	N		METHODS AND COMPOSITIONS FOR THE MANUFACTURE OF REPLICATION INCOMPETENT ADENOVIRUS	GENOVO, INC.	HIMES, Vaughn, B.|RASTY, Siyamak|PELUSO, Richard, W.
WO0166137A1	N	Y	N	N	N	N	N		ADENOVIRUS FORMULATIONS	MERCK & CO., INC.	EVANS, Robert, K.|VOLKIN, David, B.
WO0181607A2	Y	Y	N	Y	N	N	N		ADENOVIRUS VECTORS WITH KNOBLESS FIBERS, AND THEIR USES	CRUCELL HOLLAND B.V.; VRIJE UNIVERSITEIT MEDISCH CENTRUM (VUMC)	VAN ES, Helmuth, Hendrikus, Gerardus|VAN BEUSECHEM, Victor, Willem
WO0198513A2	Y	Y	N	N	N	N	N		METHODS AND MEANS FOR THE COMPLEMENTATION OF VIRAL PROTEIN EXPRESSION IN STABLE CELL LINES	VERENIGING VOOR CHRISTELIJK WETENSCHAPPELIJK ONDERWIJS	VAN BEUSECHEM, Victor, Willem|GERRITSEN, Willem-Ronald

WO0231170A1	Y	Y	Y	N	N	N	N		METHOD FOR CIRCULARIZING ADENOVIRAL NUCLEIC ACID VIA HOMOLOGOUS RECOMBINATION	MERCK & CO., INC.	YOUIL, Rima
WO0232943A2	Y	Y	N	N	Y	Y	N		MODIFICATIONS OF HIV ENV, GAG, AND POL ENHANCE IMMUNOGENICITY FOR GENETIC IMMUNIZATION	US GOVERNMENT; CHADRABARTI	NABEL, Gary, J.|HUANG, Yue
WO0240693A1	Y	Y	Y	N	N	N	N		ADENOVIRAL REPLICONS	CRUCELL HOLLAND B.V.	HAVENGA, Menzo, Jans, Emco|BRUS, Ronald, Hendrik, Peter
WO04027073A1	Y	Y	Y	Y	Y	Y	N		MODIFIED ADENOVIRAL VECTORS FOR USE IN VACCINES AND GENE THERAPY	CRUCELL HOLLAND B.V.	KOSTENSE, Stefan|OPHORST, Olga, Johanna, Alberdina, Elisa|HAVENGA, Menzo, Jans, Emco
WO04044155A2	N	N	N	N	Y	Y	N		MIP-1α AND GM-CSF AS ADJUVANTS OF IMMUNE RESPONSE	BETH ISRAEL DEACONESS MEDICAL CENTER	MCKAY, Paul|BAROUCH, Dan|LETVIN, Norman
WO05027835A2	Y	N	Y	N	Y	N	N		THERAPEUTIC IMMUNIZATION OF HIV-INFECTED INDIVIDUALS	MERCK & CO., INC.	EMINI, Emilio, A.|SHIVER, John, W.|CASIMIRO, Danilo, R.|HAZUDA, Daria|SCHLEIF, William, A.

WO05027840A2	Y	N	N	N	Y	N	N		COMBINATION APPROACHES FOR GENERATING IMMUNE RESPONSES	CHIRON CORPORATION; NATIONAL INSTITUTES OF HEALTH; NATIONAL CANCER INSTITUTE	BARNETT, Susan, W.|GÓMEZ-ROMÁN, Victor, Raúl c/o National Institutes of Health, National Cancer Institute|LIAN, Ying|PENG, Bo c/o National Institutes of Health, National Cancer Institute|ROBERT-GUROFF, Marjorie c/o National Institutes of Health, National Cancer Institute|SRIVASTAVA, Indresh, K.
WO05071093A2	Y	Y	Y	N	Y	Y	N		CHIMPANZEE ADENOVIRUS VACCINE CARRIERS	ISTITUTO DI RICERCHE DI BIOLOGIA MOLECOLARE P ANGELETTI SPA	CIRILLO, Agostino|COLLOCA, Stefano|ERCOLE, Bruno, Bruni|MEOLA, Annalisa|NICOSIA, Alfredo|SPORENO, Elisabetta
WO05075506A1	Y	Y	Y	N	N	N	N		IDENTIFICATION OF ENDOGENOUS TRIMERIZATION DOMAINS IN THE ADENOVIRUS FIBER PROTEIN THAT ALLOW DETARGETING AND RETARGETING OF VIRAL VECTORS	SCRIPPS RESEARCH INSTITUTE	NEMEROW, Glen, R.|LI, Erguang
WO05086658A3	N	Y	N	N	N	N	N		PROCESSES FOR ADENOVIRUS PURIFICATION USING CONTINUOUS FLOW CENTRIFUGATION	ALFA WASSERMANN, INC.	FORRESTER, Kathy

WO05094415A2	Y	N	N	N	Y	N	N		RECOMBINANT VECTORS AND METHODS FOR INDUCING AN IMMUNE RESPONSE	WISTAR INSTITUTE	HENSLEY, Scott, E.|ERTL, Hildegund, C., J.
WO06033672A2	N	N	Y	N	Y	Y	N		IMMUNIZATION REGIMEN WITH E4-DELETED ADENOVIRUS PRIME AND E1-DELETED ADENOVIRUS BOOST	UNIVERSITY OF PENNSYLVANIA	WILSON, James, M.|ZHI, Yan
WO06086284A2	Y	Y	Y	N	Y	Y	N		ADENOVIRUS SEROTYPE 26 VECTORS, NUCLEIC ACID AND VIRUSES PRODUCED THEREBY	MERCK & CO., INC.	BETT, Andrew, J.|CASIMIRO, Danilo, R.|SHIVER, John, W.|EMINI, Emilio, A.|CHASTAIN, Michael|KASLOW, David, C.
WO06086357A2	Y	Y	Y	N	Y	Y	N		ADENOVIRUS SEROTYPE 36 VECTORS, NUCLEIC ACID AND VIRUSES PRODUCED THEREBY	MERCK & CO., INC.	BETT, Andrew, J.|CASIMIRO, Danilo, R.|SHIVER, John, W.|EMINI, Emilio, A.|CHASTAIN, Michael|KASLOW, David, C.
WO06108707A1	N	Y	N	N	N	N	N		VIRUS PURIFICATION USING ULTRAFILTRATION	CRUCELL HOLLAND B.V.	WEGGEMAN, Miranda
WO06120034A1	Y	Y	Y	N	Y	N	N		VACCINE COMPOSITION	GLAXO GROUP LIMITED	ERTL, Peter, Franz|TITE, John, Philip|VAN WELY, Catherine Ann
WO9516772A1	Y	Y	N	N	N	N	N		ADENOVIRUS GENE EXPRESSION SYSTEM	CORNELL RESEARCH FOUNDATION, INC.	FALCK-PEDERSEN, Erik, S.
WO9524485A2	Y	N	N	Y	N	N	N		COORDINATE IN VIVO GENE EXPRESSION	MERCK & CO., INC.	LIU, Margaret, A.|SHIVER, John, W.|PERRY, Helen, C.

WO9622378A1	N	Y	N	N	N	N	N		CELLS FOR THE PRODUCTION OF RECOMBINANT ADENOVIRUSES	Aventis SA	DEDIEU, Jean-François|LATTA, Martine|ORSINI, Cécile|PERRICAUDET, Michel|VIGNE, Emmanuelle|YEH, Patrice
WO9731115A2	N	N	N	Y	N	N	N		SYNTHETIC HIV GENES	MERCK & CO., INC.	SHIVER, John, W.|DAVIES, Mary-Ellen|FREED, Daniel, C.|LIU, Margaret, A.|PERRY, Helen, C.
WO9738723A1	Y	N	N	N	N	N	N		TARGETED VIRAL VECTORS	IMMUSOL INCORPORATED	MAMOUNAS, Michael|YU, Gang|YANG, Qicheng|LI, Qi-Xiang|BARBER, Jack|YU, Mang
WO9909194A1	Y	N	N	N	N	N	N		RECOMBINANT CELO AVIAN ADENOVIRUS AND USE AS VACCINATING VECTOR	CENTRE NATIONAL D'ETUDES VETERINAIRES ET ALIMENTAIRES	LANGLOIS, Patrick
WO9916466A2	N	N	N	N	N	N	Y		VACCINE COMPOSITIONS AND METHODS OF ENHANCING VACCINE EFFICACY	BETH ISRAEL DEACONESS MEDICAL CENTER	LETVIN, Norman, L.|BAROUCH, Dan, H.
WO9954441A1	N	Y	N	N	N	N	N		EFFICIENT PURIFICATION OF ADENOVIRUS	GENVEC, INC.	CARRIÓN, Miguel, E.|MENGER, Marilyn|KOVESDI, Imre
WO9955894A1	Y	Y	N	N	N	N	N		CONSTRUCTION OF RETROVIRAL PRODUCER CELLS FROM ADENOVIRAL AND RETROVIRAL VECTORS	OKLAHOMA MEDICAL RESEARCH FOUNDATION	LIN, Xinli|TANG, Jordan, J., N.
WO9964577A1	Y	Y	N	N	N	N	N		NOVEL ADENOVIRAL VECTORS FOR GENE THERAPY	MERCK & CO., INC.	MORSY, Manal, A.|SANDIG, Volker

WO07059473A2	N	Y	N	N	N	N	N		METHODS FOR THE PRODUCTION AND PURIFICATION OF ADENOVIRAL VECTORS	INTROGEN THERAPEUTICS, INC.	ZHANG, Shuyuan|PHAM, Hai|SONG, Ping|CLARKE, Peter
WO07071997A2	N	N	Y	N	Y	Y	Y		METHOD OF ELICITING IMMUNE RESPONSE	GLAXO GROUP LIMITED	BARBER, Karen, A|BAXTER, Gillian, Margaret|BRETT, Sara, Jane|HAMBLIN, Paul, Andrew|TITE, John, Philip|VIDALIN, Olivier
WO07094653A1	N	Y	N	Y	N	N	N		ADENOVIRUS PARTICLES HAVING A CHIMERIC ADENOVIRUS SPIKE PROTEIN, USE THEREOF AND METHODS FOR PRODUCING SUCH PARTICLES.	VERENIGING VOOR CHRISTELIJK HO; VAN BEUSECHEM VICTOR WILLEM; SCHAGEN FREDERIK HUBERTUS EMAN	VAN BEUSECHEM, Victor, Willem|SCHAGEN, Frederik, Hubertus, Emanuel
WO07104792A2	Y	Y	Y	N	Y	N	N		RECOMBINANT ADENOVIRUSES BASED ON SEROTYPE 26 AND 48, AND USE THEREOF	CRUCELL HOLLAND B.V.; BETH ISRAEL DEACONESS MEDICAL CENTER INC.	BAROUCH, Dan H.|HAVENGA, Menzo Jans Emko
WO07136763A2	N	N	N	N	Y	Y	N		IMMUNOLOGICAL COMPOSITION	SANOFI PASTEUR, INC.	TARTAGLIA, James|PANTALEO, Guiseppe|HARARI, Alexandri
WO28025015A2	N	N	N	N	Y	Y	Y		EPITOPE-TRANSPLANT SCAFFOLDS AND THEIR USE	US GOVERNMENT; UNIVERSITY OF WASHINGTON	KWONG, Peter|OFEK, Gilad|GUENAGA, Javier|WYATT, Richard, T.|YANG, Zhi-yong|ZHOU, Tongqing|NABEL, Gary|TANG, Min|SCHIEF, William|BAKER, David

WO03084479A2	N	Y	N	N	N	N	N		LARGE SCALE METHODS OF PRODUCING ADENOVIRUS AND ADENOVIRUS SEED STOCKS	MERCK & CO., INC.	ZHOU, Weichang|XIE, Liangzhi|ALTARAS, Nedim Emil|AUNINS, John, G.
US2002168342A1	Y	Y	N	N	N	N	N		Novel adenoviral vectors, packaging cell lines, recombinant adenoviruses and methods	Cell Genesys, Inc.	Wang, Qing|Finer, Mitchell H.|Jia, Xiao-Chi
US2002182723A1	N	Y	N	N	N	N	N		AN IMPROVED METHOD FOR THE PRODUCTION AND PURIFICATION OF ADENOVIRAL VECTORS	Introgen Therapeutics, Inc.	Zhang, Shuyuan|Thwin, Capucine|Wu, Zheng|Cho, Toohyon|Gallagher, Shawn
US2003017597A1	Y	N	N	N	N	N	N		Hybrid vectors for gene therapy	University of California	Kasahara, Noriyuki|Higo, Collin|Soifer, Harris|Mitani, Kohnosuke
US2003054555A1	Y	Y	N	N	N	N	N		Site specific recombinase based method for producing adenoviral vectors	Becton Dickinson	Farmer, Andrew Alan|Quinn, Thomas Patrick
US2003073072A1	Y	N	Y	Y	N	N	N		Chimeric adenoviruses	Crucell Holland B.V.,	Havenga, Menzo|Vogels, Ronald|Bout, Abraham
US2003092161A1	N	Y	N	N	N	N	N		Compositions and methods for production of recombinant viruses, and uses therefor	University of Pennsylvania	Gao, Guangping|Wilson, James M.|Alvira, Mauricio R.
US2003096787A1	Y	Y	N	N	Y	N	N		Defective adenovirus vectors and use thereof in gene therapy	CENTELION	Perricaudet, Michel|Vigne, Emmanuelle|Yeh, Patrice
US2003138459A1	N	N	Y	N	Y	Y	N		Method of vaccination through serotype rotation	Genphar, Inc.	Wang, Danher
US2003143200A1	Y	Y	N	N	N	N	N		Porcine adenovirus E1 region	University of Saskatchewan	Tikoo, Suresh K.
US2003148520A1	Y	Y	N	N	N	N	N		Cell-specific adenovirus vectors comprising an internal ribosome entry site	CELL GENESYS, INC.	Yu, De-Chao|Li, Yuanhao|Little, Andrew S.|Henderson, Daniel R.

US5712136	Y	N	N	Y	N	N	N		Adenoviral-mediated cell targeting commanded by the adenovirus penton base protein	GenVec, Inc.	Wickham; Thomas J.|Kovesdi; Imre|Roelvink; Petrus W.|Brough; Douglas E.|McVey; Duncan L.|Bruder; Joseph T.
US5846546	Y	N	N	N	Y	Y	Y		Preparation and use of viral vectors for mixed envelope protein immunogenic composition against human immunodeficiency viruses	St. Jude Children's Research Hospital	Hurwitz; Julia|Slobod; Karen
US5981225	Y	Y	N	N	N	N	N		Gene transfer vector, recombinant adenovirus particles containing the same, method for producing the same and method of use of the same	Baylor College of Medicine	Kochanek; Stefan|Schiedner; Gudrun
US5994106	Y	Y	N	N	N	N	N		Stocks of recombinant, replication-deficient adenovirus free of replication-competent adenovirus	GenVec, Inc.	Kovesdi; Imre|Brough; Douglas E.|McVey; Duncan L.|Bruder; Joseph T.|Lizonova; Alena
US6066478	Y	Y	Y	N	N	N	N		Helper viruses for preparing recombinant viral vectors	Transgene S.A.	Lusky; Monika|Mehtali; Majid
US6110735	N	Y	Y	N	N	N	N		Method for the preparation of a viral vector by intermolecular homologous recombination	Transgene, S.A.	Chartier; Cecile|Degryse; Eric
US6140087	Y	Y	N	N	N	N	N		Adenovirus vectors for gene therapy	AdVec, Inc.	Graham; Frank L.|Bett; Andrew|Prevec; Ludvik|Haddara; Wael M.
US6200798	Y	N	Y	N	N	N	N		Defective recombinant adenoviruses with inactivated IVa2 gene	Rhone-Poulenc Rorer SA	Yeh; Patrice|Perricaudet; Michel|Orsini; Cecile|Vigne; Emmanuelle
US6204060	Y	Y	Y	N	N	N	N		Viral vectors and line for gene therapy	Transgene S.A.	Mehtali; Majid|Lusky; Monika|Rittner; Karola

US6211160	N	N	N	N	Y	N	N		Method for tolerizing a mammalian patient to administration of gene therapy virus vectors	University of Pennsylvania	Wilson; James M.|Chen; Youhai
US6225113	Y	N	N	Y	N	N	N		Use of trans-activation and cis-activation to modulate the persistence of expression of a transgene in an at least E4-deficient adenovirus	GenVec, Inc.	Brough; Douglas E.|Kovesdi; Imre
US6228646	Y	Y	N	N	N	N	N		Helper-free, totally defective adenovirus for gene therapy	University of California	Hardy; Stephen F.
US6232120	N	N	N	N	Y	N	Y		Methods to inhibit replication of infective virus	Johns Hopkins University School of Medicine	Dropulic; Boro|Pitha; Paula M.
US6312946	Y	N	Y	N	N	N	N		Viable contaminant particle free adenoviruses, their prepartion and use	Rhone-Poulenc Rorer S.A.	Yeh; Patrice|Perricaudet; Michel|Orsini; Cecile
US6821512	Y	Y	N	N	N	N	N		Compositions and methods for increasing packaging and yield of recombinant adenoviruses using multiple packaging signals	University of Pennsylvania	Gao; Guangping|Wilson; James M.
US6824770	Y	N	N	N	N	N	N		Adenovirus gene expression system	Cornell Research Foundation, Inc.	Falck-Pedersen; Erik S.
US6841540	Y	N	N	Y	N	N	N		Immunomodulation by genetic modification of dendritic cells and B cells	UAB Research Foundation	Curiel; David T.|Tillman; Bryan Walter
US6867022	Y	Y	N	N	N	N	N		Replication deficient adenovirus vectors and methods of making and using them	University of Michigan	Imperiale; Michael J.
US6905678	Y	N	Y	Y	N	N	N		Gene delivery vectors with cell type specificity for mesenchymal stem cells	Crucell Holland B.V.	Havenga; Menzo Jans Emco|Bout; Abraham|Vogels; Ronald

US6995010	Y	N	N	N	N	N	N		Gene transfer method	Takara Bio Inc.	Ueno; Takashi|Matsumura; Hajime|Tanaka; Keiji|Iwasaki; Tomoko|Ueno; Mitsuhiro|Fujinaga; Kei|Asada; Kiyozo|Kato; Ikunoshin
US7232899	Y	Y	N	N	N	N	N		Adenovirus vectors, packaging cell lines, compositions, and methods for preparation and use	Scripps Research Institute	Von Seggern; Daniel J.|Nemerow; Glen R.
US7264958	N	Y	N	N	N	N	N		Method for obtaining a purified viral preparation	Transgene, S.A.	Koehl; Michel|Gaillac; David
US7285265	Y	N	Y	N	Y	N	Y		Stable adenoviral vectors and methods for propagation thereof	Crucell Holland B.V.	Vogels; Ronald|Havenga; Menzo Jans Emco|Zuijdgeest; David Adrianus Theodorus Maria
US7326555	N	Y	N	N	N	N	N		Methods of adenovirus purification	Merck & Co., Inc.	Konz, Jr.; John O.|Lee; Ann L.|To; Chi Shung Brian|Goerke; Aaron R
US7410954	N	N	N	Y	N	N	N		Adenovirus serotype 30 (Ad30)	University of Iowa Research Foundation	Davidson; Beverly L.|Law; Lane K.
US2004170647A1	N	N	Y	N	Y	N	N		Recombinant adenovirus vaccines	Wyeth	Davis, Alan R.|Lubeck, Michael D.|Natuk, Robert J.|Chanda, Pranab K.|Murthy, Shridhara C. S.|Lee, Shaw-Guang L.|Hung, Paul P.
US2004185555A1	Y	Y	Y	N	Y	Y	N		Adenovirus serotype 24 vectors, nucleic acids and virus produced thereby	Merck & Co., Inc.	Emini, Emilio A.|Shiver, John W.|Bett, Andrew J.|Casimiro, Danilo R.|Chastain, Michael|Kaslow, David C.|Morsy, Manal
US2004234549A1	Y	N	N	N	N	N	N		Novel recombinant and mutant adenoviruses	Schering-Plough Veterinary Corporation	Chiang, Christina H.|Cochran, Mark D.

US2004241181A1	Y	N	N	N	Y	N	N		Methods of inducing a cytotoxic immune response and recombinant simian adenovirus compositions useful therein	WISTAR INSTITUTE OF ANATOMY AND BIOLOGY; University of Pennsylvania	Ertl, Hildeghund C. J.|Wilson, James M.
US2005079158A1	Y	N	N	N	N	N	N		Construct of anti-cancer recombinant adenovirus, method for preparing the same and use thereof	Shenzhen Allucks BioTech Co., Ltd.	Zhou; Jianfeng|Ma; Ding|Lu; Yunping|Wang; Shixuan|Chen; Gang|Gao; Qinglei
US2005100558A1	Y	N	N	N	N	Y	N		Heterologous boosting immunizations	US Government	Chamberlain; Ronald S.|Irvine; Kari R.|Rosenberg; Steven A.|Restifo; Nicholas P.
US2005158283A1	N	Y	N	N	N	N	N		Methods and compositions for the production of adenoviral vectors	INTROGEN THERAPEUTICS, INC.,	Zhang; Shuyuan|Pham; Hai
US2006019393A1	N	N	N	Y	N	N	N		Minimal lentiviral vector system	LOS ANGELES CHILDRENS HOSPITAL	Cannon; Paula M.|Ngiam; Celina
US2006057113A1	Y	N	N	N	N	N	N		Novel adenoviruses, nucleic acids coding therefor, and use thereof	Holm, Per Sonne	Holm; Per Sonne
US2006063259A1	Y	Y	N	N	N	N	N		Production of adenovirus vectors with reduced levels of replication competent adenovirus contamination	AdVec, Inc.	Graham; Frank L.
US2006216272A1	N	N	N	N	Y	N	N		Therapeutic immunization of hiv-infected individuals	MERCK AND CO., INC	Emini; Emilio A.|Shiver; John W.|Casimiro; Danilo R.|Hazuda; Daria|Scheilf; William A.
US2006269572A1	Y	N	N	N	Y	N	N		Accelerated vaccination	US GOVERNMENT	Nabel; Gary J.|Sullivan; Nancy J.|Geisbert; Thomas W.|Jahrling; Peter B.

US2007231303A1	N	Y	Y	Y	N	N	N		METHODS OF GENERATING CHIMERIC ADENOVIRUSES AND USES FOR SUCH CHIMERIC ADENOVIRUSES	University of Pennsylvania	Roy; Soumitra|Wilson; James M.
US2007248679A1	Y	N	N	Y	Y	Y	Y		VACCINE	Glaxo Group Limited	ERTL; PETER Franz

4. Patent Search Analytics

After the coding period, we analyzed the 267 relevent patents using commercial analytic tools. The final step was to produce refined analytics using Microsoft Excel.

4.1 Search Analysis through MicroPatent, Aureka®, Patent Insight Pro®

After the coding period, we analyzed the 267 patents which we found relevant using the analytic tools of MicroPatent®, Aureka® and Patent Insight Pro®.

4.1.1 MicroPatent® Results

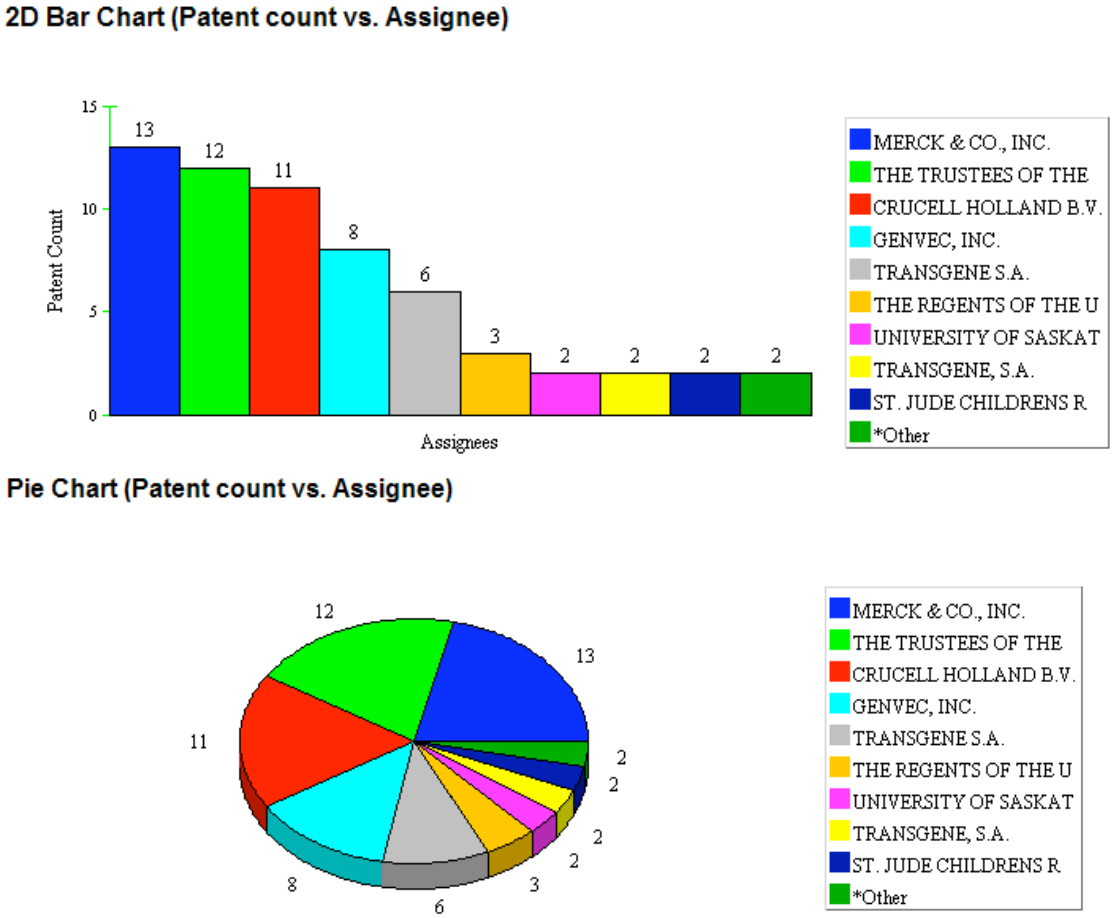
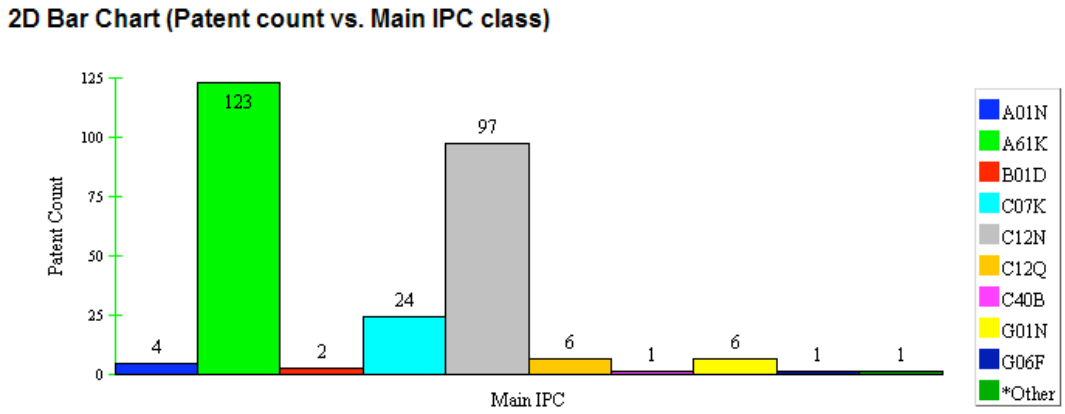


Figure 1: Patent count versus Assignees: the top three assignees for adenovirus vaccine related patents are Merck, University of Pennsylvania and Crucell Holland. Those three encompasses about 50% of the patents.

According to Figure 1, Merck, University of Pennsylvania and Crucell Holland occupies about 50% of the adenovirus vaccine related patents. This suggests that these companies are powerhouses in research and development projects addressing adenoviral vaccine technology for HIV.



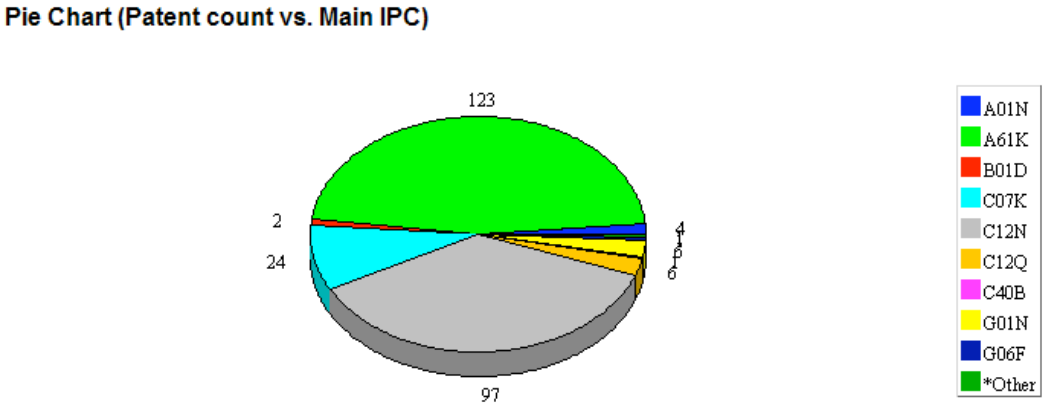


Figure 2: Patent count versus main IPC class: the top two IPC classes for adenovirus vaccine technology are A61K and C12N.

According to Figure 2, the most frequently cited international classifications include A61K and C12N.

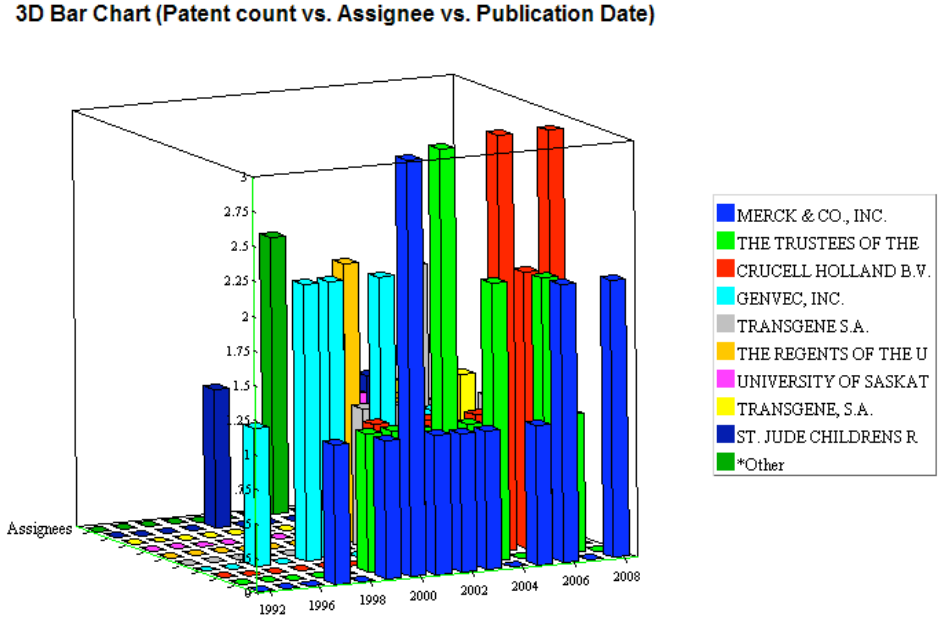


Figure 3: Patent count versus assignee versus publication date:

According to Figure 3, GenVec started to file the patents related to adenovirus vaccine from 1996.

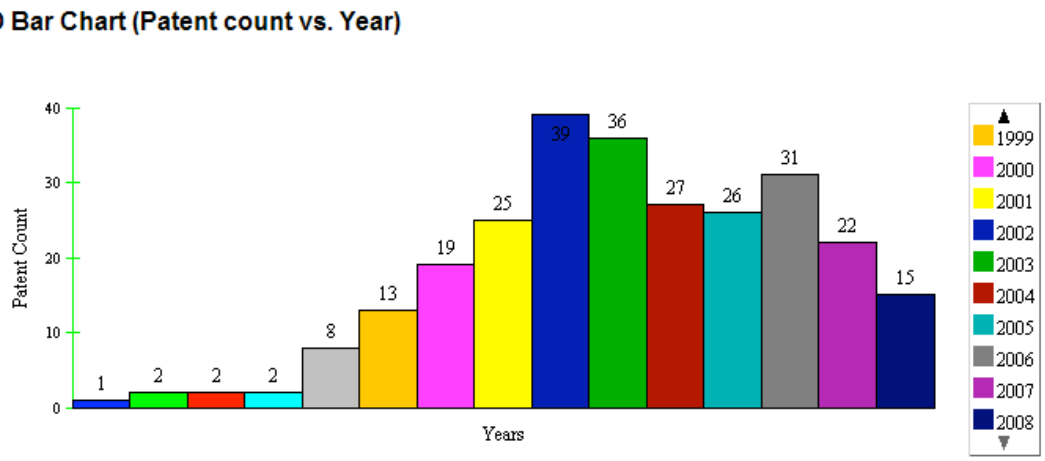


Figure 4: Patent count versus publication year

According to Figure 4, the number of adenovirus vaccine related patents has increased upto 2002 and has been decreased slightly after 2002.

4.1.2 Aureka® ThemeMap® Results

By using Aureka®, we generated Preliminary Aureka Thememaps for HIV Adenoviral Vaccine Landscapes. Thememaps were generated from the 267 relevant patent documents, using language from either the claims or the title and abstract as the data foundation. Maps therefore represent a very broad view of the representative technologies which are embodied in the entire patent landscape. As such, these thememaps provide an overview of potentially applicable technologies. For example, from the Claims Map, it appears that a larger proportion of technologies are in the area of cell packaging and purification. In addition, the relative proximity of the packaging and vaccine peaks suggests possible co-development of these approaches as a strategy for securing a broad spectrum of patent rights.



Figure 5 : Thememap based on the languages from the patent **claims** in the 267 relevant patents



Figure 6 : Thememap based on the languages from the patent **title** and **abstract** in the 267 relevant patents

4.1.3 Patent Insight Pro® Results

By using Patent Insight Pro®, we could understand the Filing Trend of the adenoviral HIV vaccine technology. As we saw the Publication Trend in the Figure 4, patent filing number of adenoviral HIV vaccine also has increased upto 2002 and has been decreased slightly after 2002.

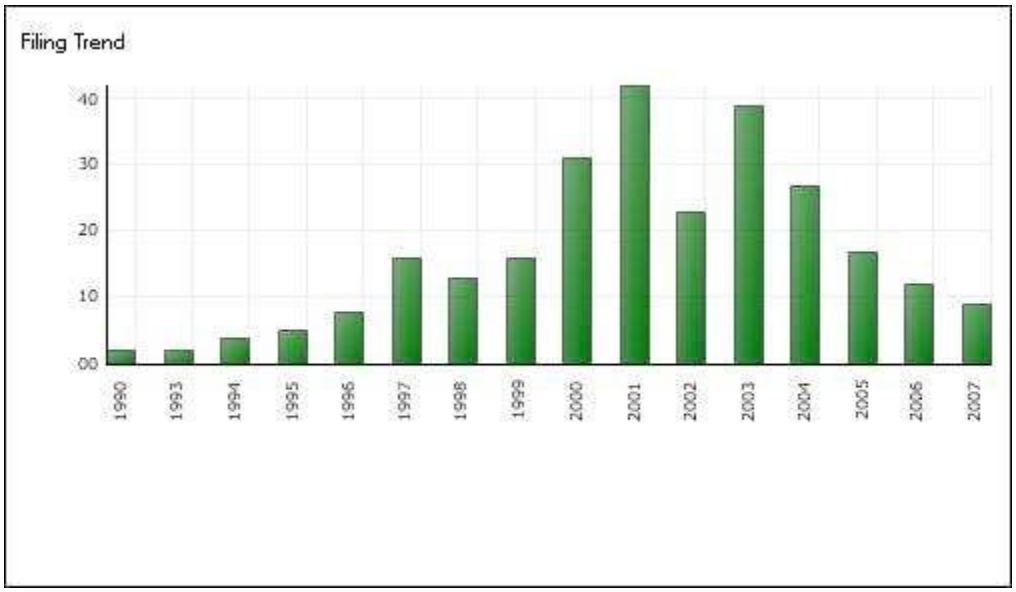


Figure 7: Patent count versus filing year

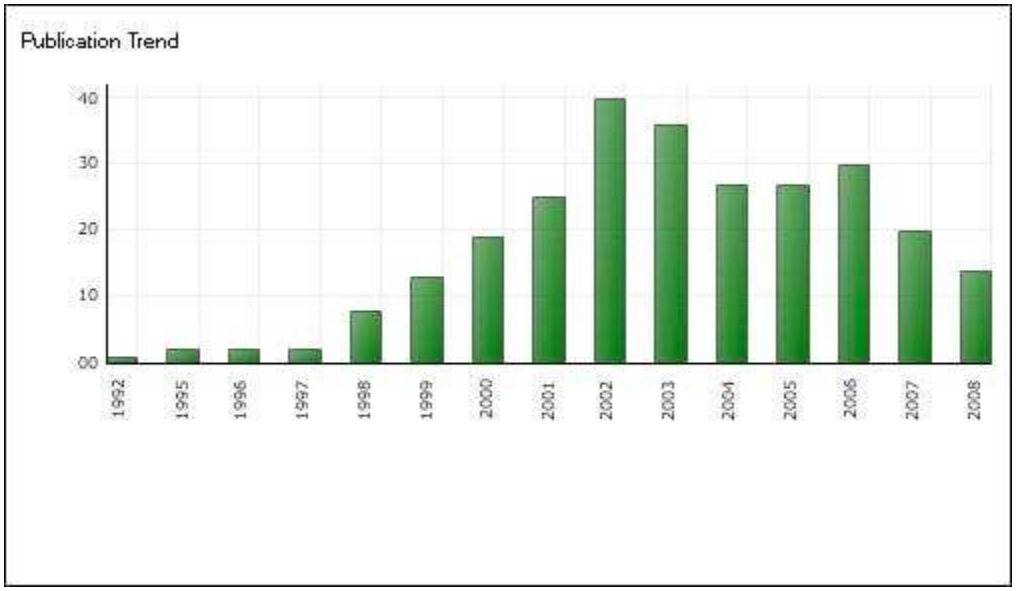


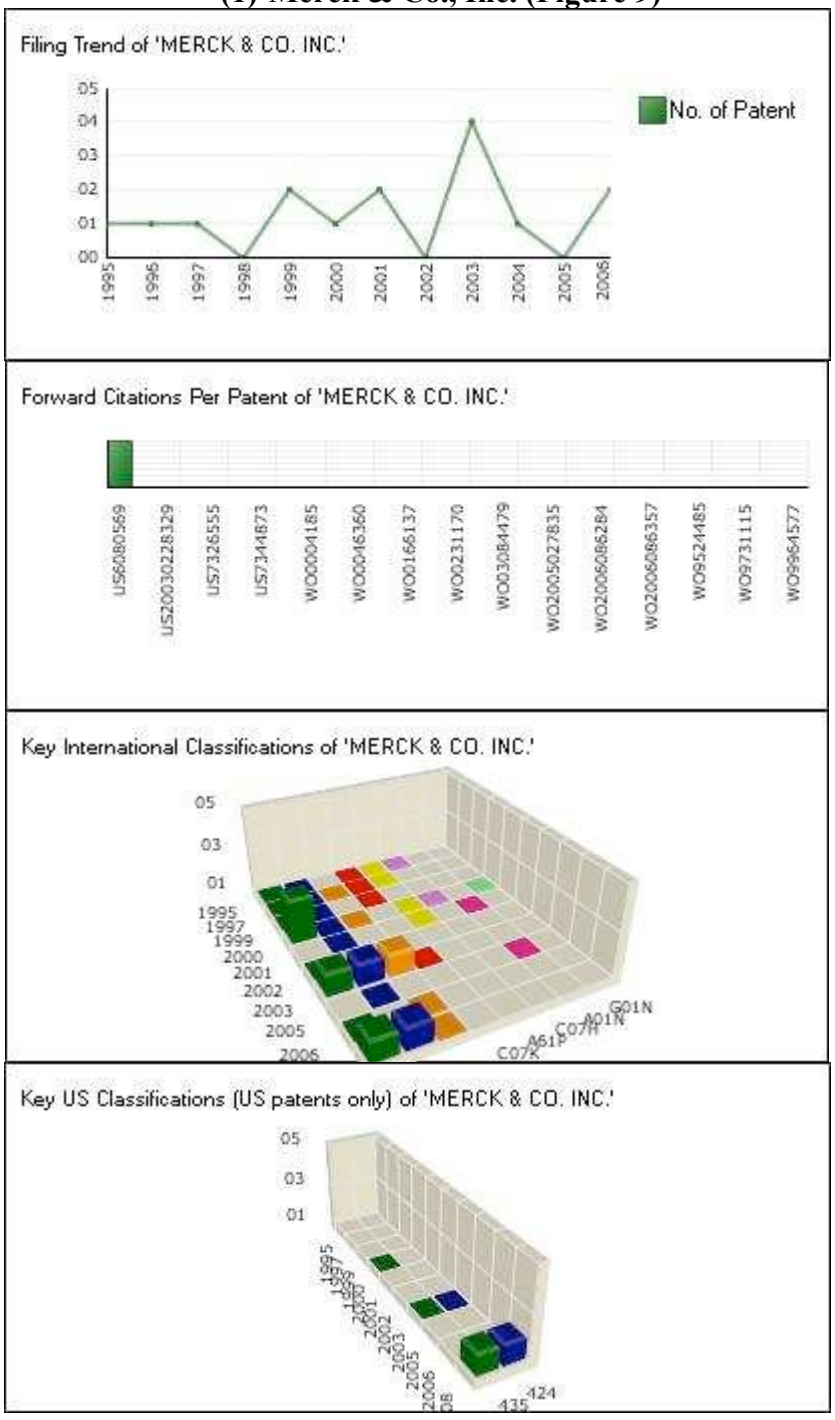
Figure 8: Patent count versus publication year

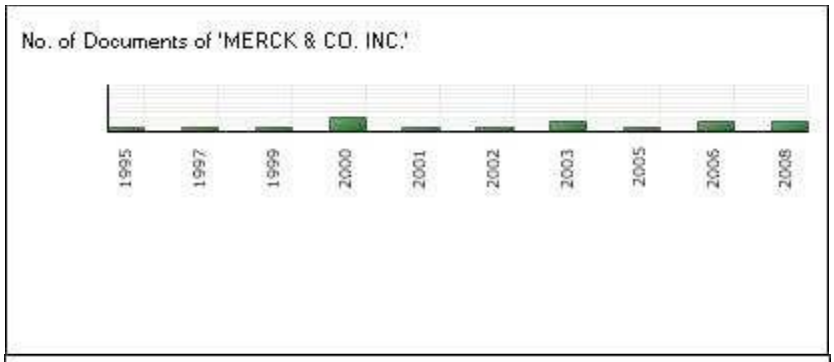
We were able to generate several valuable datas from Patent Insight Pro® for each top 5 assinee (Merck, Crucell, Transgene, U Penn, GenVec) including Filing trend, Forward citations, Key IPC, Publication trend and Prolific inventors. We were also able to generate Collaborating

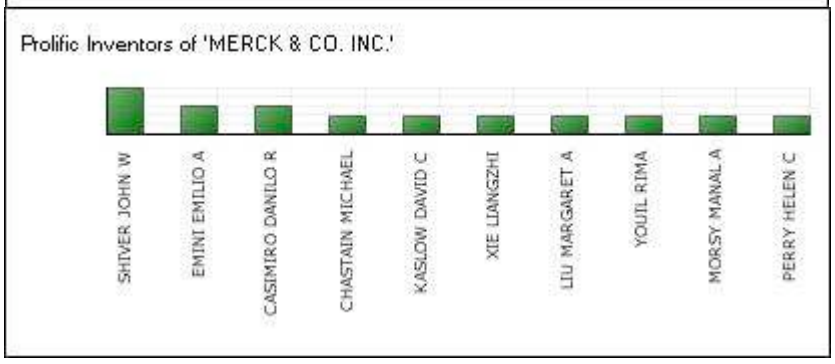
inventors, Key IPC, Key US classification and Publication trend for each top 5 inventor (Shiver, Wilson, Vogels, Casimiro, Emini).

4.1.3.1 Top 5 Assignees

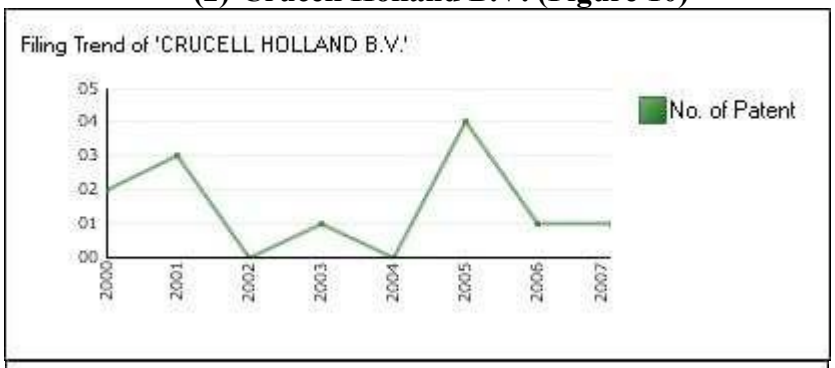
(1) Merck & Co., Inc. (Figure 9)

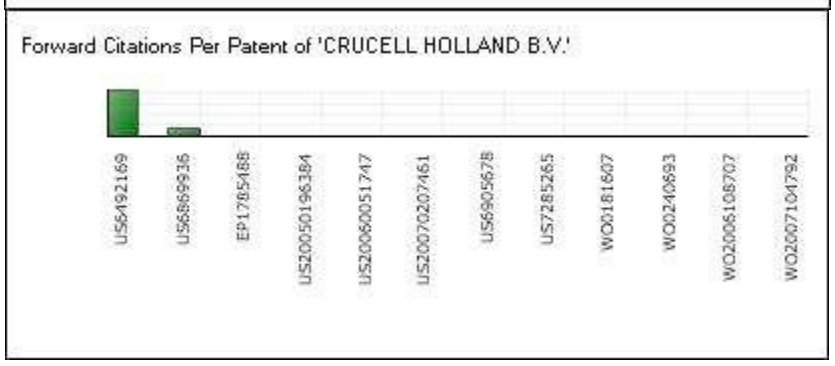




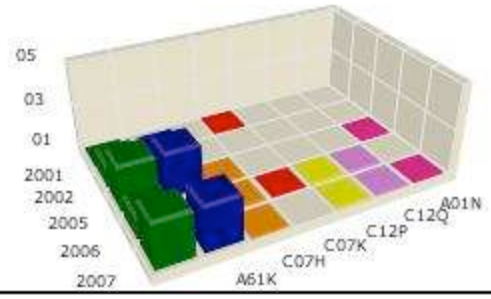


(2) Crucell Holland B.V. (Figure 10)

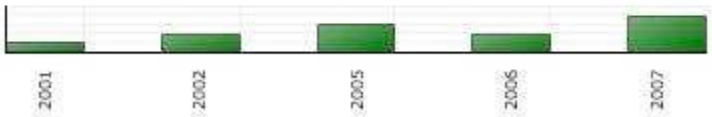




Key International Classifications of 'CRUCELL HOLLAND B.V.'



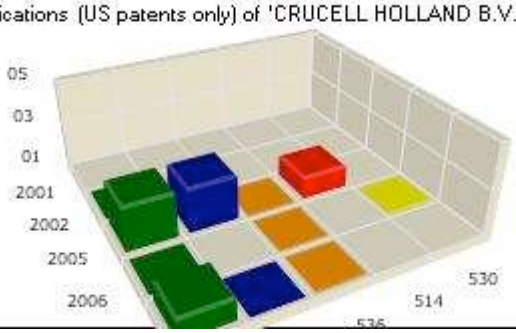
No. of Documents of 'CRUCELL HOLLAND B.V.'



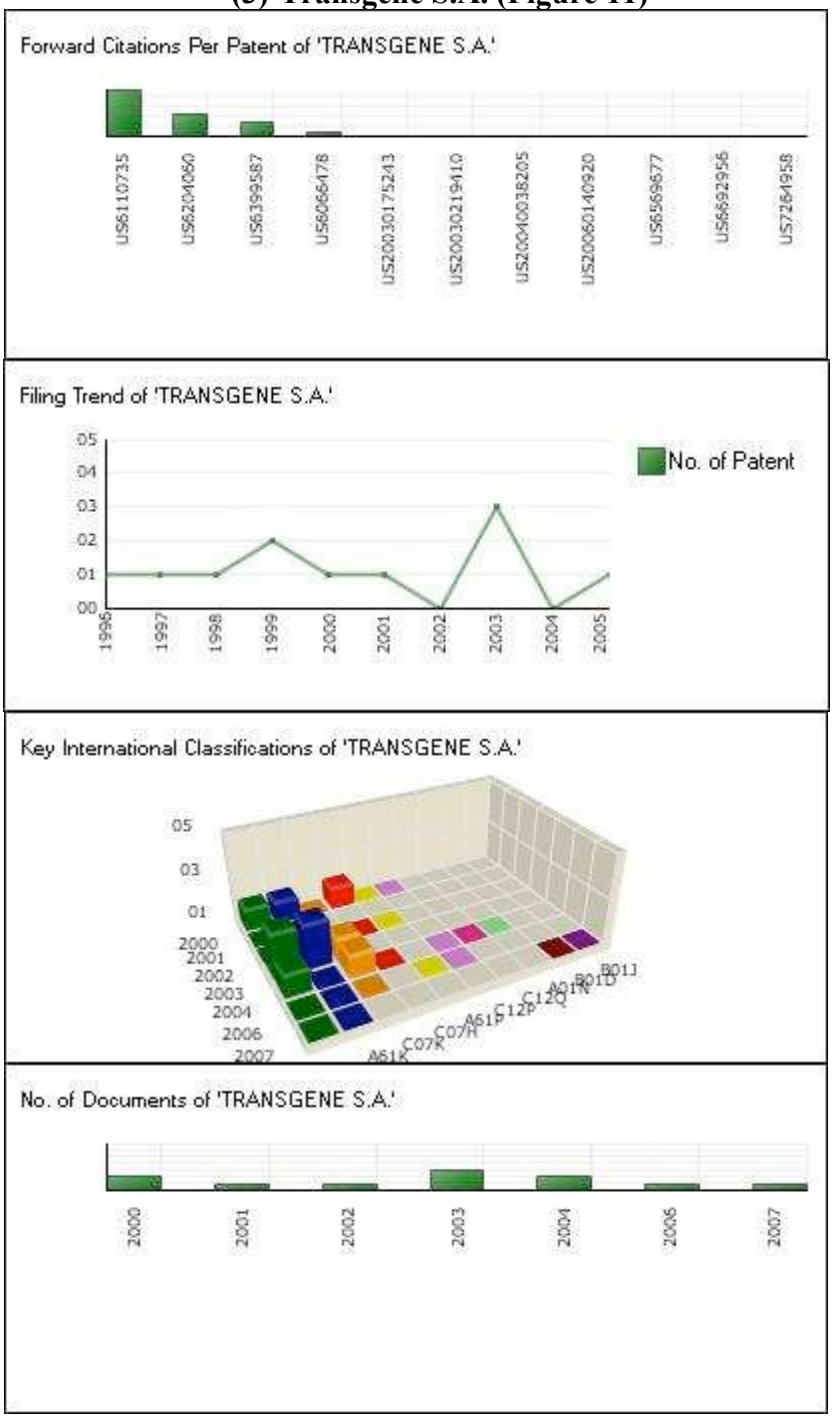
Prolific Inventors of 'CRUCELL HOLLAND B.V.'

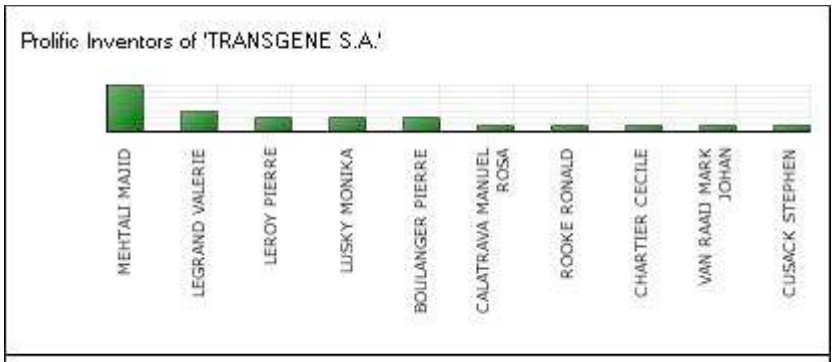


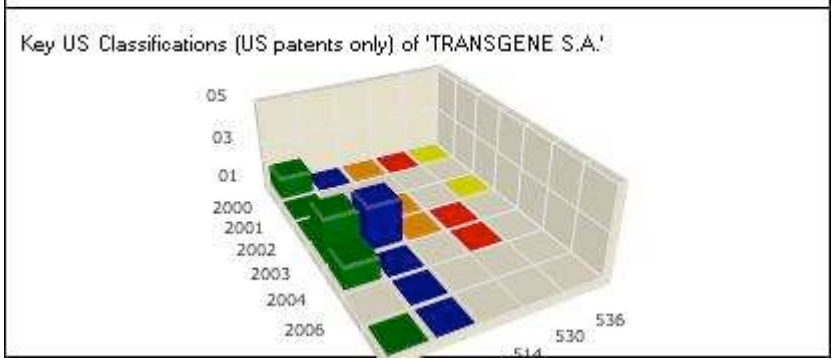
Key US Classifications (US patents only) of 'CRUCELL HOLLAND B.V.'



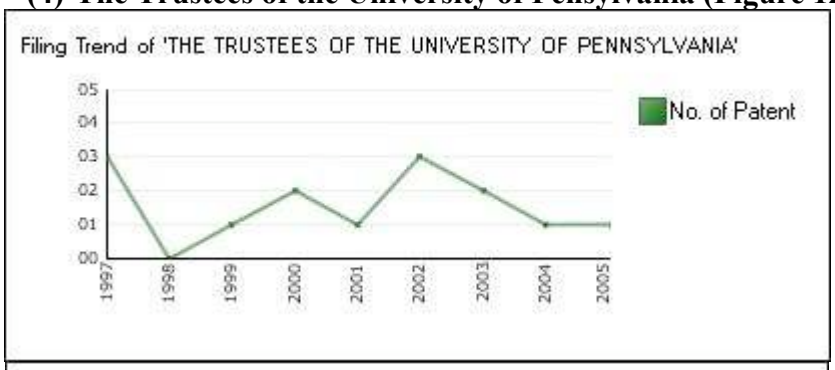
(3) Transgene S.A. (Figure 11)

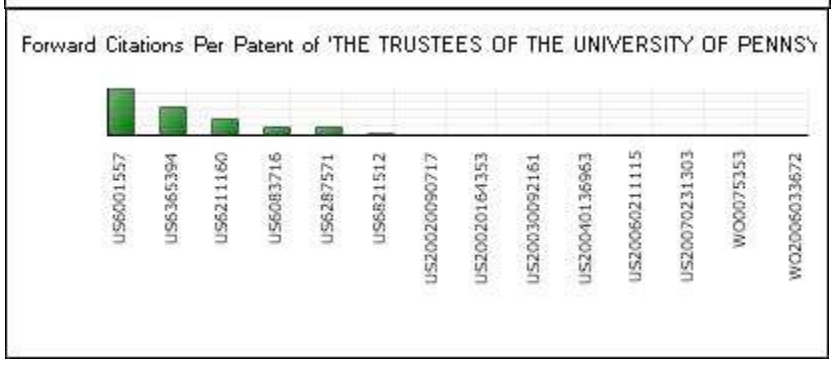


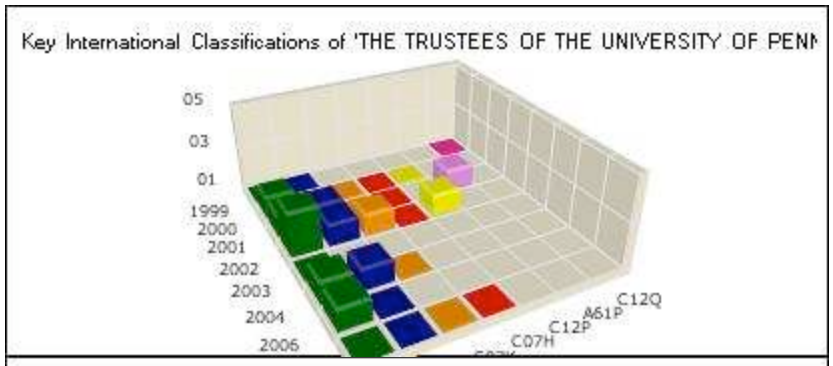




(4) The Trustees of the University of Pensylvania (Figure 12)






Key International Classifications of 'THE TRUSTEES OF THE UNIVERSITY OF PENN
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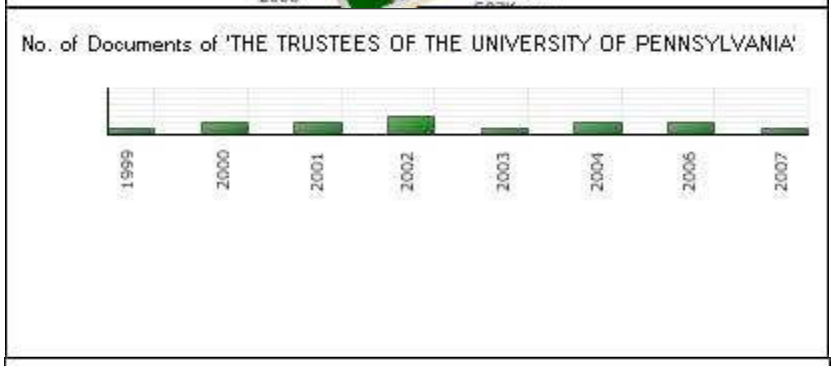
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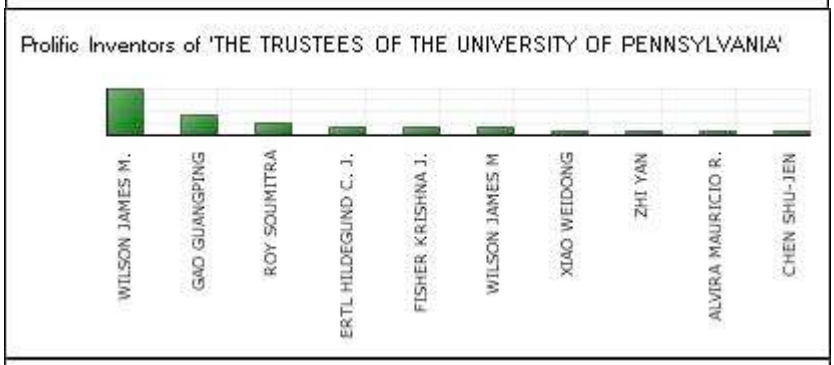
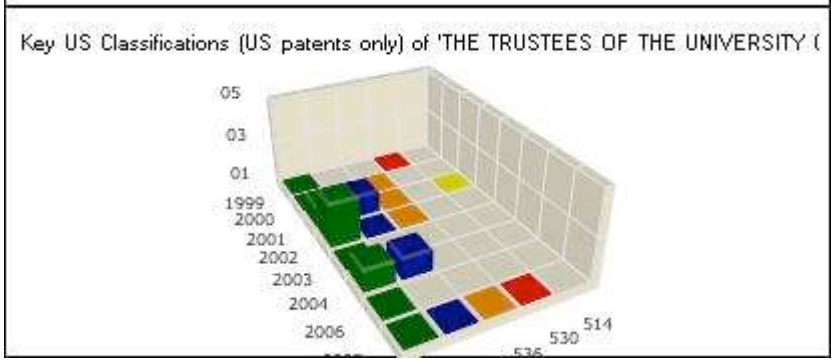

Prolific Inventors of 'THE TRUSTEES OF THE UNIVERSITY OF PENNSYLVANIA'
WILSON JAMES M.
GAO GUANGPING
ROY SOUMITRA
ERTL HILDEGUND C. J.
FISHER KRISHNA J.
WILSON JAMES M
XIAO WEIDONG
ZHI YAN
ALVIRA MAURICIO R.
CHEN SHU-JEN


Key US Classifications (US patents only) of 'THE TRUSTEES OF THE UNIVERSITY (
05
03
01
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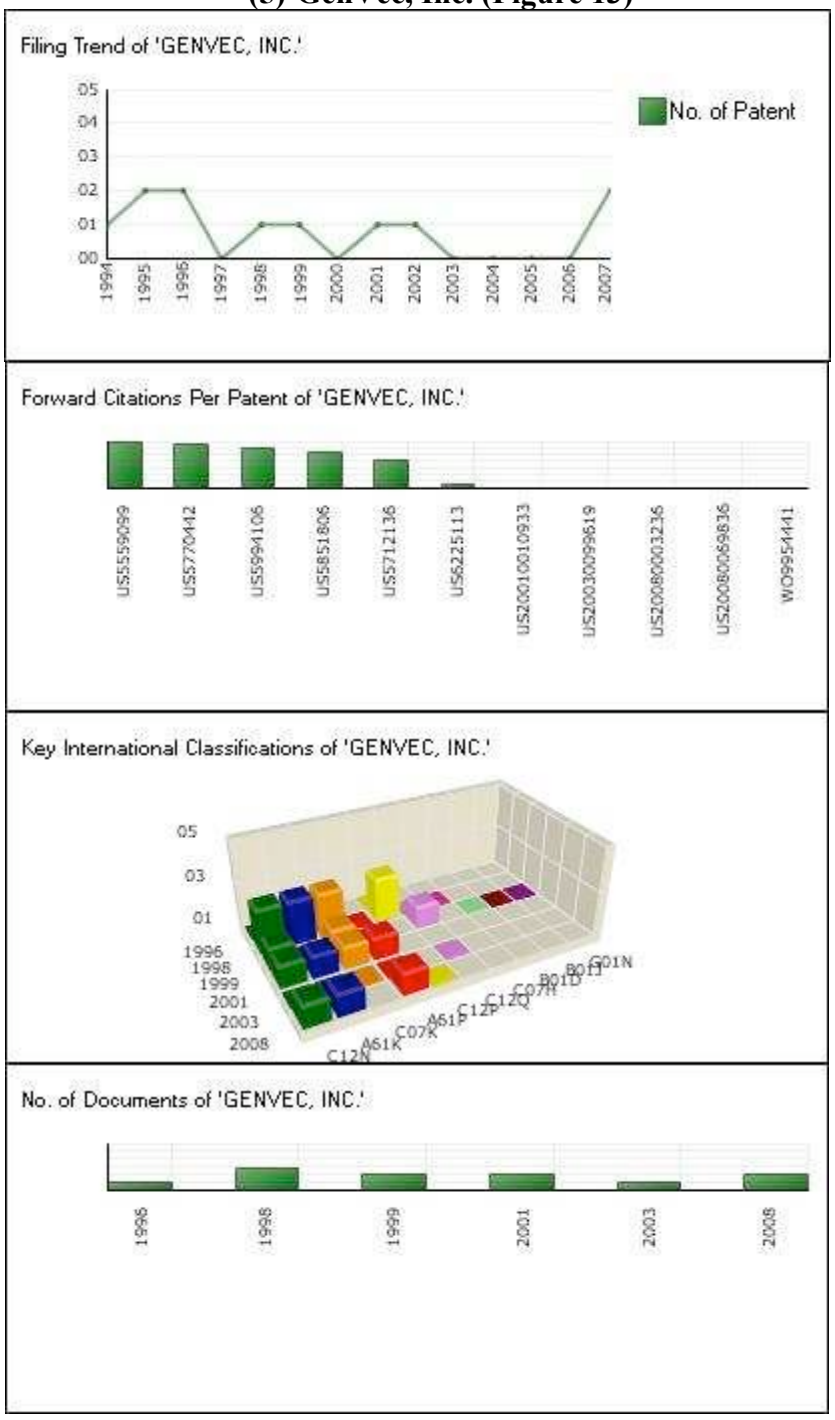
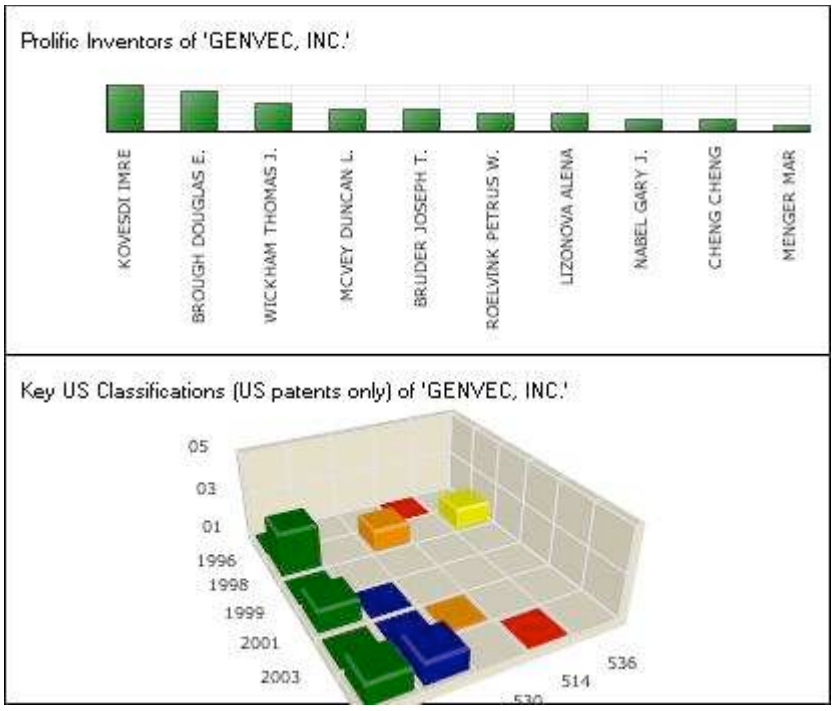
2000
2001
2002
2003
2004
2006
514
530

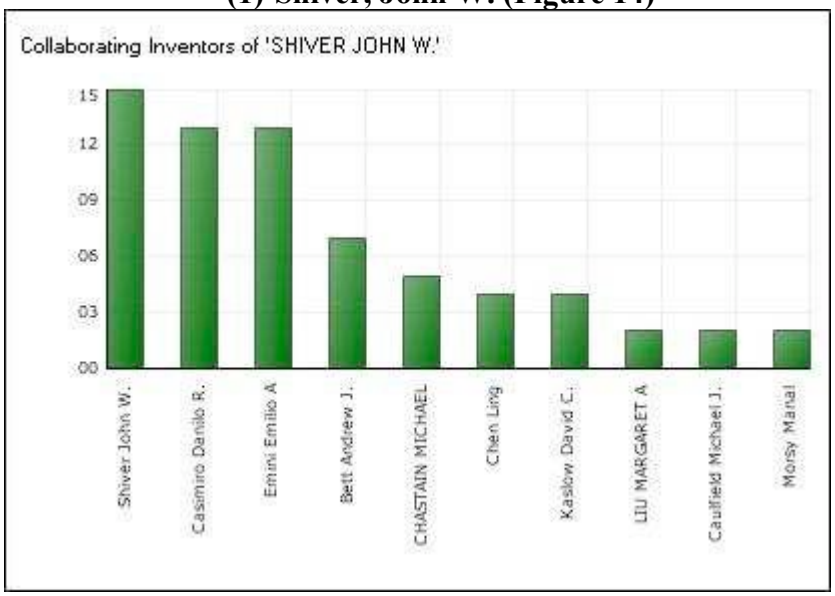
(5) GenVec, Inc. (Figure 13)



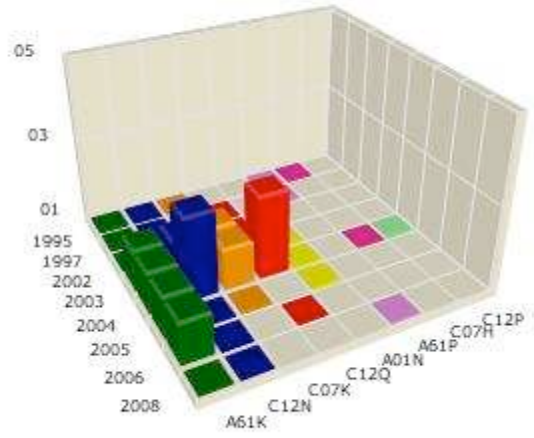


4.1.3.2 Top 5 Inventors

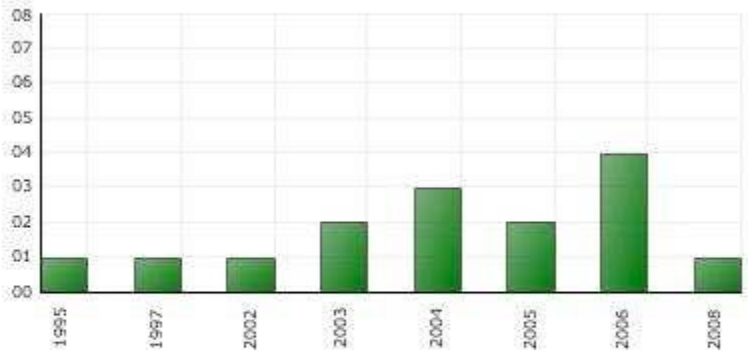
(1) Shiver, John W. (Figure 14)



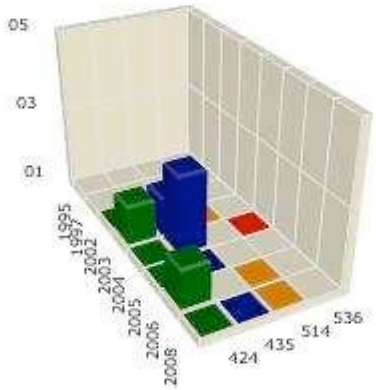
Key International Classifications of 'SHIVER JOHN W.'



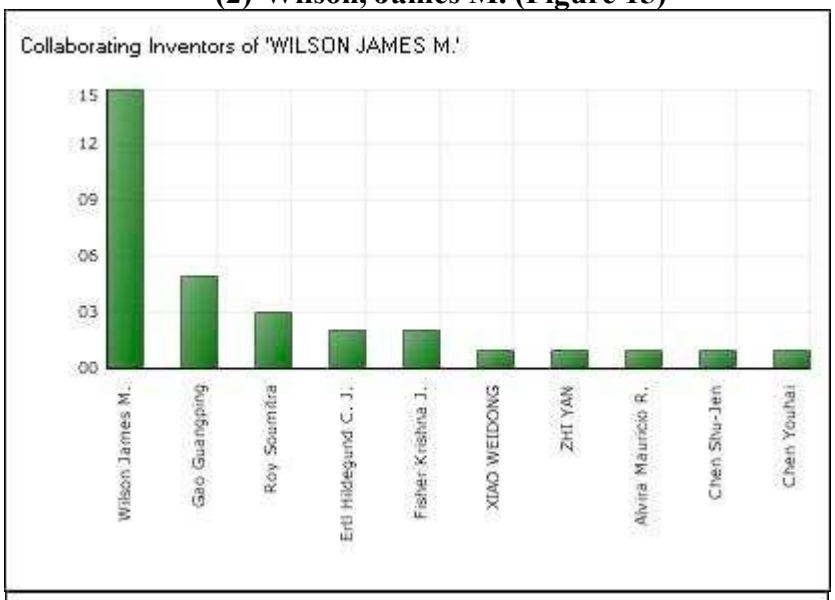
No. of Documents of 'SHIVER JOHN W.'

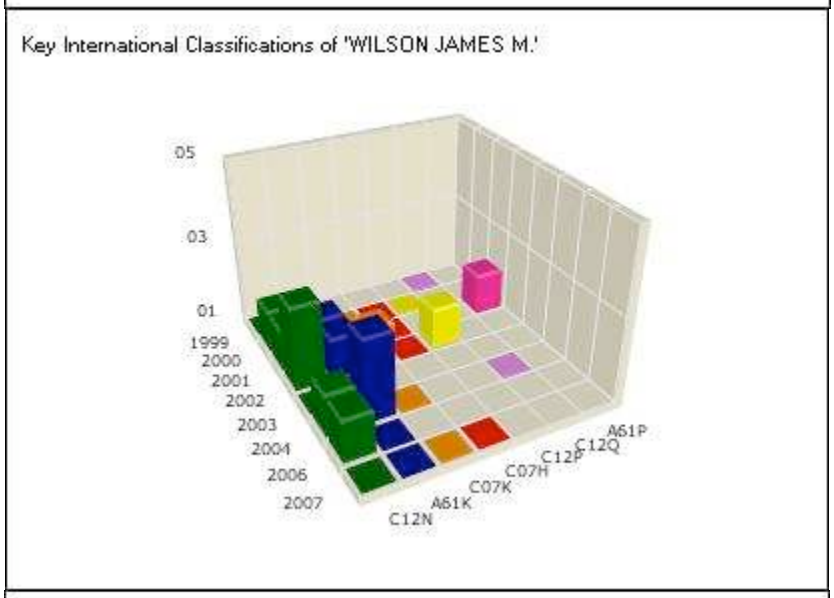


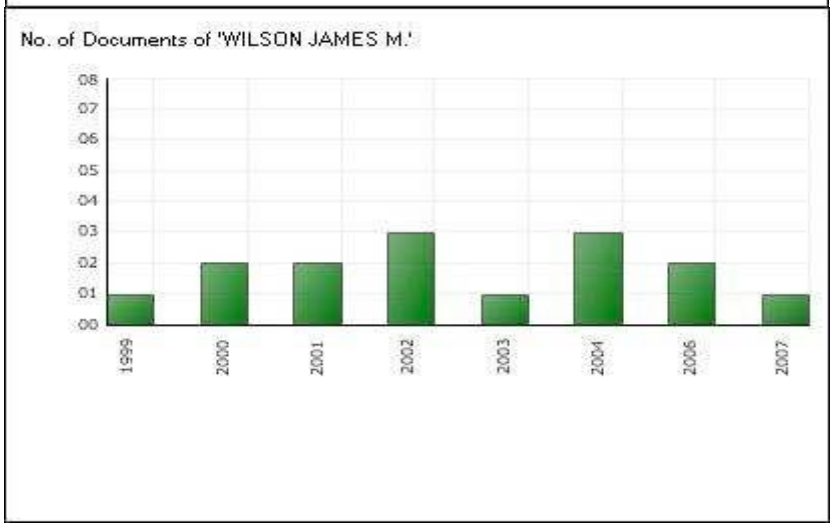
Key US Classifications (US patents only) of 'SHIVER JOHN W.'

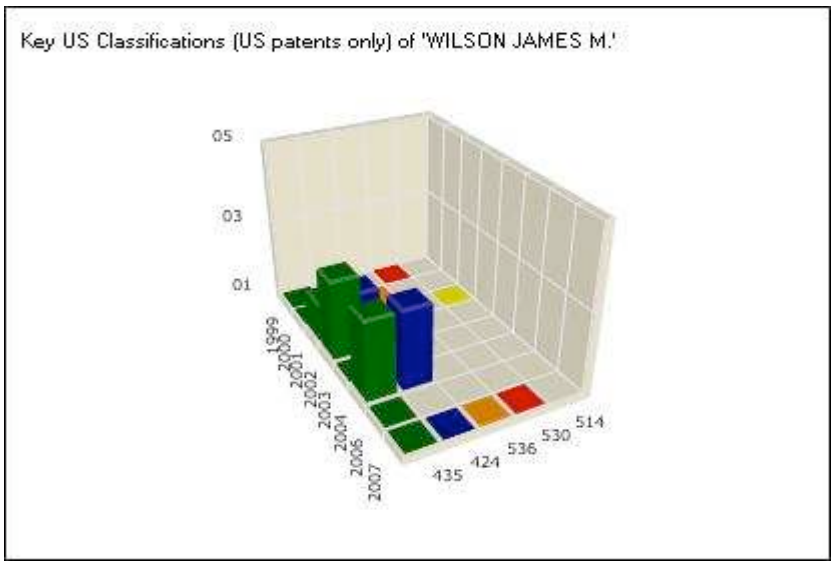


(2) Wilson, James M. (Figure 15)

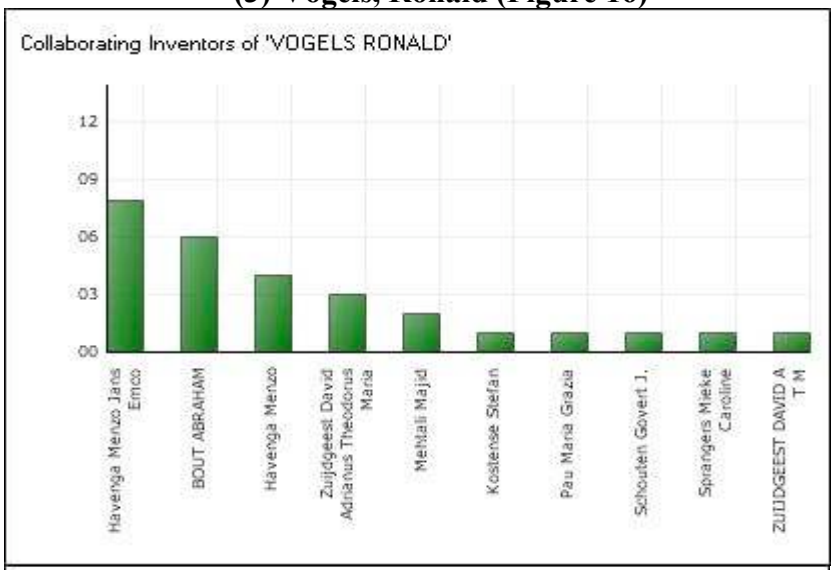


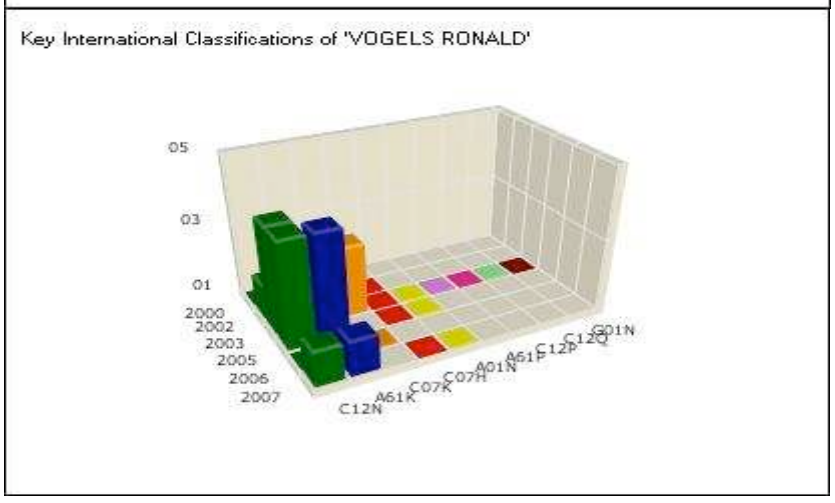


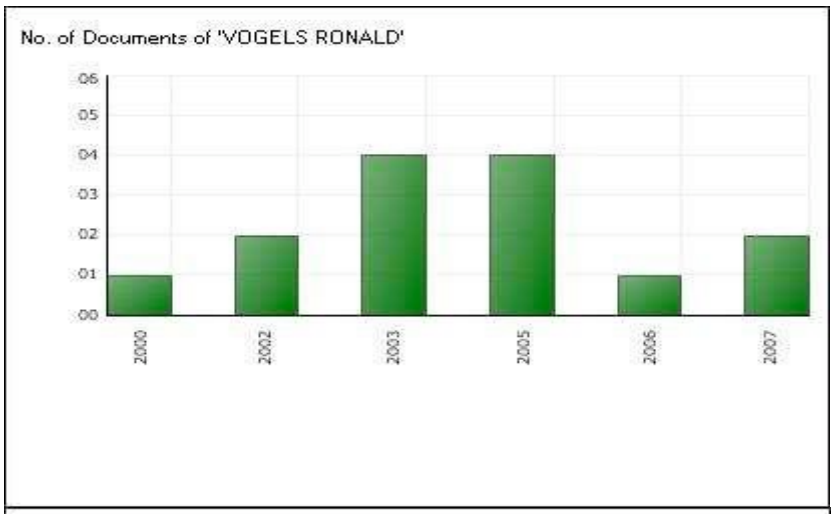


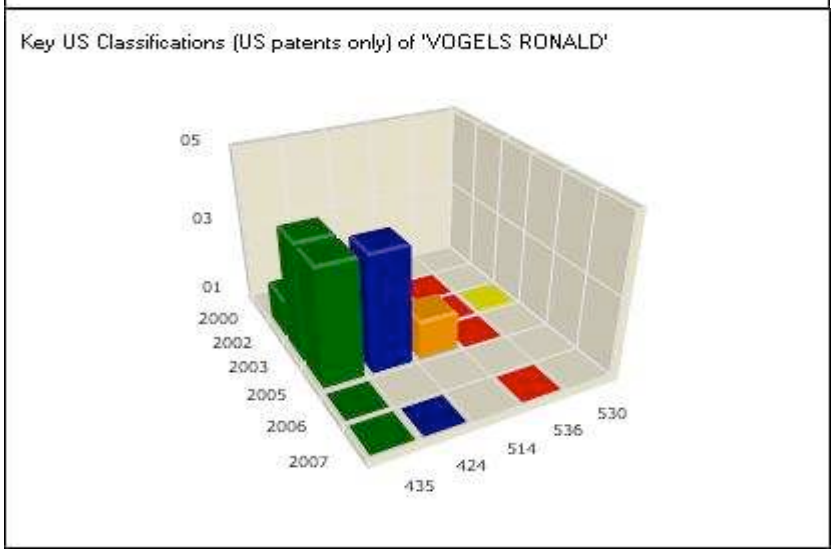


(3) Vogels, Ronald (Figure 16)

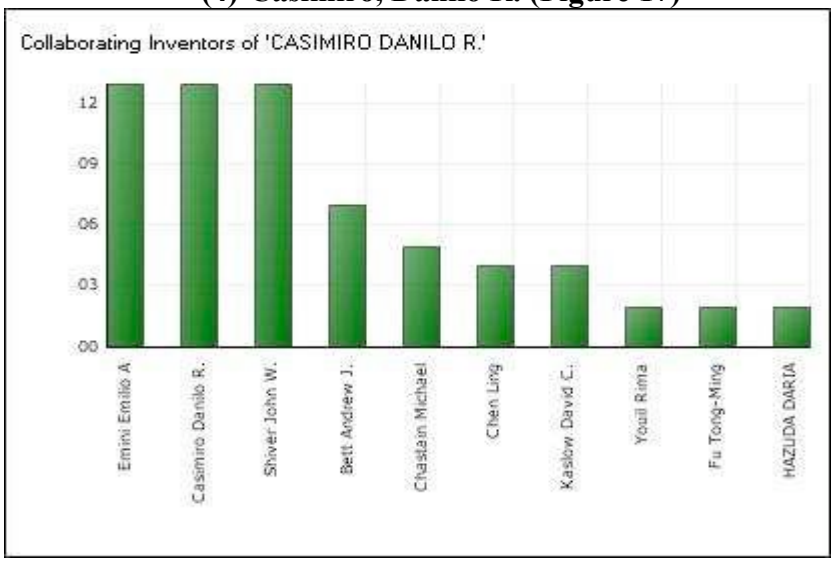




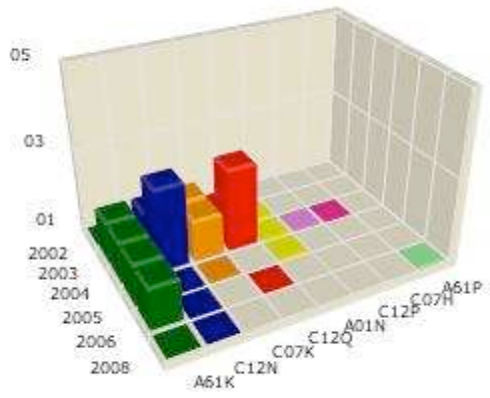




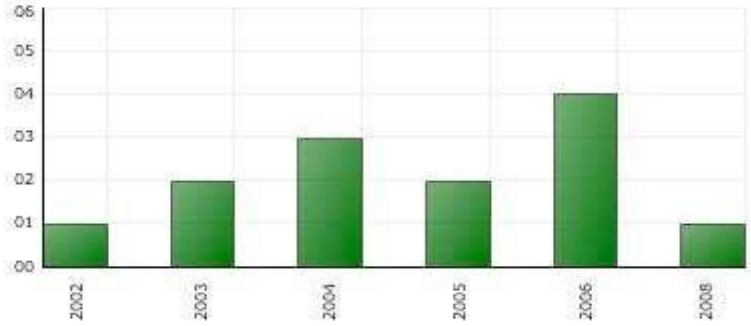
(4) Casimiro, Danilo R. (Figure 17)



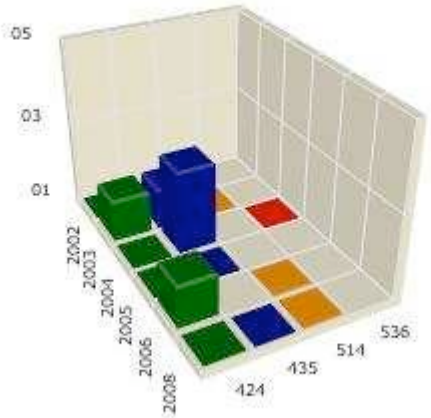
Key International Classifications of 'CASIMIRO DANILO R.'



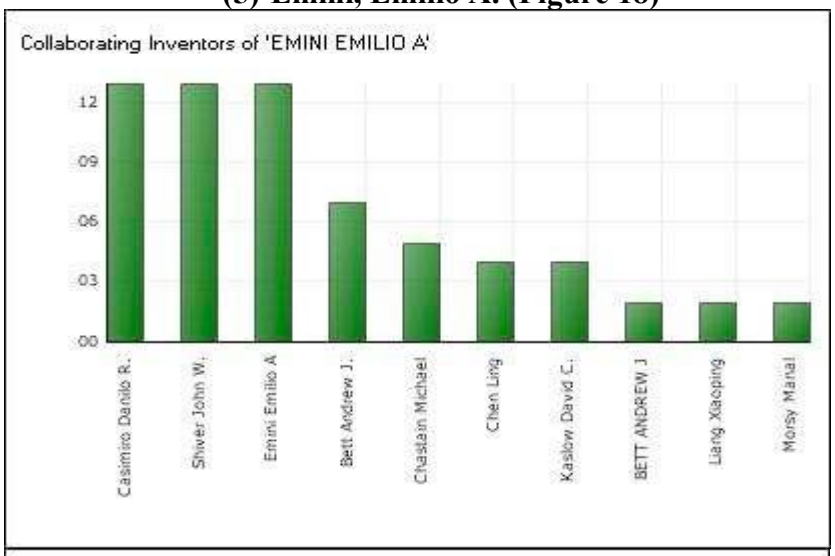
No. of Documents of 'CASIMIRO DANILO R.'

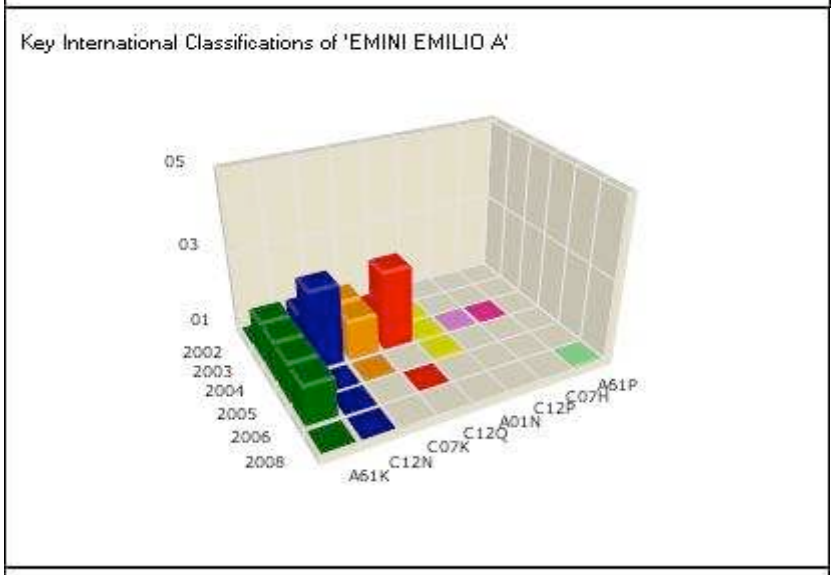


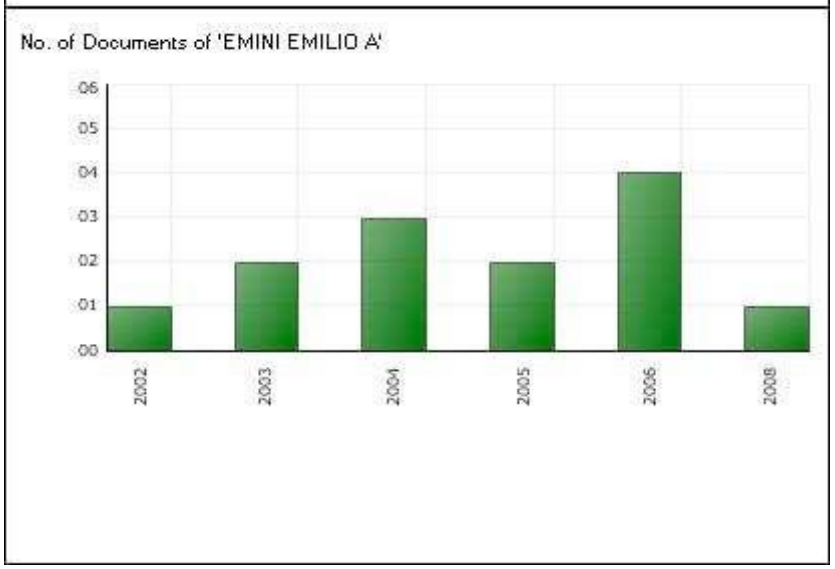
Key US Classifications (US patents only) of 'CASIMIRO DANILO R.'

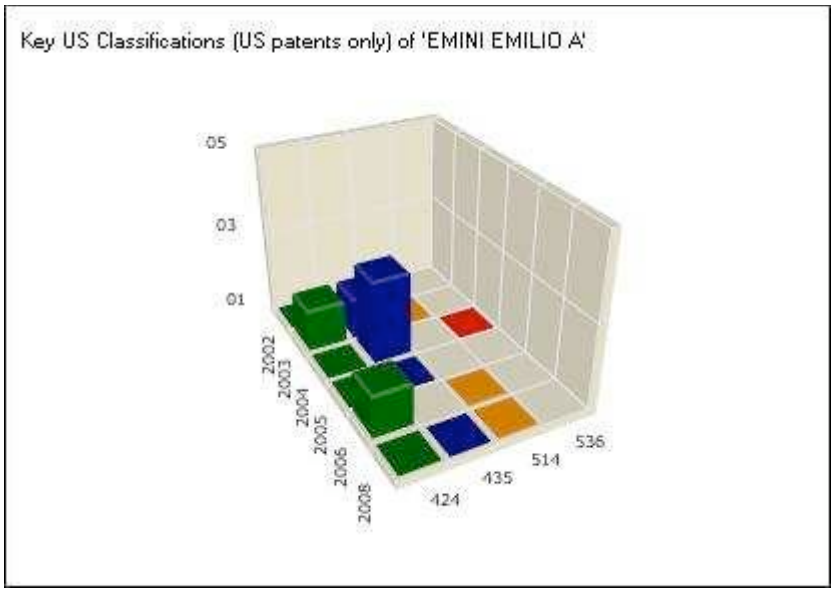


(5) Emini, Emilio A. (Figure 18)









4.2 Final Analysis after Consolidating Adjusting Assignee Names

As shown above, we found that each commercial analysis tool doesn't reflect the slight variation of the assignee's name (for example, 'Merck and Co.' is recognized differently from 'Merck & Co.') thereby the total patent counts are varied in each tool. For adjusting this problem, we reviewed and manually consolidated the same assignees by using our master spreadsheet, and generated additional tables and graphs.

4.2.1. Patent Count vs. Country

(A)

Country	**Patent Count**
EP	5
US	214
WO	48
Total	267

(B)

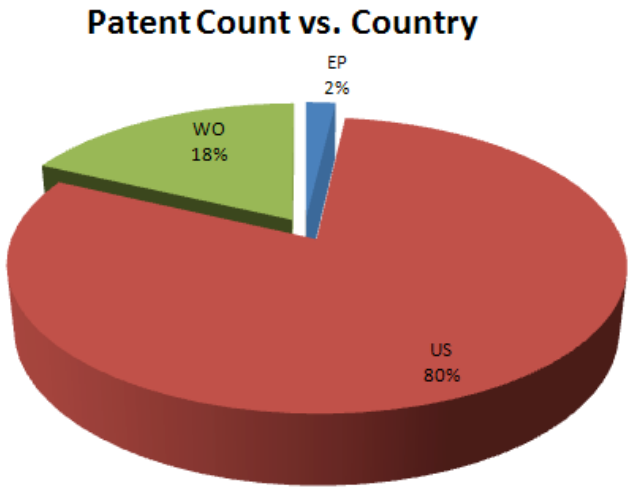


Figure 19. Patent counts according to publication country. Shown in a table (A) and a pie chart (B).

4.2.2 Patent Count vs. Publication Date

(A)

Year of Publication Date	Patent Count
2008	15
2007	21
2006	30
2005	27
2004	27
2003	36
2002	39
2001	25
2000	19
1999	13
1998	8
1997	2
1996	2
1995	2
1992	1

(B)

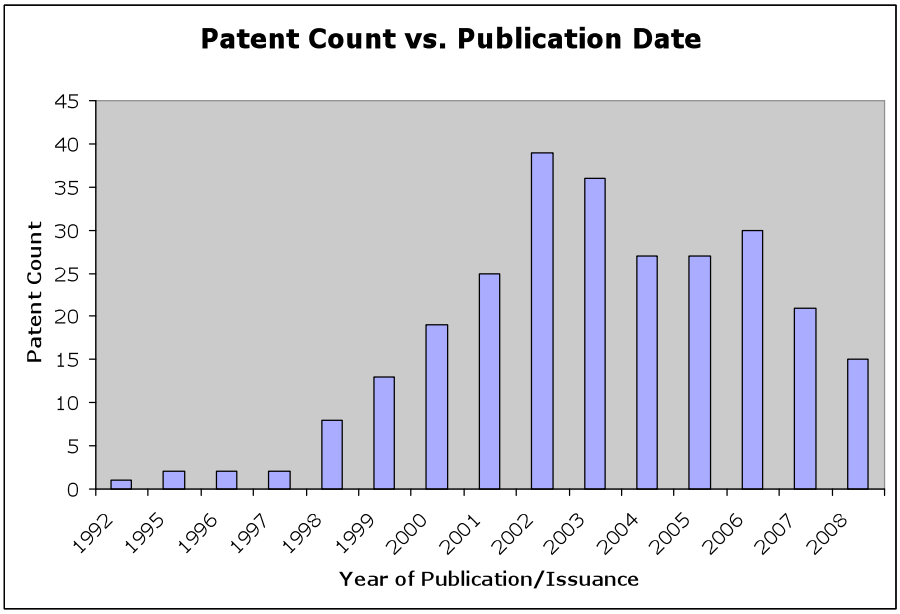


Figure 20. Patent counts according to publication date. Shown in a table (A) and a bar graph (B).

4.2.3 Patent Count vs. Filing Date

(A)

Year of Filing date	Patent Count
2007	10
2006	12
2005	17
2004	21
2003	43
2002	26
2001	42
2000	30
1999	17
1998	12
1997	16
1996	8
1995	5
1994	4
1993	2
1990	2

(B)

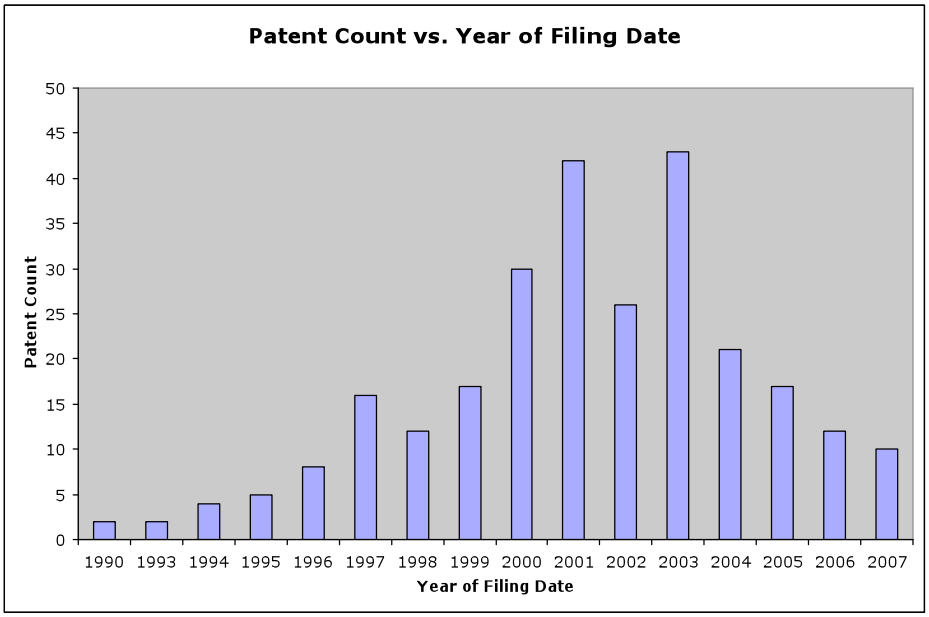


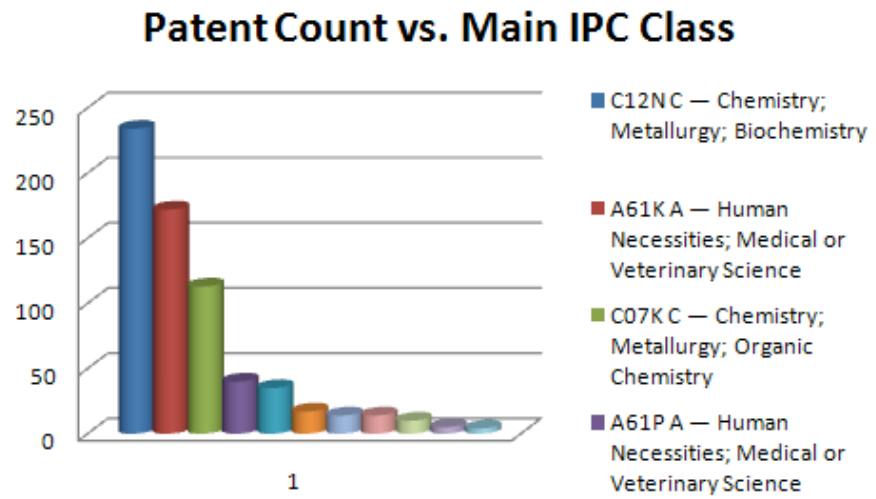
Figure 21. Patent counts according to the filing date. Shown in a table (A) and a bar graph (B).

4.2.4 Patent Count vs. Main IPC Class

(A)

IPC Code- 4 digit	Patent Count
C12N C — Chemistry; Metallurgy; Biochemistry	234
A61K A — Human Necessities; Medical or Veterinary Science	172
C07K C — Chemistry; Metallurgy; Organic Chemistry	113
A61P A — Human Necessities; Medical or Veterinary Science	40
C12Q C — Chemistry; Metallurgy; Biochemistry	35
C07H C — Chemistry; Metallurgy; Organic Chemistry	17
C12P C — Chemistry; Metallurgy; Biochemistry	14
C12R C — Chemistry; Metallurgy; Biochemistry	14
G01N G — Physics; Measuring	10
A01N A — Human Necessities; Agriculture; Forestry	5
B01D B — Performing Operations; Transporting	4
B01J B — Performing Operations; Transporting	3
C40B C — Chemistry; Metallurgy; Combinatorial Technology	2
A01K A — Human Necessities; Agriculture; Forestry	1
G06F G — Physics; Computing; Calculating	1

(B)



(C)

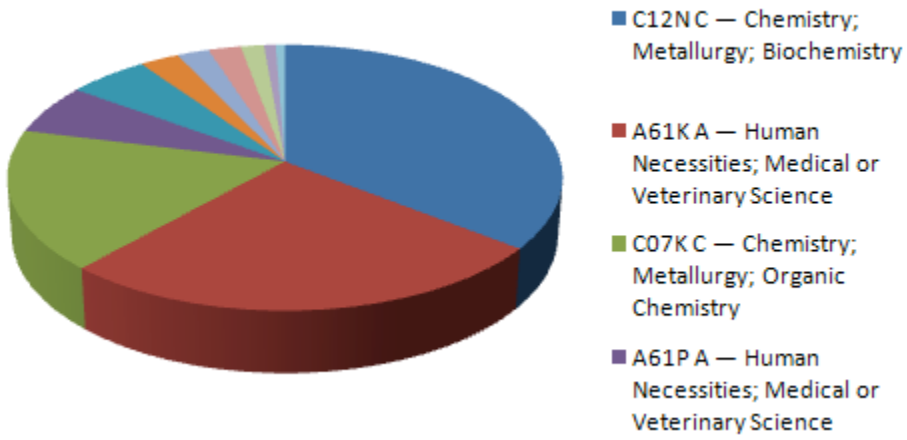


Figure 22. Patent counts according to IPC classification. More than 60% of Adenovirus vaccine patents within the scope of the present search fall under C21N and A61N. Shown in a table (A), a bar graph (B), and a pie chart (C).

4.2.5 Patent Count vs. Derwent Main Class

(A)

Top 5 Derwent Main Class	Patent Count
B04 Natural products and polymers.	266
D16 Fermentation industry.	264
C06 Biotechnology - including plant genetics and veterinary vaccines.	23
A96 Medical, dental, veterinary, cosmetic.	9
S03 Scientific Instrumentation.	6

(B)

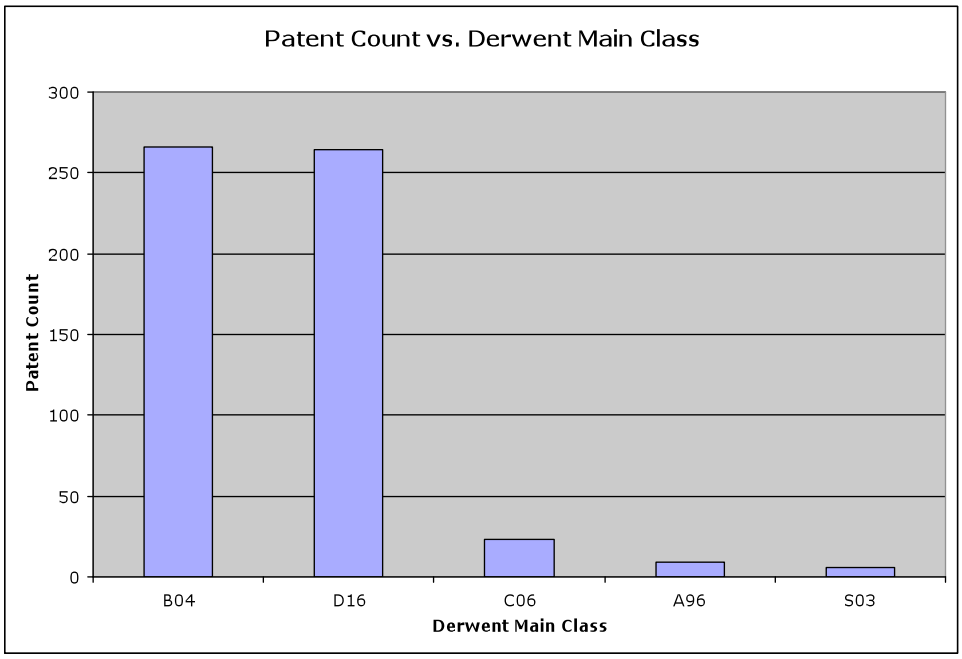


Figure 23. Patent counts according to Derwent Main classification. Most of Adenovirus vaccine patents within the scope of the present search fall under B04 and D16. Shown in a table (A) and a bar graph (B).

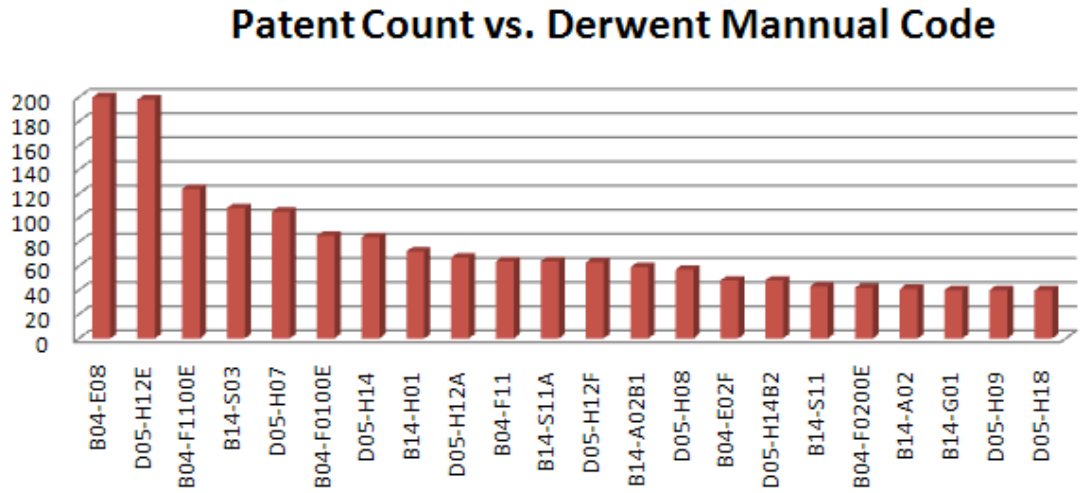
4.2.6 Patent Count vs. Derwent Mannual Code

(A)

	Top 20 Derwent Manual Code	**Patent Count**
1	B04-E08 Natural products (or genetically engineered), polymers: Vectors, plasmids, cosmids, transposons	200
2	D05-H12E Fermentation industry: Vectors	198
3	B04-F1100ENatural products (or genetically engineered), polymers: Viruses (genetically engineered)	124
4	B14-S03 Pharmaceutical activities: Gene therapy (general)	108
5	D05-H07 Fermentation industry: Production of vaccines, antigens	105
6	B04-F0100ENatural products (or genetically engineered), polymers: Cells, microorganisms, transformants, hosts, cell lines, tissue [general] (genetically engineered)	85
7	D05-H14 Fermentation industry: Recombinant cells	84
8	B14-H01 Pharmaceutical activities: Anticancer general and other	72
9	D05-H12A Fermentation industry: Wild-type coding sequences	67
10	B04-F11 Natural products (or genetically engineered), polymers: Viruses	64
11	B14-S11A Pharmaceutical activities: Antiviral vaccine	64
12	D05-H12F Fermentation industry: Recombinant viruses [excluding viral vectors]	63
13	B14-A02B1 Pharmaceutical activities: Retrovirus	59
14	D05-H08 Fermentation industry: Cell or tissue culture	57
15	B04-E02F Natural products (or genetically engineered), polymers: Encoding other protein/polypeptide	48
16	D05-H14B2 Fermentation industry: Recombinant mammalian cells	48

17	B14-S11 Pharmaceutical activities: Vaccine [general]	43
18	B04-F0200ENatural products (or genetically engineered), polymers: Mammal (including human) (genetically engineered)	42
19	B14-A02 Pharmaceutical activities: Antiviral [general]	41
20	B14-G01 Pharmaceutical activities: Immunostimulant general and other	40
20	D05-H09 Fermentation industry: Testing and detection [exc. bacteria, fungi, viruses]	40
20	D05-H18 Fermentation industry: Genetic engineering techniques, new methods	40

(B)



(c)

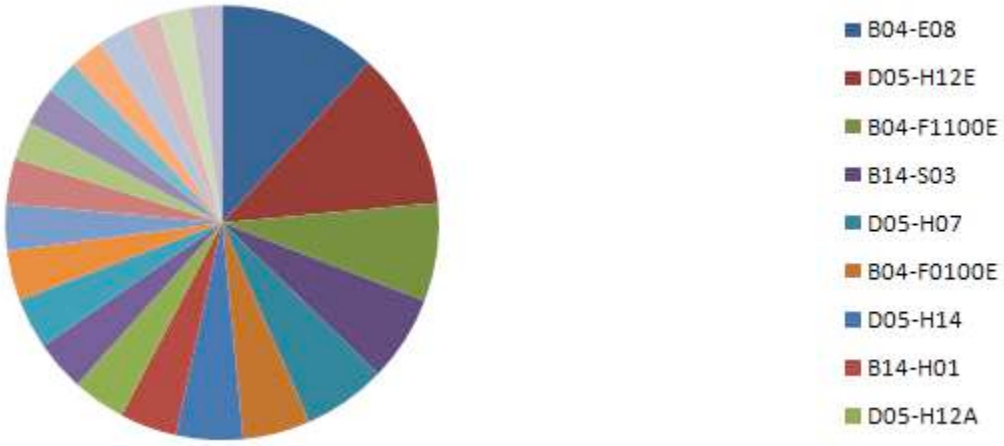


Figure 24. Patent counts according to Top 20 Derwent Manual Code. More than 30% of Adenovirus vaccine patents within the scope of the present search fall under B04-E08 and following by D05-H12E and B04-f1100E. Shown in a table (A), a bar graph (B), and a pie chart (C).

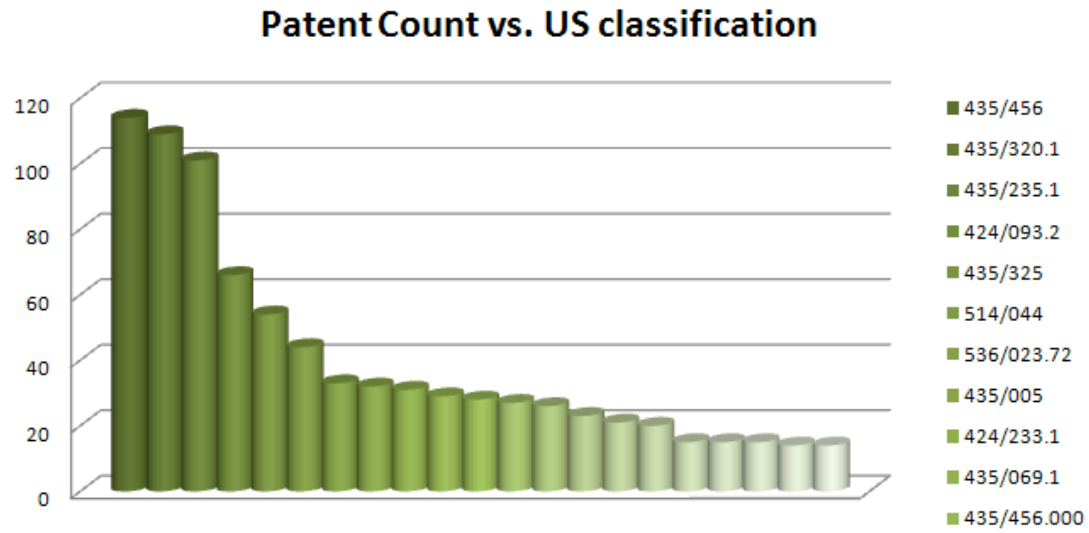
4.2.7 Patent Count vs. US classification

(A)

	Top 20 US class-subclass	Patent count

1	435/456	114
2	435/320.1	109
3	435/235.1	101
4	424/093.2	66
5	435/325	54
6	514/044	44
7	536/023.72	33
8	435/005	32
9	424/233.1	31
10	435/069.1	29
11	435/456.000	28
12	435/455	27
13	424/199.1	26
14	424/093.21	23
15	530/350	21
16	536/023.1	20
17	435/006	15
17	435/235.100	15
17	435/457	15
20	424/204.1	14
20	435/366	14

(B)



(C)

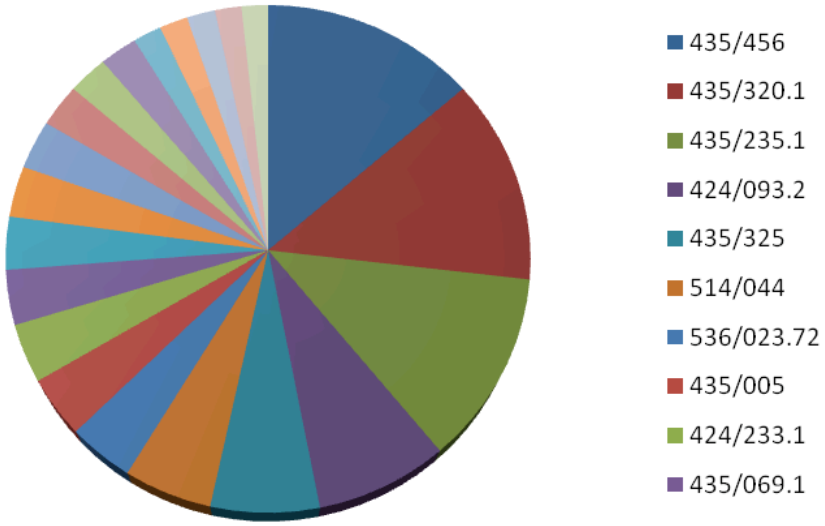


Figure 25. Patent counts according to Top 20 US class-subclass. 39% of Adenovirus vaccine patents within the scope of the present search fall under 435/456 (14%), 435/320.1(13%) and 435/235.1(12%). Shown in a table (A), a bar graph (B), and a pie chart (C).

4.2.8 Patent Count vs. Assignee

(A)

	Top Assignee	**Patent Count**
1	Merck & Co., Inc.	27
2	Crucell Holland B.V.	22
3	Transgene S.A.	16
4	University of Pennsylvania	15
5	GenVec, Inc.	13
6	US GOVERNMENT	12
7	University of Saskatchewan	9
8	Scripps Research Institute	7
9	GLAXO GROUP LIMITED	6
9	Introgen Therapeutics, Inc.	6
11	Cell Genesys, Inc.	5
11	University of California	5
11	WISTAR INSTITUTE OF ANATOMY AND BIOLOGY	5
14	Aventis Pharma S.A	4
14	Cornell Research Foundation, Inc.	4
14	NOVARTIS PHARMA AG	4
14	Rhone-Poulenc Rorer S.A.	4

18	BETH ISRAEL DEACONESS MEDICAL CENTER	3
18	CANJI, INC	3
18	Genzyme Corporation	3
18	Introgene B.V.	3
18	University of Michigan	3
18	University of Washington	3

(B)

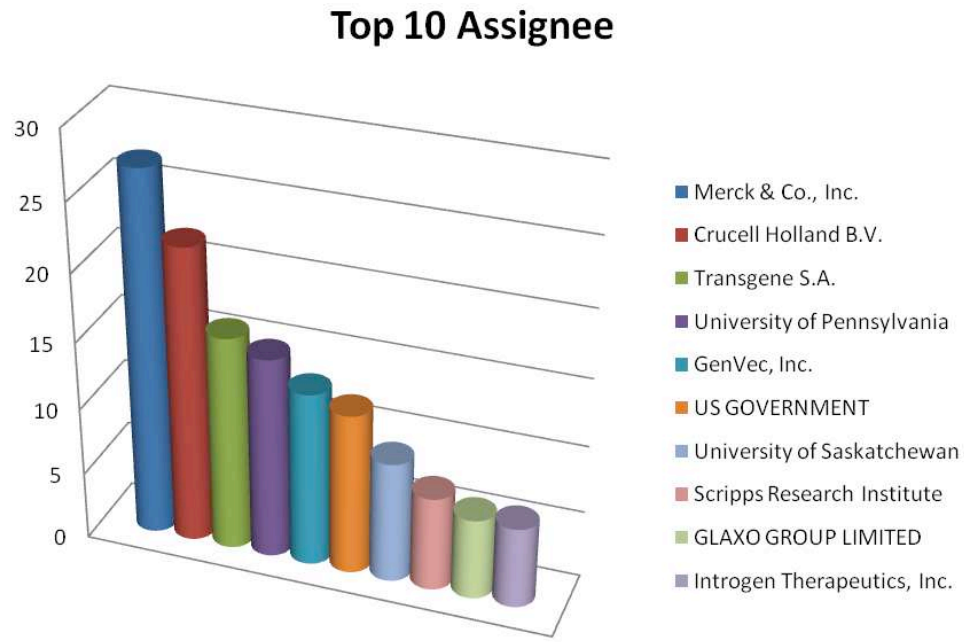


Figure 26. Patent counts according to assignee. Shown in a table (A) and a bar graph (B).

4.2.9 Patent Count vs. Inventor

(A)

	Top 20 Inventor	Patent Count
1	SHIVER, JOHN W.	15
2	WILSON, JAMES M.	15
3	VOGELS, RONALD	14
4	CASIMIRO, DANILO R.	13
4	EMINI, EMILIO A.	13
6	BETT, ANDREW J.	12
7	MEHTALI, MAJID	11
8	HAVENGA; MENZO JANS EMCO	10
8	KOVESDI, IMRE	10
10	BOUT, ABRAHAM	9
10	TIKOO, SURESH K.	9
12	BROUGH; DOUGLAS E.	8

13	CHASTAIN, MICHAEL	7
13	PERRICAUDET, MICHEL	7
13	YEH, PATRICE	7
16	ERTL, HILDEGHUND C. J.	6
16	KASLOW, DAVID C.	6
16	NABEL, GARY	6
16	NEMEROW, GLEN R.	6
16	WICKHAM, THOMAS J.	6

(B)

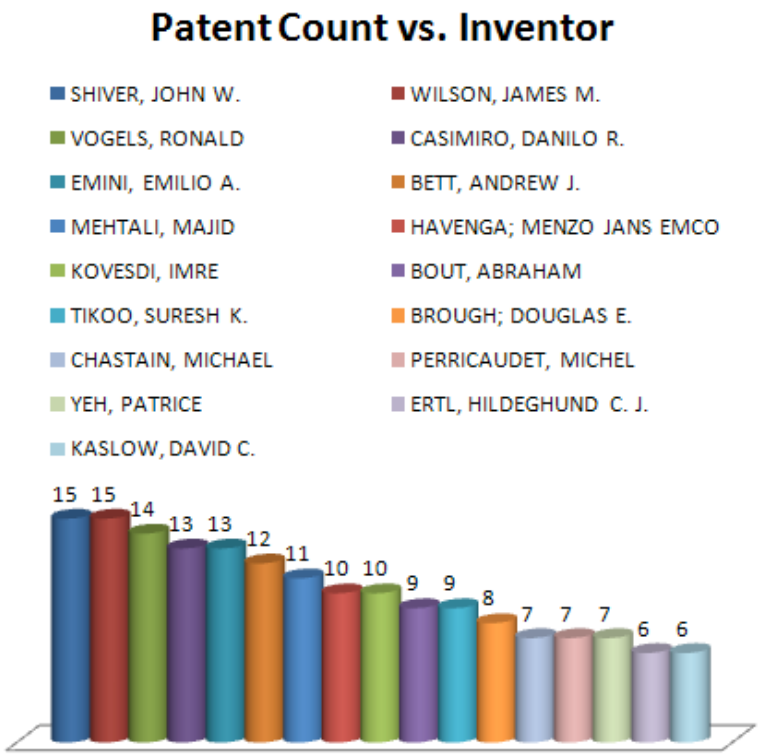


Figure 27. Patent counts according to Inventor. Shown in a table (A) and a bar graph (B).

APPENDIX A: Scientific Papers

1. Curr Gene Ther. 2007 Jun;7(3):189-204.

Current advances and future challenges in Adenoviral vector biology and targeting.

Campos SK, **Barry MA**.

Gene delivery vectors based on Adenoviral (Ad) vectors have enormous potential for the treatment of both hereditary and acquired disease. Detailed structural analysis of the Ad virion, combined with functional studies has broadened our knowledge of the structure/function relationships between Ad vectors and host cells/tissues and substantial achievement has been made towards a thorough understanding of the biology of Ad vectors. The widespread use of Ad vectors for clinical gene therapy is compromised by their inherent immunogenicity. The generation of safer and more effective Ad vectors, targeted to the site of disease, has therefore become a great ambition in the field of Ad vector development. This review provides a synopsis of the structure/function relationships between Ad vectors and host systems and summarizes the many innovative approaches towards achieving Ad vector targeting.
http://www.ncbi.nlm.nih.gov/pubmed/17584037

2. Hum Gene Ther. 2005 Feb;16(2):149-56.

Adenovirus vector-based vaccines for human immunodeficiency virus type 1.

Barouch DH, **Nabel GJ**.

Recombinant adenovirus (rAd) vectors have received considerable attention for gene therapy because of their high transduction efficiency. However, recombinant gene expression from rAd vectors elicits rapid and potent immune responses to foreign transgene products. Such immunogenicity limits the duration of transgene expression and poses a major challenge to the use of rAd vectors for gene therapy. In contrast, the inherent immunogenicity of these vectors is a desirable feature for vaccine development. The immunogenicity and protective efficacy of rAd vector-based vaccines have now been demonstrated in a number of animal models, and rAd vaccines for a variety of pathogens are currently being explored in early-phase clinical trials. In this review, we describe progress in the development of rAd vector-based vaccines with a focus on human immunodeficiency virus type 1.
http://www.ncbi.nlm.nih.gov/sites/entrez

3. Mol Ther. 2004 Oct;10(4):616-29.

Adenoviruses as vaccine vectors.

Tatsis N, **Ertl HC**.

Adenoviruses have transitioned from tools for gene replacement therapy to bona fide vaccine delivery vehicles. They are attractive vaccine vectors as they induce both innate and adaptive immune responses in mammalian hosts. Currently, adenovirus vectors are being tested as subunit vaccine systems for numerous infectious agents ranging from malaria to HIV-1. Additionally, they are being explored as vaccines against a multitude of tumor-associated antigens. In this review we describe the molecular biology of adenoviruses as well as ways the adenovirus vectors can be manipulated to enhance their efficacy as vaccine carriers. We describe methods of evaluating immune responses to transgene products expressed by adenoviral vectors and discuss data on adenoviral vaccines to a selected number of pathogens. Last, we comment on the limitations of using human adenoviral vectors and provide alternatives to circumvent these problems. This field is growing at an exciting and rapid pace, thus we have limited our scope to the use of adenoviral vectors as vaccines against viral pathogens.

http://www.ncbi.nlm.nih.gov/pubmed/15451446?ordinalpos=6&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

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The adenovirus hexon protein. The primary structure of the polypeptide and its correlation with the hexon gene.

Jörnvall H, **Akusjärvi G**, **Aleström P**, **von Bahr-Lindström H**, **Pettersson U**, **Appella E**, **Fowler AV**, **Philipson L**.

The primary structure of the adenovirus hexon polypeptide has been determined by amino acid sequence studies of peptides from all regions of the molecule combined with sequence analysis of selected areas of its gene. The sequence presented contains 966 unique amino acid residues. Overlapping peptides recovered from CNBr cleavage and from digestions with proteolytic enzymes were analyzed, as well as DNA segments around sites for restriction endonucleases in the hexon gene. The primary structure is in good agreement with the total composition of the protein, with the compositions of individual CNBr fragments, and with known locations of restriction enzyme cleavage sites in the gene. Distinct regions of internal homology do not occur in the structure. The entire hexon polypeptide is encoded by a contiguous DNA sequence without intervening sequences.
http://www.ncbi.nlm.nih.gov/pubmed/6263909?dopt=Abstract

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Structural and functional determinants in adenovirus type 2 penton base recombinant protein.

Karayan L, **Hong SS**, **Gay B**, **Tournier J**, **d'Angeac AD**, **Boulanger P**.

Discrete domains involved in structural and functional properties of adenovirus type 2 (Ad2) penton base were investigated with site-directed mutagenesis of the recombinant protein expressed in baculovirus-infected cells. Seventeen substitution mutants were generated and

phenotyped for various functions in insect and human cells as follows. (i) Pentamerization of the penton base protein was found to be dependent on three amino acid side chains, the indole ring of Trp119, the hydroxylic group of Tyr553, and the basic group of Lys556. (ii) Arg254, Cys432, and Trp439, the stretch of basic residues at positions 547 to 556, and Arg340 of the RGD motif played a critical role in stable fiber-penton base interactions in vivo. (iii) Nuclear localization of penton base in Sf9 cells was negatively affected in mutants W119H or W165H, and, to a lesser extent, by substitutions in the consensus polybasic signal at positions 547 to 549. (iv) Penton base mutants were also assayed for HeLa cell binding, cell detachment, plasmid DNA internalization, and Ad-mediated gene delivery. The results obtained suggested that the previously identified integrin-binding motifs RGD340 and LDV287 were functionally and/or topologically related to other discrete regions which include Trp119, Trp165, Cys246, Cys432, and Trp439, all of which were involved in penton base-cell surface recognition, endocytosis, and postendocytotic steps of the virus life cycle.

http://jvi.asm.org/cgi/content/abstract/71/11/8678

6. J Virol. 2005 Feb;79(4):1992-2000.

Adenovirus protein VI mediates membrane disruption following capsid disassembly.

Wiethoff CM, **Wodrich H**, **Gerace L**, **Nemerow GR**.

In contrast to enveloped viruses, the mechanisms involved in membrane penetration by nonenveloped viruses are not as well understood. In these studies, we determined the relationship between adenovirus (Ad) capsid disassembly and the development of membrane lytic activity. Exposure to low pH or heating induced conformational changes in wild-type Ad but not in temperature-sensitive Ad (ts1) particles that fail to escape the early endosome. Wild-type Ad but not ts1 particles permeabilized model membranes (liposomes) and facilitated the cytosolic delivery of a ribotoxin. Alterations in wild-type Ad capsids were associated with the exposure of a pH-independent membrane lytic factor. Unexpectedly, this factor was identified as protein VI, a 22-kDa cement protein located beneath the peripentonal hexons in the viral capsid. Recombinant protein VI and preprotein VI, but not a deletion mutant lacking an N-terminal amphipathic alpha-helix, possessed membrane lytic activity similar to partially disassembled virions. A new model of Ad entry is proposed based on our present observations of capsid disassembly and membrane penetration.

http://jvi.asm.org/cgi/content/full/79/4/1992?view=long&pmid=15681401

7. Virus Res. 2002 Feb 26;83(1-2):197-206.

Unscheduled expression of capsid protein IIIa results in defects in adenovirus major late mRNA and protein expression.

Molin M, **Bouakaz L**, **Berenjian S**, **Akusjärvi G**.

Adenovirus gene expression is to a large extent regulated at the level of alternative RNA splicing. For example, in the major late region 1 (L1) unit, a common 5' splice site can be joined to two alternative 3' splice sites, resulting in the formation of the so-called 52,55K (proximal 3' splice site) or the IIIa (distal 3' splice site) mRNAs. Whereas, the 52,55K mRNA is expressed both early and late during infection, the IIIa mRNA is strictly confined to the late phase of the infectious cycle. We have previously shown that IIIa mRNA splicing is subjected to a tight viral control of IIIa 3 splice site usage. In an attempt to determine why adenovirus uses elaborate mechanisms to confine IIIa mRNA production to the late phase of infection, we characterized the phenotype of a recombinant adenovirus expressing the IIIa protein from an inducible tetracycline regulated gene cassette. The results show that expression of the IIIa protein during the early phase of infection results in a significant reduction in late viral protein synthesis and a moderate block to viral DNA replication. Interestingly, unscheduled IIIa protein expression resulted in a perturbation of the accumulation of alternatively spliced L1 mRNAs. Thus, 52,55K mRNA accumulation was inhibited while no effects on endogenous IIIa mRNA expression was detected.

http://www.sciencedirect.com/science?_ob=ArticleURL&_udi=B6T32-45BCRKP-J&_user=10&_rdoc=1&_fmt=&_orig=search&_sort=d&view=c&_acct=C000050221&_version=1&_urlVersion=0&_userid=10&md5=f0cf47596a587bb4abbed02e1b694b3e

8. J Virol. 2003 Mar;77(6):3586-94.

Requirement of the adenovirus IVa2 protein for virus assembly.

Zhang W, **Imperiale MJ**.

The adenovirus L1 52/55-kDa protein is required for viral DNA packaging and interacts with the viral IVa2 protein, which binds to the viral packaging sequence. Previous reports suggest that the IVa2 protein plays a role in viral DNA packaging and that this function of the IVa2 protein is serotype specific. To further examine the function of the IVa2 protein in viral DNA packaging, a mutant virus that does not express the IVa2 protein was constructed by introducing two stop codons at the beginning of the IVa2 open reading frame in a full-length bacterial clone of adenovirus type 5. The mutant virus, pm8002, was defective for growth in 293 cells, although it replicated its DNA and produced early and late viral proteins. Electron microscopic and gradient analyses revealed that the mutant virus did not assemble any viral particles in 293 cells. In 293-IVa2 cells, which express the IVa2 protein, infectious viruses were produced, although the titer of the mutant virus was lower than that of the wild-type virus, indicating that these cells may not fully complement the mutation. The mutant viral particles produced in 293-IVa2 cells were heterogeneous in size and shape, less stable, and did not traffic efficiently to the nucleus. Marker rescue experiments with a wild-type IVa2 DNA fragment confirmed that the only mutations present in pm8002 were in the IVa2 gene. The results indicate that the IVa2 protein is required for adenovirus assembly and suggest that virus particles may be assembled around the DNA rather than DNA being packaged into preformed capsids.

http://jvi.asm.org/cgi/content/full/77/6/3586?view=long&pmid=12610134

9. J Gen Virol. 2004 Jan;85(Pt 1):185-96.

Precursor of human adenovirus core polypeptide Mu targets the nucleolus and modulates the expression of E2 proteins.

Lee TW, **Lawrence FJ**, **Dauksaite V**, **Akusjärvi G**, **Blair GE**, **Matthews DA**.

We have examined the subcellular localization properties of human adenovirus 2 (HAdV-2) preMu and mature Mu (pX) proteins as fusions with enhanced green fluorescence protein (EGFP). We determined that preMu is exclusively a nucleolar protein with a single nucleolar accumulation signal within the Mu sequence. In addition, we noted that both preMu-EGFP and Mu-EGFP are excluded from adenovirus DNA-binding protein (DBP)-rich replication centres in adenovirus-infected cells. Surprisingly, we observed that cells in which preMu-EGFP (but not Mu-EGFP) is transiently expressed prior to or shortly after infection with Ad2 did not express late adenovirus genes. Further investigation suggested this might be due to a failure to express pre-terminal protein (preTP) from the E2 region, despite expression of another E2 protein, DBP. Deletion mutagenesis identified a highly conserved region in the C terminus of preMu responsible for these observations. Thus our data suggest that preMu may play a role in modulating accumulation of proteins from the E2 region.

http://vir.sgmjournals.org/cgi/content/full/85/1/185

10. Mol Cell Biol. 1985 Aug;5(8):1933-9.

Control functions of adenovirus transformation region E1A gene products in rat and human cells.

Bellett AJ, **Li P**, **David ET**, **Mackey EJ**, **Braithwaite AW**, **Cutt JR**.

Altered control of the rat cell cycle induced by adenovirus requires expression of transformation region E1A, but not of E1B, E2A, E2B, or late genes. We show here that neither E3 nor E4 is required, so the effect results directly from an E1A product. Mutants with defects in the 289-amino-acid (aa) E1A product had little or no effect on the rat cell cycle even at 1,000 IU per cell. A mutant (pm975) lacking the 243-aa E1A product altered cell cycle progression, but less efficiently than did wild-type virus. The 289-aa E1A protein is therefore essential for cell cycle effects; the 243-aa protein is also necessary for the full effect but cannot act alone. Mutants with altered 289-aa E1A proteins showed different extents of leak expression of viral early region E2A as the multiplicity was increased; each leaked more in human than in rat cells. dl312, with no E1A products, failed to produce E2A mRNA or protein at 1,000 IU per cell in rat cells but did so in some experiments in human cells. There appears to be a very strict dependence of viral early gene expression on E1A in rat cells, whereas dependence on E1A is more relaxed in HeLa cells, perhaps due to a cellular E1A-like function. Altered cell cycle control is more dependent on E1A function than is early viral gene expression.

http://mcb.asm.org/cgi/content/abstract/5/8/1933

11. Mol Cell Biol. 2000 Aug;20(15):5540-53.

Adenovirus E1B 55-kilodalton oncoprotein inhibits p53 acetylation by PCAF.

Liu Y, **Colosimo AL**, **Yang XJ**, **Liao D**.

The adenovirus E1B 55-kDa protein binds to cellular tumor suppressor p53 and inactivates its transcriptional transactivation function. p53 transactivation activity is dependent upon its ability to bind to specific DNA sequences near the promoters of its target genes. It was shown recently that p53 is acetylated by transcriptional coactivators p300, CREB bidning protein (CBP), and PCAF and that acetylation of p53 by these proteins enhances p53 sequence-specific DNA binding. Here we show that the E1B 55-kDa protein specifically inhibits p53 acetylation by PCAF in vivo and in vitro, while acetylation of histones and PCAF autoacetylation is not affected. Furthermore, the DNA-binding activity of p53 is diminished in cells expressing the E1B 55-kDa protein. PCAF binds to the E1B 55-kDa protein and to a region near the C terminus of p53 encompassing Lys-320, the specific PCAF acetylation site. We further show that the E1B 55-kDa protein interferes with the physical interaction between PCAF and p53, suggesting that the E1B 55-kDa protein inhibits PCAF acetylase function on p53 by preventing enzyme-substrate interaction. These results underscore the importance of p53 acetylation for its function and suggest that inhibition of p53 acetylation by viral oncoproteins prevent its activation, thereby contributing to viral transformation.

http://mcb.asm.org/cgi/content/full/20/15/5540?view=long&pmid=10891493

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Production of first generation adenovirus vectors: a review.

Danthinne X, **Imperiale MJ**.

In the past decade, adenovirus vectors have generated tremendous interest, especially in gene therapy applications. In the so-called 'first generation' adenovirus vectors, the transgenes are inserted in place of the E1 region, or less often the E3 region. Although second-generation and helper-dependent adenovirus vectors will probably prevail in the future in applications that require long-term gene expression, first generation adenovirus vectors will remain very useful in other settings, such as cancer and vaccination, or simply to transfect cell lines that are refractory to other transfection methods. Until a few years ago, the construction of first generation adenovirus vectors was a labor-intensive and time-consuming process. More than 20 methods have appeared that facilitate their construction and are reviewed below.

http://www.nature.com/gt/journal/v7/n20/abs/3301301a.html

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Adenovirus early region 3(E3) immunomodulatory genes decrease the incidence of autoimmune diabetes in NOD mice.

Efrat S, **Serreze D**, **Svetlanov A**, **Post CM**, **Johnson EA**, **Herold K**, **Horwitz M**.

The early three (E3) region of the adenovirus (Ad) encodes a number of immunomodulatory proteins that interfere with class I major histocompatibility-mediated antigen presentation and

confer resistance to cytokine-induced apoptosis in cells infected by the virus. Transgenic expression of Ad E3 genes under the rat insulin II promoter (RIP-E3) in beta-cells in nonobese diabetic (NOD) mice decreases the incidence and delays the onset of autoimmune diabetes. The immune effector cells of RIP-E3/NOD mice maintain the ability to infiltrate the islets and transfer diabetes into NOD-scid recipients, although at a significantly reduced rate compared with wild-type littermates. The islets of RIP-E3/ NOD mice can be destroyed by adoptive transfer of splenocytes from wild-type NOD mice; however, the time to onset of hyperglycemia is delayed significantly, and 40% of these recipients were not diabetic at the end of the experiment. These findings suggest that expression of E3 genes in beta-cells affects both the activation of immune effector cells and the intrinsic resistance of beta-cells to autoimmune destruction.

http://diabetes.diabetesjournals.org/cgi/content/full/50/5/980

14. J Virol. 1991 Mar;65(3):1440-9.

Adenovirus E4-dependent activation of the early E2 promoter is insufficient to promote the early-to-late-phase transition.

Hemström C, **Virtanen A**, **Bridge E**, **Ketner G**, **Pettersson U**.

The adenovirus E4 ORF6/7 protein has been shown to activate the cellular transcription factor E2F. E2F activation leads to activation of the adenovirus early E2 promoter which controls the production of viral DNA replication proteins. In the present study an adenovirus type 5 cDNA mutant, H5ilE4L, was constructed. This mutant is capable of making the ORF6/7 polypeptide but lacks the coding sequences for all other E4 products. H5ilE4L trans activates the early E2 promoter to wild-type levels, but still it is defective for viral DNA replication. A mutant expressing ORF6 in addition to ORF6/7, H5ilE4I, is normal for viral DNA replication. This indicates that activation of the early E2 promoter is insufficient to promote efficient viral DNA replication and that another E4-encoded function is necessary. The ORF6 protein seems to provide this function. We suggest that ORF6/7-induced activation of E2F is not necessary for adenovirus growth in HeLa cells. Rather, this activation might be of importance in the normal, growth-arrested host cell, since E2F has been shown to bind to the promoter regions of a number of immediate-early genes involved in regulation of cell proliferation (M. Mudryj, S. W. Hiebert, and J. R. Nevins, EMBO J. 9:2179-2184, 1990).

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Viral transactivating proteins.

Flint J, **Shenk T**.

Department of Molecular Biology, Princeton University, New Jersey 08544-1014, USA.

Many viruses utilize the cellular transcription apparatus to express their genomes, and they

encode transcriptional regulatory proteins that modulate the process. Here we review the current understanding of three viral regulatory proteins. The adenovirus E1A protein acts within the nucleus to regulate transcription through its ability to bind to other proteins. The herpes simplex type 1 virus VP16 protein acts within the nucleus to control transcription by binding to DNA in conjunction with cellular proteins. The human T-cell leukemia virus Tax protein influences transcription through interactions with cellular proteins in the nucleus as well as the cytoplasm.

http://arjournals.annualreviews.org/doi/abs/10.1146/annurev.genet.31.1.177?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%3dncbi.nlm.nih.gov

16. Annu Rev Med. 2004;55:355-72.

Recent advances in the development of HIV-1 vaccines using replication-incompetent adenovirus vectors.

Shiver JW, **Emini EA**.

An increasing body of evidence suggests that a vaccine that elicits anti-HIV-1 cellular immunity could provide the basis for an effective AIDS vaccine. Comparative immunization experiments testing a variety of vaccine approaches have demonstrated that replication-incompetent adenovirus vectors are an effective means for eliciting cytotoxic T-lymphocyte (CTL) immune responses against HIV-1 antigens. These immune responses effectively control viremia in nonhuman primates following challenge with simian AIDS viruses. Such data, coupled with epidemiology studies that identify HIV-1 gag, pol, and nef as the best antigens for broadly directed cellular immune responses, provide guidance for the development of a potential AIDS vaccine.

http://arjournals.annualreviews.org/doi/abs/10.1146/annurev.med.55.091902.104344?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%3dncbi.nlm.nih.gov

17. J Gen Virol. 2000 Nov;81(Pt 11):2573-604.

Update on adenovirus and its vectors.

Russell WC.

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18. Expert Rev Vaccines. 2007 Jun;6(3):347-56.

T-cell immunity generated by recombinant adenovirus vaccines.

Yang TC, **Millar JB**, **Grinshtein N**, **Bassett J**, **Finn J**, **Bramson JL**.

Recombinant adenovirus vaccines show great promise for generating protective immunity against infectious agents and tumors. Our studies have identified several interesting biological features of the adenovirus vector that influence the T-cell response. Notably, we have

demonstrated that following immunization with adenovirus vaccines, the transgene antigen remains available to the system for a longer period than would be expected, resulting in a T-cell population with a sustained effector phenotype. The implications of these observations with regards to the utility of adenovirus vaccines are discussed.

http://www.expert-reviews.com/doi/abs/10.1586/14760584.6.3.347?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%3dncbi.nlm.nih.gov

19. ILAR J. 2004;45(3):334-42.

Nonhuman primate models in type 1 diabetes research.

Contreras JL, **Smyth CA**, **Curiel DT**, **Eckhoff DE**.

The recent success of "steroid-free" immunosuppressive protocols and improvements in islet preparation techniques have proven that pancreatic islet transplantation (PIT) is a valid therapeutic approach for patients with type 1 diabetes. However, there are major obstacles to overcome before PIT can become a routine therapeutic procedure, such as the need for chronic immunosuppression, the loss of functional islet mass after transplantation requiring multiple islet infusion to achieve euglycemia without exogenous administration of insulin, and the shortage of human tissue for transplantation. With reference to the first obstacle, stable islet allograft function without immunosuppressive therapy has been achieved after tolerance was induced in diabetic primates. With reference to the second obstacle, different strategies, including gene transfer of antiapoptotic genes, have been used to protect isolated islets before and after transplantation. With reference to the third obstacle, pigs are an attractive islet source because they breed rapidly, there is a long history of porcine insulin use in humans, and there is the potential for genetic engineering. To accomplish islet transplantation, experimental opportunities must be balanced by complementary characteristics of basic mouse and rat models and preclinical large animal models. Well-designed preclinical studies in primates can provide the quality of information required to translate islet transplant research safely into clinical transplantation.

http://dels.nas.edu/ilar_n/ilarjournal/45_3/pdfs/v4503contreras.pdf

20. Expert Opinion on Therapeutic Patents 2008;18(3): 293-307

Adenovirus-vectored vaccines

Chawla T, **Khanna N**, **Swaminathan S.**

Background: Engineered adenoviruses are being increasingly explored as immunoprophylactic or immunotherapeutic vaccine vectors. Encouraging data from preclinical studies using human adenovirus vectors carrying different antigen genes have resulted in many currently ongoing clinical trials. *Objective*: The article seeks to review the current status of the use of adenoviruses as vaccine vectors. *Methods*: This review is based on the patent literature since 2000 pertaining to the development of adenovirus vaccine vectors for infectious and non-infectious diseases.

Conclusion: Human adenovirus-vectored vaccines have important limitations that stem from their immunogenicity and restrict their utility. This has spurred intensive efforts to find alternative adenovirus vectors and strategies, each with its own advantages and shortcomings.

http://www.informapharmascience.com/doi/abs/10.1517/13543776.18.3.293

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Replication-incompetent adenoviral vaccine vector elicits effective anti-immunodeficiency-virus immunity.

Shiver JW, **Fu TM**, **Chen L**, **Casimiro DR**, **Davies ME**, **Evans RK**, **Zhang ZQ**, **Simon AJ**, **Trigona WL**, **Dubey SA**, **Huang L**, **Harris VA**, **Long RS**, **Liang X**, **Handt L**, **Schleif WA**, **Zhu L**, **Freed DC**, **Persaud NV**, **Guan L**, **Punt KS**, **Tang A**, **Chen M**, **Wilson KA**, **Collins KB**, **Heidecker GJ**, **Fernandez VR**, **Perry HC**, **Joyce JG**, **Grimm KM**, **Cook JC**, **Keller PM**, **Kresock DS**, **Mach H**, **Troutman RD**, **Isopi LA**, **Williams DM**, **Xu Z**, **Bohannon KE**, **Volkin DB**, **Montefiori DC**, **Miura A**, **Krivulka GR**, **Lifton MA**, **Kuroda MJ**, **Schmitz JE**, **Letvin NL**, **Caulfield MJ**, **Bett AJ**, **Youil R**, **Kaslow DC**, **Emini EA**.

Recent studies of human immunodeficiency virus type 1 (HIV-1) infection in humans and of simian immunodeficiency virus (SIV) in rhesus monkeys have shown that resolution of the acute viral infection and control of the subsequent persistent infection are mediated by the antiviral cellular immune response. We comparatively assessed several vaccine vector delivery systems-three formulations of a plasmid DNA vector, the modified vaccinia Ankara (MVA) virus, and a replication incompetent adenovirus type 5 (Ad5) vector-expressing the SIV gag protein for their ability to elicit such immune responses in monkeys. The vaccines were tested either as a single modality or in combined modality regimens. Here we show that the most effective responses were elicited by a replication-incompetent Ad5 vector, used either alone or as a booster inoculation after priming with a DNA vector. After challenge with a pathogenic HIV-SIV hybrid virus (SHIV), the animals immunized with Ad5 vector exhibited the most pronounced attenuation of the virus infection. The replication-defective adenovirus is a promising vaccine vector for development of an HIV-1 vaccine.

http://www.ncbi.nlm.nih.gov/pubmed/11797011?ordinalpos=3&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

22. J Virol. 2000 Jan;74(1):505-12.

Canine adenovirus vectors: an alternative for adenovirus-mediated gene transfer.

Kremer EJ, **Boutin S**, **Chillon M**, **Danos O**.

Preclinical studies have shown that gene transfer following readministration of viral vectors is often inefficient due to the presence of neutralizing antibodies. Vectors derived from ubiquitous human adenoviruses may have limited clinical use because preexisting humoral and cellular immunity is found in 90% of the population. Furthermore, risks associated with the use of human

adenovirus vectors, such as the need to immunosuppress or tolerize patients to a potentially debilitating virus, are avoidable if efficient nonhuman adenovirus vectors are feasible. Plasmids containing recombinant canine adenovirus (CAV) vectors from which the E1 region had been deleted were generated and transfected into a CAV E1-transcomplementing cell line. Vector stocks, with titers greater than or equal to those obtained with human adenovirus vectors, were free of detectable levels of replication-competent CAV and had a low particle-to-transduction unit ratio. CAV vectors were replication defective in all cell lines tested, transduced human-derived cells at an efficiency similar to that of a comparable human adenovirus type 5 vector, and are amenable to in vivo use. Importantly, 49 of 50 serum samples from healthy individuals did not contain detectable levels of neutralizing CAV antibodies.

http://www.pubmedcentral.nih.gov/articlerender.fcgi?tool=pubmed&pubmedid=10590140

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Molecular characterization of replication-competent variants of adenovirus vectors and genome modifications to prevent their occurrence.

Hehir KM, **Armentano D**, **Cardoza LM**, **Choquette TL**, **Berthelette PB**, **White GA**, **Couture LA**, **Everton MB**, **Keegan J**, **Martin JM**, **Pratt DA**, **Smith MP**, **Smith AE**, **Wadsworth SC**.

Adenovirus (Ad) vectors for gene therapy are made replication defective by deletion of E1 region genes. For isolation, propagation, and large-scale production of such vectors, E1 functions are supplied in trans from a stable cell line. Virtually all Ad vectors used for clinical studies are produced in the 293 cell, a human embryonic kidney cell line expressing E1 functions from an integrated segment of the left end of the Ad type 5 (Ad5) genome. Replication-competent vector variants that have regained E1 sequences have been observed within populations of Ad vectors grown on 293 cells. These replication-competent variants presumably result from recombination between vector and 293 cell Ad5 sequences. We have developed Ad2-based vectors and have characterized at the molecular level examples of replication-competent variants. All such variants analyzed are Ad2-Ad5 chimeras in which the 293 cell Ad5 E1 sequences have become incorporated into the viral genome by legitimate recombination events. A map of Ad5 sequences within the 293 cell genome developed in parallel is consistent with the proposed recombination events. To provide a convenient vector production system that circumvents the generation of replication-competent variants, we have modified the Ad2 vector backbone by deleting or rearranging the protein IX coding region normally present downstream from the E1 region such that the frequency of recombination between vector and 293 cell Ad5 sequences is greatly reduced. Twelve serial passages of an Ad2 vector lacking the protein IX gene were carried out without generating replication-competent variants. In the course of producing and testing more than 30 large-scale preparations of vectors lacking the protein IX gene or having a rearranged protein IX gene, only three examples of replication-competent variants were observed. Use of these genome modifications allows use of conventional 293 cells for production of large-scale preparations of Ad-based vectors lacking replication-competent variants.

http://www.pubmedcentral.nih.gov/articlerender.fcgi?tool=pubmed&pubmedid=8970968

24. Gene Ther. 1996 Jun;3(6):521-30.

Stabilization of transgene expression by incorporation of E3 region genes into an adenoviral factor IX vector and by transient anti-CD4 treatment of the host.

Poller W, **Schneider-Rasp S**, **Liebert U**, **Merklein F**, **Thalheimer P**, **Haack A**, **Schwaab R**, **Schmitt C**, **Brackmann HH**.

Complex interactions between replication deficient adenoviral vectors (Ad5) and the immune system of the host influence the stability of transgenes in vivo. Vector-infected cells are attacked by diverse cellular immune mechanisms which limit transgene persistence. On the other hand, the products of several E3 region genes of wild-type adenovirus can suppress host immune reactions by interference with the expression of MHC class I molecules and by other mechanisms. We have developed an adenoviral vector for human factor IX (Ad5E3+FIX) which carries the E3 region of wild-type adenovirus, and an E3-deleted vector of otherwise similar structure (ad5 delta E3FIX). Intravenous injection of Ad5E3+FIX in C57BI/6 mice resulted in expression levels up to 6000 ng/ml of recombinant human factor IX in the mouse plasma and in enhanced transgene stability as compared with the vector Ad5 delta E3FIX. Whereas expression from E3-deleted vectors was essentially turned off 8 weeks after the gene transfer, the vector Ad5E3+FIX3+FIX supported transgene expression with therapeutic levels of human factor IX in the mouse plasma for > 4 months. The enhanced stability of the vector Ad5E3+FIX appears to be a consequence of efficient E3 region-mediated suppression of the host's antivector immune response. As an additional approach to improving transgene stability the influence of transient CD4+ T cell depletion of the host was investigated. CD4+ cytotoxic T lymphocytes contribute to the clearance of adenovirus-infected cells and play a pivotal role in the activation of CD8+ cytotoxic T cells and as helper T cells in the formation of human adenovirus neutralizing antibodies (HANA). Transient anti-CD4 treatment of the host limited to the time of vector injection resulted in a significant prolongation of transgene expression from the factor IX vector Ad5E3+FIX and a luciferase vector Ad5Luc. The combination of transient anti-CD4 treatment of the host and integration of a complete E3 region in an adenoviral vector resulted in markedly improved transgene stability after gene transfer to the liver (therapeutic factor IX levels for > 6 months).

http://www.ncbi.nlm.nih.gov/pubmed/8789802?dopt=Abstract

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In vitro and in vivo biology of recombinant adenovirus vectors with E1, E1/E2A, or E1/E4 deleted.

Lusky M, **Christ M**, **Rittner K**, **Dieterle A**, **Dreyer D**, **Mourot B**, **Schultz H**, **Stoeckel F**, **Pavirani A**, **Mehtali M**.

Isogenic, E3-deleted adenovirus vectors defective in E1, E1 and E2A, or E1 and E4 were generated in complementation cell lines expressing E1, E1 and E2A, or E1 and E4 and characterized in vitro and in vivo. In the absence of complementation, deletion of both E1 and E2A completely abolished expression of early and late viral genes, while deletion of E1 and E4

impaired expression of viral genes, although at a lower level than the E1/E2A deletion. The in vivo persistence of these three types of vectors was monitored in selected strains of mice with viral genomes devoid of transgenes to exclude any interference by immunogenic transgene-encoded products. Our studies showed no significant differences among the vectors in the short-term maintenance and long-term (4-month) persistence of viral DNA in liver and lung cells of immunocompetent and immunodeficient mice. Furthermore, all vectors induced similar antibody responses and comparable levels of adenovirus-specific cytotoxic T lymphocytes. These results suggest that in the absence of transgenes, the progressive deletion of the adenovirus genome does not extend the in vivo persistence of the transduced cells and does not reduce the antivirus immune response. In addition, our data confirm that, in the absence of transgene expression, mouse cellular immunity to viral antigens plays a minor role in the progressive elimination of the virus genome.

http://www.ncbi.nlm.nih.gov/pubmed/9499056?ordinalpos=7&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

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Genomic DNA transfer with a high-capacity adenovirus vector results in improved in vivo gene expression and decreased toxicity.

Schiedner G, **Morral N**, **Parks RJ**, **Wu Y**, **Koopmans SC**, **Langston C**, **Graham FL**, **Beaudet AL**, **Kochanek S**.

Many applications for human gene therapy would be facilitated by high levels and long duration of physiologic gene expression. Adenoviral vectors are frequently used for gene transfer because of their high cellular transduction efficiency in vitro and in vivo. Expression of viral proteins and the low capacity for foreign DNA limits the clinical application of first- and second-generation adenoviral vectors. Adenoviral vectors with all viral coding sequences deleted offer the prospect of decreased host immune responses to viral proteins, decreased cellular toxicity of viral proteins and increased capacity to accommodate large regulatory DNA regions. Currently most vectors used in vivo for preclinical and clinical studies express cDNAs under the control of heterologous eukaryotic or viral promoters. Using an adenoviral vector with all viral coding sequences deleted and containing the complete human alpha1-antitrypsin (PI) locus, we observed tissue-specific transcriptional regulation in cell culture and in vivo; intravenous injection in mice resulted in high levels of very stable expression for more than ten months and decreased acute and chronic toxicity. These results indicate significant advantages of regulated gene expression using genomic DNA for gene transfer and of adenoviral gene transfer vectors devoid of all viral coding sequences.

http://www.ncbi.nlm.nih.gov/entrez/utils/fref.fcgi?PrId=3094&itool=AbstractPlus-def&uid=9462752&db=pubmed&url=http://dx.doi.org/10.1038/ng0298-180

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Improved production of gutted adenovirus in cells expressing adenovirus preterminal protein and DNA polymerase.

Hartigan-O'Connor D, **Amalfitano A**, **Chamberlain JS**.

Production of gutted, or helper-dependent, adenovirus vectors by current methods is inefficient. Typically, a plasmid form of the gutted genome is transfected with helper viral DNA into 293 cells; the resulting lysate is serially passaged to increase the titer of gutted virions. Inefficient production of gutted virus particles after cotransfection is likely due to suboptimal association of replication factors with the abnormal origins found in these plasmid substrates. To test this hypothesis, we explored whether gutted virus production would be facilitated by transfection into cells expressing various viral replication factors. We observed that C7 cells, coexpressing adenoviral DNA polymerase and preterminal protein, converted plasmid DNA into replicating virus approximately 50 times more efficiently than did 293 cells. This property of C7 cells can be used to greatly increase the efficiency of gutted virus production after cotransfection of gutted and helper viral DNA. These cells should also be useful for generation of recombinant adenovirus from any plasmid-based precursor.

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Generation of adenovirus by transfection of plasmids.

Berkner KL, **Sharp PA**.

Biologically active fragments of Adenovirus 5 (Ad5) DNA that span the entire genome have been cloned into plasmids. The covalently attached terminal protein was removed and Eco RI linkers added in a fashion that preserves the Ad5 terminal sequences. When plasmids containing overlapping fragments that represent the entire genome are cotransfected onto 293 cells, infectious virus is obtained. Generation of virus depends upon the release of the 0 or 100 mu Ad5 terminus from pBR322 DNA by Eco RI cleavage. During virus production the modified termini of the transfected fragments are corrected exactly to that of wt viral DNA. The above method for preparing adenovirus recombinants has been used to construct a mutant, Ad5 delta (78.9-84.3), lacking most of the non-essential EIII transcriptional unit. This mutant is phenotypically wild type with respect to burst size and kinetics of growth. Surprisingly, it inhibits wt viral growth upon mixed infections of HeLa or 293 cells, apparently at the level of DNA replication.

http://www.ncbi.nlm.nih.gov/pubmed/6310523?ordinalpos=&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.SmartSearch&log$=citationsensor

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Efficient construction of a recombinant adenovirus vector by an improved in vitro ligation method.

Mizuguchi H, **Kay MA**.

An efficient method for constructing a recombinant adenovirus (Ad) vector, based on an in vitro ligation, has been developed. To insert the foreign gene into an adenoviral DNA, we introduced three unique restriction sites, I-CeuI, SwaI, and PI-SceI, into the E1 deletion site of the vector plasmid, which contains a complete E1, E3-deleted adenovirus type 5 genome. I-CeuI and PI-SceI are intron-encoded endonucleases with a sequence specificity of at least 9-10 and 11 bp, respectively. A shuttle plasmid, pHM3, containing multiple cloning sites between the I-CeuI and PI-SceI sites, was constructed. After the gene of interest was inserted into this shuttle plasmid, the plasmid for E1-deleted adenovirus vector could be easily prepared by in vitro ligation using the I-CeuI and PI-SceI sites. SwaI digestion of the ligation products prevented the production of a plasmid containing a parental adenovirus genome (null vector). After transformation into E. coli, more than 90% of the transformants had the correct insert. To make the vector, a PacI-digested, linearized plasmid was transfected into 293 cells, resulting in a homogeneous population of recombinant virus. The large number and strategic location of the unique restriction sites will not only increase the rapidity of production of new first-generation vectors for gene transfer but will allow for rapid further improvements in the vector DNA backbone.

http://www.ncbi.nlm.nih.gov/entrez/utils/fref.fcgi?PrId=3043&itool=AbstractPlus-def&uid=9853524&db=pubmed&url=http://dx.doi.org/10.1089/10430349850019418

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A cell line for high-yield production of E1-deleted adenovirus vectors without the emergence of replication-competent virus.

Gao GP, **Engdahl RK**, **Wilson JM**.

Production of E1-deleted adenovirus vectors for gene therapy has been plagued by the emergence of replication-competent adenovirus. A number of investigators have minimized homologous sequences between the vector and transfected E1 DNA in an attempt to avoid replication-competent adenovirus. We describe a HeLa-based cell line called GH329 that stably expresses the E1 locus from a promoter derived from the phosphoglycerate kinase gene. Overlap sequences with a standard E1-deleted vector that retains a full pIX transcriptional unit have been eliminated at the 5' end and minimized at the 3' end. The GH329 cell line plaques and produces E1-deleted adenovirus as well as 293 cells. Replication-competent virus has emerged after 5 passages of vector on 293 cells but was not detected after 20 passages on GH329 cells.

http://www.ncbi.nlm.nih.gov/entrez/utils/fref.fcgi?PrId=3043&itool=AbstractPlus-def&uid=10646652&db=pubmed&url=http://dx.doi.org/10.1089/10430340050016283

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Construction of nondefective adenovirus type 5 bearing a 2.8-kilobase hepatitis B virus DNA near the right end of its genome.

Saito I, **Oya Y**, **Yamamoto K**, **Yuasa T**, **Shimojo H**.

A novel helper-free adenovirus type 5 (Ad5) vector system, which utilizes a cloning site 0.2 kilobase (kb) from the right end of the genome, has been developed. To construct a nondefective

Ad5 bearing the 2.8-kb DNA fragment of hepatitis B virus (HBV) at this site, we deleted the 2.1-kb nonessential E3 fragment from cloned DNA covering the right one-fourth of the Ad5 genome (76 to 100 map units), inserted the HBV DNA into this site, ligated the recombinant DNA to the rest of the Ad5 genome, and transfected the ligated DNA into human embryo kidney cells. Most of the recovered virus clones had only the E3 deletion and no HBV insertion, suggesting that a homologous recombination occurs between transfected DNAs in these cells. The isolated Ad5 virus bearing the HBV DNA (Ad5-HBL) grew without helper virus in HeLa cells as efficiently as wild-type Ad5, although the 1.9-kb major E4 transcript was detected only poorly in the early phase in the Ad5-HBL-infected cells, suggesting that the HBV DNA inserted upstream of the E4 promoter reduces the E4 transcript. HBV mRNAs transcribed from the inserted DNA were at least as abundant as Ad5 early mRNAs in the late phase of Ad5-HBL infection, but the HBV surface antigen was barely detectable in the infected-cell lysate and culture medium. This result suggests that HBV mRNAs can be transcribed from the inserted genes but no protein can be translated from the HBV mRNAs, presumably because of the translational suppression of cellular mRNAs caused by adenovirus in its late phase.

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Adenovirus E1A N-terminal amino acid sequence requirements for repression of transcription in vitro and in vivo correlate with those required for E1A interference with TBP-TATA complex formation.

Boyd JM, **Loewenstein PM**, **Tang Qq QQ**, **Yu L**, **Green M**.

The adenovirus (Ad) E1A 243R oncoprotein encodes an N-terminal transcription repression domain that is essential for early viral functions, cell immortalization, and cell transformation. The transcription repression function requires sequences within amino acids 1 to 30 and 48 to 60. To elucidate the roles of the TATA-binding protein (TBP), p300, and the CREB-binding protein (CBP) in the mechanism(s) of E1A repression, we have constructed 29 amino acid substitution mutants and 5 deletion mutants spanning the first 30 amino acids within the E1A 1-80 polypeptide backbone. These mutant E1A polypeptides were characterized with regard to six parameters: the ability to repress transcription in vitro and in vivo, to disrupt TBP-TATA box interaction, and to bind TBP, p300, and CBP. Two regions within E1A residues 1 to 30, amino acids 2 to 6 and amino acid 20, are critical for E1A transcription repression in vitro and in vivo and for the ability to interfere with TBP-TATA interaction. Replacement of 6Cys with Ala in the first region yields the most defective mutant. Replacement of 20Leu with Ala, but not substitutions in flanking residues, yields a substantially defective phenotype. Protein binding assays demonstrate that replacement of 6Cys with Ala yields a mutant completely defective in interaction with TBP, p300, and CBP. Our findings are consistent with a model in which the E1A repression function involves interaction of E1A with p300/CBP and interference with the formation of a TBP-TATA box complex.

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Adenovirus types 5 and 35 seroprevalence in AIDS risk groups supports type 35 as a vaccine vector.

Kostense S, **Koudstaal W**, **Sprangers M**, **Weverling GJ**, **Penders G**, **Helmus N**, **Vogels R**, **Bakker M**, **Berkhout B**, **Havenga M**, **Goudsmit J**.

The seroprevalence of adenovirus types 5 (Ad5) and 35 (Ad35) was investigated in patients at risk of AIDS. The seroprevalence of Ad5 was higher than Ad35 in HIV-infected patients from The Netherlands (60% versus 7%) and sub-Saharan Africa (90% versus 20%). The seroprevalence was similar among HIV-infected and uninfected individuals, and remained constant during progression to AIDS. Ad35 is less prone to neutralization than Ad5, encouraging the further development of Ad35 for vaccination against HIV.

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Immunogenicity of recombinant adenovirus serotype 35 vaccine in the presence of pre-existing anti-Ad5 immunity.

Barouch DH, **Pau MG**, **Custers JH**, **Koudstaal W**, **Kostense S**, **Havenga MJ**, **Truitt DM**, **Sumida SM**, **Kishko MG**, **Arthur JC**, **Korioth-Schmitz B**, **Newberg MH**, **Gorgone DA**, **Lifton MA**, **Panicali DL**, **Nabel GJ**, **Letvin NL**, **Goudsmit J**.

The high prevalence of pre-existing immunity to adenovirus serotype 5 (Ad5) in human populations may substantially limit the immunogenicity and clinical utility of recombinant Ad5 vector-based vaccines for HIV-1 and other pathogens. A potential solution to this problem is to use vaccine vectors derived from adenovirus (Ad) serotypes that are rare in humans, such as Ad35. However, cross-reactive immune responses between heterologous Ad serotypes have been described and could prove a major limitation of this strategy. In particular, the extent of immunologic cross-reactivity between Ad5 and Ad35 has not previously been determined. In this study we investigate the impact of pre-existing anti-Ad5 immunity on the immunogenicity of candidate rAd5 and rAd35 vaccines expressing SIV Gag in mice. Anti-Ad5 immunity at levels typically found in humans dramatically blunted the immunogenicity of rAd5-Gag. In contrast, even high levels of anti-Ad5 immunity did not substantially suppress Gag-specific cellular immune responses elicited by rAd35-Gag. Low levels of cross-reactive Ad5/Ad35-specific CD4(+) T lymphocyte responses were observed, but were insufficient to suppress vaccine immunogenicity. These data demonstrate the potential utility of Ad35 as a candidate vaccine vector that is minimally suppressed by anti-Ad5 immunity. Moreover, these studies suggest that using Ad vectors derived from immunologically distinct serotypes may be an effective and general strategy to overcome the suppressive effects of pre-existing anti-Ad immunity.

http://www.ncbi.nlm.nih.gov/entrez/utils/fref.fcgi?PrId=3051&itool=AbstractPlus-def&uid=15128818&db=pubmed&url=http://www.jimmunol.org/cgi/pmidlookup?view=long&pmid=15128818

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Isolation of a common receptor for Coxsackie B viruses and adenoviruses 2 and 5.

Bergelson JM, **Cunningham JA**, **Droguett G**, **Kurt-Jones EA**, **Krithivas A**, **Hong JS**, **Horwitz MS**, **Crowell RL**, **Finberg RW**.

A complementary DNA clone has been isolated that encodes a coxsackievirus and adenovirus receptor (CAR). When transfected with CAR complementary DNA, nonpermissive hamster cells became susceptible to coxsackie B virus attachment and infection. Furthermore, consistent with previous studies demonstrating that adenovirus infection depends on attachment of a viral fiber to the target cell, CAR-transfected hamster cells bound adenovirus in a fiber-dependent fashion and showed a 100-fold increase in susceptibility to virus-mediated gene transfer. Identification of CAR as a receptor for these two unrelated and structurally distinct viral pathogens is important for understanding viral pathogenesis and has implications for therapeutic gene delivery with adenovirus vectors.

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Targeting adenovirus.

Wickham TJ.

The use of targeted viral vectors to localize gene transfer to specific cell types holds many advantages over conventional, non-targeted vectors currently used in gene therapy. The resulting improvements in gene localization from targeted adenovirus vectors are likely to reduce immunogenicity and toxicity, increase safety, and enable the systemic administration of these vectors for multiple indications including cancer, cardiovascular disease, and inflammatory disease. Recent advances in the biological understanding of adenovirus structure and adenovirus receptor interactions have fueled the rapid development of targeted adenovirus vectors. Two basic requirements are necessary to create a targeted adenovirus vector: interaction of adenovirus with its native receptors must be removed and novel, tissue-specific ligands must be added to the virus. Two general approaches have been used to achieve these basic requirements. In the 'two-component' approach, a bispecific molecule is complexed with the adenovirus. The bispecific component simultaneously blocks native receptor binding and redirects virus binding to a tissue-specific receptor. In the 'one-component' approach the adenovirus is genetically modified to ablate native receptor interactions and a novel ligand is genetically incorporated into one of the adenovirus coat proteins. Two-component systems offer great flexibility in rapidly validating the feasibility of targeting via a particular receptor. One-component systems offer the best advantages in producing a manufacturable therapeutic and in more completely ablating all native adenovirus receptor interactions. The coming challenges for targeted adenovirus vectors will be the demonstration that the technology performs in vivo. Ultimately, or in parallel, 'receptor-targeting' technology can be combined with improved adenovirus backbones and with 'transcriptional targeting' approaches to create adenovirus which deliver genes selectively, safely, and with little immune response.

http://www.ncbi.nlm.nih.gov/pubmed/10673715?ordinalpos=8&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

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Replication-deficient human adenovirus type 35 vectors for gene transfer and vaccination: efficient human cell infection and bypass of preexisting adenovirus immunity.

Vogels R, **Zuijdgeest D**, **van Rijnsoever R**, **Hartkoorn E**, **Damen I**, **de Béthune MP**, **Kostense S**, **Penders G**, **Helmus N**, **Koudstaal W**, **Cecchini M**, **Wetterwald A**, **Sprangers M**, **Lemckert A**, **Ophorst O**, **Koel B**, **van Meerendonk M**, **Quax P**, **Panitti L**, **Grimbergen J**, **Bout A**, **Goudsmit J**, **Havenga M**.

Replication-deficient human adenovirus type 5 (Ad5) can be produced to high titers in complementing cell lines, such as PER.C6, and is widely used as a vaccine and gene therapy vector. However, preexisting immunity against Ad5 hampers consistency of gene transfer, immunological responses, and vector-mediated toxicities. We report the identification of human Ad35 as a virus with low global prevalence and the generation of an Ad35 vector plasmid system for easy insertion of heterologous genes. In addition, we have identified the minimal sequence of the Ad35-E1B region (molecular weight, 55,000 [55K]), pivotal for complementation of fully E1-lacking Ad35 vector on PER.C6 cells. After stable insertion of the 55K sequence into PER.C6 cells a cell line was obtained (PER.C6/55K) that efficiently transcomplements both Ad5 and Ad35 vectors. We further demonstrate that transduction with Ad35 is not hampered by preexisting Ad5 immunity and that Ad35 efficiently infects dendritic cells, smooth muscle cells, and synoviocytes, in contrast to Ad5.

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T cell vaccines for microbial infections.

Robinson HL, **Amara RR**.

Vaccination, or the deliberate induction of protective immunity by administering nonpathogenic forms of a microbe or its antigens to induce a memory immune response, is the world's most cost-effective medical procedure for preventing morbidity and mortality caused by infectious disease. Historically, most vaccines have worked by eliciting long-lived plasma cells. These cells produce antibodies that limit disease by neutralizing a toxin or blocking the spread of the infectious agent. For these 'B cell vaccines,' the immunological marker, or correlate, for protection is the titer of protective antibodies. With the discovery of HIV/AIDS, vaccine development has been confronted by an agent that is not easily blocked by antibody. To overcome this, researchers who are developing HIV/AIDS vaccines have turned to the elicitation of cellular immunity, or 'T cell vaccines,' which recognize and kill infected cells.

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DNA vaccines for HIV: challenges and opportunities.

Hokey DA, **Weiner DB**.

In December 2005, the UNAIDS and WHO reported that the global epidemic known as acquired immunodeficiency syndrome (AIDS) has claimed the lives of more than 25 million adults and children over the past 26 years. These figures included an estimated 3.1 million AIDS-related deaths in 2005. Despite enormous efforts to control the spread of human immunodeficiency virus (HIV) new infection rates are on the rise. An estimated 40.3 million people are now living with HIV, including 4.9 million new infections this past year. Nearly half of new HIV infections are in young people between the ages of 15 and 24. While drug therapies have helped sustain the lives of infected individuals in wealthy regions, they are relatively unavailable to the poorest global regions. This includes sub-Saharan Africa which has approximately 25.8 million infected individuals, more than triple the number of infections of any other region in the world. It is widely believed that the greatest hope for controlling this devastating pandemic is a vaccine. In this review, we will discuss the current state of DNA-based vaccines and how they compare to other vaccination methods currently under investigation. We will also discuss innovative ideas for enhancing DNA vaccine efficacy and the progress being made toward developing an effective vaccine.

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A review of vaccine research and development: the human immunodeficiency virus (HIV).

Girard MP, **Osmanov SK**, **Kieny MP**.

Since the discovery of AIDS in 1981, the global spread of HIV has reached pandemic proportions, representing a global developmental and public health threat. The development of a safe, globally effective and affordable HIV vaccine offers the best hope for the future control of the pandemic. Significant progress has been made over the past years in the areas of basic virology, immunology, pathogenesis of HIV/AIDS and the development of antiretroviral drugs. However, the development of an HIV vaccine faces formidable scientific challenges related to the high genetic variability of the virus, the lack of immune correlates of protection, limitations with the existing animal models and logistical problems associated with the conduct of multiple clinical trials. More than 35 vaccine candidates have been tested in Phase I/II clinical trials, involving more than 10,000 volunteers, and two Phase III trials have been completed, themselves involving more than 7500 volunteers. Multiple vaccine concepts and vaccination strategies have been tested, including DNA vaccines, subunit vaccines, live vectored recombinant vaccines and various prime-boost vaccine combinations. This article reviews the state of the art in HIV

vaccine development, summarizes the results obtained so far and discusses the challenges to be met in the development of the various vaccine candidates.

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Current progress in the development of HIV vaccines.

Spearman P.

The greatest hope for controlling the expanding HIV epidemic is the development of a preventive HIV vaccine. Despite almost twenty years of effort, the search for an effective HIV vaccine continues at the present time. Advances in the understanding of HIV immunopathogenesis, and especially viral immune evasion mechanisms, have provided important insights into HIV vaccine design. HIV vaccine approaches based solely on recombinant monomeric envelope glycoproteins have failed dramatically and have been discarded. Modern vector technologies with the potential for generating protective cellular immune responses against HIV are undergoing intensive evaluation in clinical trials. Adenoviral vector systems appear to be very promising for this purpose, while the ability of poxvirus-based regimens to elicit potent HIV-specific cellular immune responses in humans is less certain. A number of novel live vector-based approaches are in development. This review presents the current state of the HIV vaccine field, with an emphasis on those vaccines that are in clinical trials or in an advanced stage of preclinical testing. The HIV vaccine field is a very active and challenging one that will continue to push forward our understanding of basic immunology and drive the development of new vaccine technologies. New breakthroughs in methods to generate effective neutralizing antibody responses against HIV are urgently needed.

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The failed HIV Merck vaccine study: a step back or a launching point for future vaccine development?

Sekaly RP.

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The world of human immunodeficiency virus (HIV) vaccines has suffered a baffling setback. The first trial of a vaccine designed to elicit strong cellular immunity has shown no protection against infection. More alarmingly, the vaccine appeared to increase the rate of HIV infection in individuals with prior immunity against the adenovirus vector used in the vaccine. A new study in this issue suggests that a different vaccine approach-using a DNA prime/poxvirus boost strategy-induces polyfunctional immune responses to an HIV immunogen. The disappointing

results of the recent vaccine trial suggest that a more thorough assessment of vaccine-induced immune responses is urgently needed, and that more emphasis should be placed on primate models before efficacy trials are undertaken.

http://www.ncbi.nlm.nih.gov/entrez/utils/fref.fcgi?PrId=3494&itool=AbstractPlus-nondef&uid=18195078&db=pubmed&url=http://www.pubmedcentral.nih.gov/articlerender.fcgi?tool=pubmed&pubmedid=18195078

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Human versus HIV: round 2 defeat in AIDS vaccine development.
Lu S.

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Challenges in the development of an HIV-1 vaccine.

Barouch DH.

The development of a safe and effective human immunodeficiency virus (HIV)-1 vaccine is a critically important global health priority. Despite recent advances in our understanding of HIV-1 pathogenesis and immunology, however, major scientific obstacles remain. Prototype HIV-1 vaccine candidates aimed at eliciting humoral and cellular immune responses have so far failed to protect against HIV-1 infection or to reduce viral loads after infection in clinical efficacy studies. A renewed and coordinated commitment to basic discovery research, preclinical studies and clinical trials will therefore be required to overcome the hurdles currently facing the field. Here I review key challenges and future prospects in the quest to develop a prophylactic HIV-1 vaccine.

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Comparative seroprevalence and immunogenicity of six rare serotype recombinant adenovirus vaccine vectors from subgroups B and D.

Abbink P, **Lemckert AA**, **Ewald BA**, **Lynch DM**, **Denholtz M**, **Smits S**, **Holterman L**, **Damen I**, **Vogels R**, **Thorner AR**, **O'Brien KL**, **Carville A**, **Mansfield KG**, **Goudsmit J**, **Havenga MJ**, **Barouch DH**.

Recombinant adenovirus serotype 5 (rAd5) vector-based vaccines are currently being developed for both human immunodeficiency virus type 1 and other pathogens. The potential limitations associated with rAd5 vectors, however, have led to the construction of novel rAd vectors derived

from rare Ad serotypes. Several rare serotype rAd vectors have already been described, but a detailed comparison of multiple rAd vectors from subgroups B and D has not previously been reported. Such a comparison is critical for selecting optimal rAd vectors for advancement into clinical trials. Here we describe the construction of three novel rAd vector systems from Ad26, Ad48, and Ad50. We report comparative seroprevalence and immunogenicity studies involving rAd11, rAd35, and rAd50 vectors from subgroup B; rAd26, rAd48, and rAd49 vectors from subgroup D; and rAd5 vectors from subgroup C. All six rAd vectors from subgroups B and D exhibited low seroprevalence in a cohort of 200 individuals from sub-Saharan Africa, and they elicited Gag-specific cellular immune responses in mice both with and without preexisting anti-Ad5 immunity. The rAd vectors from subgroup D were also evaluated using rhesus monkeys and were shown to be immunogenic after a single injection. The rAd26 vectors proved the most immunogenic among the rare serotype rAd vectors studied, although all rare serotype rAd vectors were still less potent than rAd5 vectors in the absence of anti-Ad5 immunity. These studies substantially expand the portfolio of rare serotype rAd vectors that may prove useful as vaccine vectors for the developing world.

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Human immunodeficiency virus type 1 vaccine development: recent advances in the cytotoxic T-lymphocyte platform "spotty business".

Schoenly KA, **Weiner DB**.

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A simian replication-defective adenoviral recombinant vaccine to HIV-1 gag.

Fitzgerald JC, Gao GP, Reyes-Sandoval A, Pavlakis GN, Xiang ZQ, Wlazlo AP, Giles-Davis W, Wilson JM, Ertl HC.

In animal models, E1-deleted human adenoviral recombinants of the serotype 5 (AdHu5) have shown high efficacy as vaccine carriers for different Ags including those of HIV-1. Humans are infected by common serotypes of human adenovirus such as AdHu5 early in life and a significant percentage has high levels of neutralizing Abs to these serotypes, which will very likely impair the efficacy of recombinant vaccines based on the homologous virus. To circumvent this problem, a novel replication-defective adenoviral vaccine carrier based on an E1-deleted recombinant of the chimpanzee adenovirus 68 (AdC68) was developed. An AdC68 construct expressing a codon-optimized, truncated form of gag of HIV-1 induces CD8(+) T cells to gag in mice which at the height of the immune response encompass nearly 20% of the entire splenic CD8(+) T cell population. The vaccine-induced immune response provides protection to challenge with a vaccinia gag recombinant virus. Induction of transgene-specific CD8(+) T cells and protection against viral challenge elicited by the AdC68 vaccines is not strongly inhibited in

animals preimmune to AdHu5 virus. However, the response elicited by the AdHu5 vaccine is greatly attenuated in AdHu5 preimmune animals.

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A CD46-binding chimpanzee adenovirus vector as a vaccine carrier.

Tatsis N, **Blejer A**, **Lasaro MO**, **Hensley SE**, **Cun A**, **Tesema L**, **Li Y**, **Gao GP**, **Xiang ZQ**, **Zhou D**, **Wilson JM**, **Ertl HC**.

A replication-defective chimeric vector based on the chimpanzee adenovirus serotype C1 was developed and tested as a vaccine carrier in mice. The AdC1 virus is closely related to human adenoviruses of subgroup B2 and uses CD46 for cell attachment. To overcome poor growth of E1-deleted AdC1 vectors on cell lines that provide the E1 of adenovirus of the human serotype 5 (AdHu5) virus in trans, the inverted terminal repeats and some of the early genes of AdC1 were replaced with those from AdC5, a chimpanzee origin adenovirus of subfamily E. The chimeric AdC1/C5 vector efficiently transduces CD46-expressing mouse dendritic cells (DCs) in vitro and initiates their maturation. Transduction of DCs in vivo is inefficient in CD46 transgenic mice. The AdC1/C5 vector induces transgene product-specific B- and CD8(+) T-cell responses in mice. Responses are slightly higher in wild-type mice than in CD46 transgenic mice. Transgene product-specific T-cell responses elicited by the AdC1/C5 vector can be increased by priming or boosting with a heterologous adenovirus vector. Pre-existing immunity to adenovirus of the common human serotype 5 does not affect induction of cell-mediated immune responses by the AdC1/C5 vector. This vector provides an additional tool in a repertoire of adenovirus-based vaccine vectors.

http://www.nature.com/mt/journal/v15/n3/abs/6300078a.html

APPENDIX B: Description of Patent Databases & Platforms Used in this Report

Platform Name- Aureka

- Aureka is a Thomson Reuters product
- Patent and non-patent citations are associated with every publication record
- Updated to accommodate IPC R (International Patent Classification Reform) codes
- Full text of global patent documents, including United States (US) patents and applications, European (EP) patents and applications, World Intellectual Property Organization (WO) PCT patent applications, German (DE) patents and applications, French (FR) applications, British (GB) patents and applications, and Japanese (JP) applications
- Includes non-patent citation, including journal articles, book chapters, technical reports, etc. from US, EP, WO, GB, and DE
- Ability to search for a range of PCT publication dates
- Allows the use of Boolean operators and truncation to search specified topics or patent fields
- Ability to sub-search a hitlist to the ideal detail relevant to your needs
- Can import non-patent content to analyze alongside patent information
- US litigation data is displayed in records and is available in the Legal Status view, but it is not searchable
- Document lists are the results of a search or series of searches, listed with the data and in the preferred order
- Users can post messages to make announcements or provide information with co-collaborators
- Useful text-mining module called ThemeScape, which helps companies compare portfolios using pseudo-3D maps with contoured hills representing the patent themes identified
- Clustering tool (Vivismo) extracts and groups records by like concepts into heirarchally organized folders for a quick snapshot
- Citation trees visually depict all reference and referenced patents to a source document in an interactive tool that captures the history, competitive activity, and future of a technology up to five generations

Platform Name- Patent Insight Pro

- Supports US, EP, WOPO, JP, GB, CA and other countries patents
- Users can submit a list of patent numbers in an Excel file or a CSV file and the software will download them one-by-one
- Full Claims section can be separately captured in original PDF format and exported to Word documents
- The Patent Viewer allows quick browsing of patents within the portfolio and includes multi-word highlighting capabilities
- Provides the ability to conduct advanced Boolean searching through patent sets
- The Claims Tree and Claims Comparison Viewer allows users to generate complete claims trees that show all the dependencies within the claims of a patent and allow the comparison of independent claims of different patens in a side-by-side viewer

- The Classification Browser allows users to view US Class and IPC-R details and reverse search for appropriate Class Codes based on the technology name
- The Tabular Word/Excel Export function allows the export of patent summaries with images to Excel and Word
- Automatic language detection of patents with preset nine languages stop-word lists for segmentation according to the detected language
- Includes Automated Patent term cleanup using Thesaurus
- Offers patent mapping, patent alerts, text clustering and auto-categorization, natural language searching, similarity searching, patent landscaping, and co-occurancy analysis

Platform Name - Westlaw
General Information
• Westlaw, which is owned by the Thomson Company, and can be accessed at is a premium access database that is useful for patent law practitioners. It provides access to the Derwent World Patent Index as well as relevant sources, including cases and statutes, patents and patent treatises, and post issuance information, such as KeyCite for patents.
• The value added services from Westlaw can be accessed off the "Patent Practitioner" tab of the user's account after login. This tab includes links to facilitate research in patent literature, cases, statutes, and regulations, court records and litigation tracking. It also provides information on recent developments, litigation practice guides, prosecution practice guides, and forms.
• Includes a link to Delphion that includes access to the full text of US, European, and PCT patents and patent applications, and the patent abstracts from Japan
• Includes the ability to search full-text patents and a link to display the full original patent, including drawings in PDF.
• The Westlaw database contains full-text information of patents before 1972, whereas other services just have bibliographic information.
• Links to Derwent databases, including the World Patent Index
• Citing references provide relevant previous patent literature
• Flexible pricing plans (i.e., large company or single attorney)
• A link to "KeyCites" that covers all patents granted by the USPTO beginning with 1976 utility, design, and plant patents
1. This link also includes access to reissued patents, defensive publications, and statutory invention registrations
2. Can click on the flag on the document or result list or click "Full History" or "Citing References" links on the "Links" tab to retrieve KeyCite information for the patent

Disadvantages:
• Using certain truncations and connectors is difficult when using the Westlaw database
• Hybrid searches often generate a large number of irrelevant results
• Citing references are U.S. only 157
• Data manipulation is less user-friendly in Westlaw than Dialog or Questel/Orbit
• No patent landscaping tools are available
www.westlaw.com

Database Name – Derwent World Patent Index
General Information
• Most comprehensive database of international patent information
• Approximately 19,000 patent documents from over 40 patent-issuing authorities are reviewed and value enhanced by experts
• Documents are read in their native language. Titles and abstracts are then rewritten in English to create a DWPI record
• Included in the record is the drawing from the patent that is most representative of its claims and special indexing to help search for key patent information.
• Can be accessed via Delphion
www.delphion.com

Platform Name – Delphion
General Information
Delphion gives patent collections & searching options inside the world's important patent databases.
Sources:
• United States Patents — Applications (US)
• United States Patents — Granted (US)
• Derwent World Patents Index (DWPI)
• European Patents — Applications (EP-A)
• European Patents — Granted (EP-B)
• German Patents — Applications
• German Patents — Granted
• INPADOC Family and Legal Status
• Patent Abstracts of Japan (JP)
• Switzerland (CH)
• WIPO PCT Publications (WO) Delphion analytical tools give different insights into data:
• Citation Link creates graphical maps of forward and backward references
• Snapshot allows quick online analysis of your results using bar charts
• PatentLab-II supports offline analysis of results with 3D graphs and charts
• Clustering performs keyword-based linguistic analysis
• Corporate Tree facilitates targeted Assignee name searching
The productivity tools help make the most of research efforts:
• Data Extract exports key bibliographic fields in common formats
• Work Files save, organize, annotate and share personalized lists of patents
• Saved Searches saves queries for frequently-used searches
• Alerts automatically notifies you of updates
• PDF Express bulk downloads of up to 500 PDFs
• Patent viewing options include the Delphion Integrated View, both high resolution and low-resolution image options, and a variety of download and delivery options.
www.delphion.com

Platform Name – MicroPatent Family Option

1. Reduce to One Member per Family

In this option, using the default order US-WO-EP-JP-GB-DE-FR for selecting the representative document, the WorkSheet retains only one family member and deletes the other patents from the list. This feature gives the user the basis for analysis of patents by family, eliminating the distortion that results from counting the same invention in each country.

2. Sort by Family

This option sorts all records in your WorkSheet hierarchically into patent families, using INPADOC data. The default order that determines which patent is listed first is US-WO-EP-JP-GB-DE-FR. When a family sort has been performed, the total of families and of patents is displayed at the top of the WorkSheet in the Family Options Section of the header. This feature enables the user to search multiple authorities, yet evaluate the results in family groupings.

APPENDIX C: Definitions of U.S. Classifications

United States Patent Classification System (http://www.uspto.gov/go/classification/)

•A Patent Classification is a code which provides a method for categorizing the invention.
• Classifications are typically expressed as "482/1".
• The first number, 482, represents the class of invention.
• The number following the slash is the subclass of invention within the class.
  - A Subclass definition is a complete description of the subclass.
  - The Subclass Definition can incorporate an explanation of the class, a glossary, search notes, references to subclasses within the class, and references to other classes and subclasses.

• There are about 450 Classes of invention and about 150,000 subclasses of invention in the USPC.
• Classes and subclasses have titles which provide a short description of the class or subclass.
• Classes and subclasses also have definitions which provide a more detailed explanation.
• Many Classes and subclasses have explicitly defined relationships to one another. Subclasses contain patents.
• In a sense, classes also contain patents but for classification purposes patents are always classified at the subclass level.
• That one or more classifications (i.e., class/subclass designations) are assigned to each granted patent and each published application.
• A patent classification also represents a searchable collection of patents grouped together according to similarly claimed subject matter.
• A classification is used both as a tool for finding patents (patentability searches), and for assisting in the assignment of patent applications to examiners for examination purposes.

Classification Codes applicable for this report

- Class 424: Drug, Bio-Affecting and Body Treating Compositions
  - Class 424/93.2: Genetically Modified Micro-Organism, Cell, or Virus (e.g., Transformed, Fused, Hybrid, etc.)
  - Class 424/199.1: Recombinant Virus Encoding One or More Heterologous Proteins or Fragments Thereof
  - Class 424/233.1: Adenoviridae, Adeno-Like Virus, or Parvoviridae (e.g., Adenovirus, Canine Parvovirus, Mink Enteritis Virus, Hemorrhagic Enteritis Virus, Feline Panleukopenia Virus, Egg Drop Syndrome Virus, etc.)
  - Class 424/204.1: Virus or Component Thereof
- Class 435: Chemistry: Molecular Biology and Microbiology
  - Class 435/005: Involving virus or bacteriophage
  - Class 435/069.1: Recombinant DNA Technique Included in Method of Making a Protein or Polypeptide

- Class 435/235.1: Virus or Bacteriophage, Except for Viral Vector or Bacteriophage Vector; Composition Thereof; Preparation or Purification Thereof; Production of Viral Subunits; Media for Propagating
- Class 435/320.1: Vector, Per Se (e.g., Plasmid, Hybrid Plasmid, Cosmid, Viral Vecto, Bacteriophage Vector, etc.)
- Class 435/325: Animal Cell, Per Se (E.G., Cell Lines, Etc.); Composition Thereof; Process of Propagating, Maintaining or Preserving an Animal Cell or Composition Thereof; Process of Isolating Or Separating an Animal Cell or Composition Thereof; Process of Preparing a Composition Containing an Animal Cell; Culture Media Therefore
- Class 435/455: Introduction of a Polynucleotide Molecule into or Rearrangement of Nucleic Acid within an Animal Cell
- Class 435/456: The polynucleotide is encapsidated within a virus or viral coat

• Class 514: Drug, Bio-Affecting and Body Treating Compositions
- Class 514/012: 25 or More Peptide Repeating Units in Known Peptide Chain Structure
- Class 514/044: Polynucleotide (e.g., RNA, DNA, etc.)

• Class 530: Chemistry: Natural Resins or Derivatives; Peptides or Proteins; Lignins or Reaction Products Thereof
- Class 530/350: Proteins, i.e., More than 100 Amino Acid Residues

• Class 536: Organic Compounds: Part of the Class 532-570 Series
- Class 536/ 23.72: Viral Protein

APPENDIX D: Definitions of IPC Classifications

An International Patent Classification (IPC) is a classification drawn from The International Patent Classification System, administered by the World Intellectual Property Organization (WIPO). The IPC divides technology into eight sections with approximately 69,000 subdivisions. Each subdivision has a symbol consisting of Arabic numerals and letters of the Latin alphabet.

Available at: http://www.wipo.int/classifications/fulltext/new_ipc/ipcen.html

Classification Codes applicable for this report

A61K 48/00	Medicinal preparations containing genetic material which is inserted into cells of the living body to treat genetic diseases; Gene therapy
C07K 14/435	Peptides having more than 20 amino acids; Gastrins; Somatostatins; Melanotropins; Derivatives thereof [6] from animals; from humans
C12N 15/861	Mutation or genetic engineering; DNA or RNA concerning genetic engineering, vectors, e.g. plasmids, or their isolation, preparation or purification; Use of hosts therefor (mutants or genetically engineered micro-organisms C12N 1/00, C12N 5/00, C12N 7/00; new plants A01H; plant reproduction by tissue culture techniques A01H 4/00; new animals A01K 67/00; use of medicinal preparations containing genetic material which is inserted into cells of the living body to treat genetic diseases, gene therapy A61K 48/00; peptides in general C07K) *[3,5,6] adenoviral vectors*
A61K 38/00	Medicinal preparations containing peptides (peptides containing beta-lactam rings A61K 31/00; cyclic dipeptides not having in their molecule any other peptide link than those which form their ring, e.g. piperazine-2,5-diones, A61K 31/00; ergoline-based peptides A61K 31/48; containing macromolecular compounds having statistically distributed amino acid units A61K 31/74; medicinal preparations containing antigens or antibodies A61K 39/00; medicinal preparations characterised by the non-active ingredients, e.g. peptides as drug carriers, A61K 47/00) [6]
C12N 15/09	Mutation or genetic engineering; DNA or RNA concerning genetic engineering, vectors, e.g. plasmids, or their isolation, preparation or purification; Use of hosts therefor (mutants or genetically engineered micro-organisms C12N 1/00, C12N 5/00, C12N 7/00; new plants A01H; plant reproduction by tissue culture techniques A01H 4/00; new animals A01K 67/00; use of medicinal preparations containing genetic material which is inserted into cells of the living body to treat genetic diseases, gene therapy A61K 48/00; peptides in general C07K) [3,5,6] recombinant DNA technology
C07K 14/47	Peptides having more than 20 amino acids; Gastrins; Somatostatins; Melanotropins; Derivatives thereof [6] from mammals
C07K 14/005	Peptides having more than 20 amino acids; Gastrins; Somatostatins; Melanotropins; Derivatives thereof [6] from viruses
C12N 5/10	Undifferentiated human, animal or plant cells, e.g. cell lines; Tissues; Cultivation or maintenance thereof; Culture media therefor (plant reproduction by tissue culture techniques A01H 4/00) [3 Cells modified by introduction of foreign genetic material, e.g. virus-transformed cells
C07H 21/00	Measuring or testing processes involving enzymes or micro-organisms (measuring or testing apparatus with condition measuring or sensing means, e.g. colony counters, C12M 1/34); Compositions therefor; Processes of preparing such compositions [3]
C12Q 1/68	involving nucleic acids

APPENDIX E: Derwent Classifications

Description of Derwent Patent Classifications (http://www.delphion.com/derwent/docs/derwentclass.pdf)

• Categorizes patent documents using a simple classification system for all technologies; consistently applied to all patents by Thomson Scientific subject experts, enabling effective and precise searching in a particular area of technology

• International Patent Classification (IPC) is an internationally recognized classification system, which is controlled by the World Intellectual Property Organization (WIPO) and assigned to patent documents by Patent Offices.

• Where possible we indicated next to the Class the equivalent IPC in an abbreviated form (e.g. A47, F23-5).

- However, this should only be taken as a guide, since there are areas where the DWPI
- Classes are assigned intellectually by our subject experts, and no strict correspondence is claimed.

Classification Codes applicable for this report

- Class D16: Fermentation industry – including fermentation equipment, brewing, yeast production, production of pharmaceuticals and other chemicals by fermentation, microbiology, production of vaccines and antibodies, cell and tissue culture and genetic engineering.
- Class B04: Natural products and polymers. Including testing of body fluids (other than blood typing or cell counting), pharmaceuticals or veterinary compounds of unknown structure, testing of microorganisms for pathogenicity, testing of chemicals for mutagenicity or human toxicity and fermentative production of DNA or RNA. General compositions.
- Class C06: Biotechnology – including plant genetic and veterinary vaccines.
- Class A96: Medical, dental, veterinary, cosmetic
- Class S03: Scientific Instrumentation – Photometry, calorimetry. Thermometers. Meteorology, geophysics, measurement of nuclear or X-radiation. Investigating chemical or physical properties.

APPENDIX F: Chemical Patents Index (CPI) Manual Codes

- Derwent manual codes increase the accuracy of online patent searches by arranging patents by categories
- The codes can be used by incorporating them into online search strategies when they are initially being developed
- Many of the codes are redundant by covering a single subject under several codes
- As a result, the searches are extremely narrow and produce only a handful of relevant search results

Classification Codes applicable to this report

- Adenovirus:
    - B04-F11A1 adenovirus
    - B04-F11A1E adenovirus (genetically engineered)
    - B14-A02A1 adenovirus
    - C04-F11A1 adenovirus
    - C04-F11A1E adenovirus (genetically engineered)
    - C14-A02A1 adenovirus
- Vaccine
    - B14-S11 vaccine [general]
    - B14-A06 antiviral
    - B14-S11A antiviral vaccine
    - C14-S11 vaccine [general]
    - C14-S11A antiviral vaccine

APPENDIX G: Current Clinical Trials (as of November, 2008)

Clinical Trial	Brief Description	Principal Investigator (s)	Institution (s)	Status	Access point
A Phase I Randomized, Double-Blind, Placebo Controlled Dose Escalation Clinical Trial to Evaluate the Safety and Immunogenicity of Recombinant Adenovirus Serotype 5 HVR48 HIV-1 Vaccine (Ad5HVR48.ENVA.01) in Healthy, HIV-1 Uninfected Adults	A vaccine that will prevent HIV infection will elicit a strong immune response from both CD4 and CD8 cells. Recombinant adenovirus serotype vectors have been shown to elicit just such a response. The purpose of this study is to determine the safety and immunogenicity of the recombinant adenovirus serotype 5 preventive HIV-1 vaccine.	Lindsey Baden, MD; Dan Barouch, MD	Brigham and Women's Hospital; Beth Israel Deaconess Medical Center	Not yet open for recruitment	Clinicaltrials.gov
A Phase 1B Clinical Trial to Evaluate the Safety and Immunogenicity of Recombinant Adenoviral Serotype 35 (rAd35) and Serotype 5 (rAd5) HIV-1 Vaccines When Given in Heterologous Prime-Boost Regimens or as a Boost to a Recombinant DNA Vaccine in Healthy, HIV-1-Uninfected Adult Participants With Pre-Existing Immunity to Adenovirus Serotype 5 Infection	Due to high prevalence of pre-existing immunity to adenovirus serotype Ad5 in the developing world, this study will evaluate boosting with a different serotype, Ad35, as compared to boosting with the Ad5 serotype. This study will also test the effect of the order of administration of recombinant adenoviral vector HIV vaccines when administered without the DNA plasmid vaccine. Two arms of this study will evaluate the safety and immunogenicity of the experimental multiclade, multigene HIV DNA vaccine VRC-HIVDNA044-00-VP, followed by a similarly structured adenovirus vector vaccine boost (either VRC-HIVADV027-00-VP or VRC-HIVADV038-00-VP), in HIV uninfected adults. To determine the effect of pre-existing Ad5 or Ad35 immunity, the other two arms will test the safety and immunogenicity of receiving either VRC-HIVADV027-00-VP followed by VRC-HIVADV038-00-VP, or vice versa.	Jonathan Fuchs, MD, MPH	San Francisco Department of Public Health, University of California, San Francisco	Ongoing - no longer recruiting	Clinicaltrials.gov

A Phase Ib Clinical Trial to Compare the Safety, Tolerability, and Immunogenicity of an HIV-1 Adenoviral Vector Boost Administered Intramuscularly, Intradermally, or Subcutaneously After an HIV-1 DNA Plasmid Vaccine Prime Administered Intramuscularly to Healthy Adenovirus Type 5 Seropositive HIV-1-Uninfected Adults	This study will evaluate the safety, immunogenicity, and tolerability to a DNA HIV vaccine, followed by an adenoviral vaccine boost given either intramuscularly, intradermally, or subcutaneously, in HIV uninfected adults.	Beryl Koblin, PhD; Martin Casapia, MD	New York Blood Center; Asociación Civil Impacta Salud y Educación (IMPACTA), Peru	Ongoing - no longer recruiting	Clinicaltrials.gov
A Phase I Clinical Trial to Evaluate Immune Response Kinetics and Safety of Two Different Primes, Adenoviral Vector Vaccine (VRC-HIVADV014-00-VP) and DNA Vaccine (VRC-HIVDNA009-00-VP), Each Followed by Adenoviral Vector Boost in Healthy, HIV-1 Uninfected Adults	This study will determine the safety and immune response to the administration of an adenoviral vector HIV vaccine or a DNA HIV vaccine, each followed by an adenoviral vaccine boost, in HIV uninfected adults.	Stephen De Rosa, MD; Spyros A. Kalams, MD	Fred Hutchinson Cancer Research Center and University of Washington; Vanderbilt University	Ongoing - no longer recruiting	Clinicaltrials.gov
A Multicenter Double-Blind Randomized Placebo-Controlled Phase IIB Test-of-Concept Study to Evaluate the Safety and Efficacy of a Three-Dose Regimen of the Clade B-Based Merck Adenovirus Serotype 5 HIV-1 Gag/Pol/Nef Vaccine	The purpose of this study is to evaluate the safety and efficacy of the MRKAd5 HIV-1 gag/pol/nef vaccine in HIV-uninfected participants from South Africa, where clade C is predominant. The study will address whether a clade B-based vaccine designed to elicit T-cellular immunity will demonstrate efficacy in reducing acquisition of infection, or reducing HIV viral load in persons who become infected in a non-clade B region.	Glenda Gray, MD; James Kublin, MD, MPH	Chris Hani Baragwanath Hospital; Fred Hutchinson Cancer Research Center	Suspended	Clinicaltrials.gov
A Phase 1B Open-Label Clinical Trial to Expand the Characterization of the Immune Responses to the Merck Adenovirus Serotype 5 HIV-1 Gag/Pol/Nef Vaccine in Healthy, HIV-1-Uninfected Adult Participants	This study will look for relationships among the immune responses induced by MRKAd5 HIV-1 gag/pol/nef vaccine. The study will also determine if the T cells that respond to different vaccine epitopes have correspondingly different functional profiles. The study will evaluate the safety and tolerability of the vaccine regimen as well.	Ann Duerr, MD, PhD, MPH; Mike Keefer, MD	HVTN Core Operations Center, Fred Hutchinson Cancer Research Center (FHCRC); University of Rochester	Suspended	Clinicaltrials.gov

A Phase 1 Randomized, Double-Blind, Placebo Controlled Dose Escalation Clinical Trial to Evaluate the Safety and Immunogenicity of Recombinant Adenovirus Serotype 26 HIV-1 Vaccine (Ad26.ENVA.01) in Healthy, HIV-1 Uninfected Adults	The purpose of this study is to determine the safety and immunogenicity of the recombinant adenovirus serotype 26 preventive HIV-1 vaccine.	Lindsey Baden, MD; Dan Barouch, MD, PhD; Raphael Dolin, MD	Brigham and Women's Hospital; Beth Israel Deaconess Medical Center; Brigham and Women's Hospital	Currentl y Recruitin g	Clinicaltrials .gov
A Phase II, Randomized, Placebo-Controlled, Double-Blind Trial to Evaluate the Safety and Immunogenicity of a Multiclade HIV-1 DNA Plasmid Vaccine Followed by Recombinant, Multiclade HIV-1 Adenoviral Vector Vaccine in Healthy Adult Volunteers at Risk for HIV Infection	This study will evaluate the safety, tolerability, and immunogenicity of a multiclade HIV-1 DNA plasmid vaccine,VRC-HIVDNA016-00-VP, followed by a multiclade recombinant HIV-1 adenoviral vector vaccine, HIVADV014-00-VP.	Pontiano Kaleebu, MD, PhD	Medical Research Council/Uganda Viral Research Institute (UVRI) Uganda Research Unit on AIDS, UVRI/International AIDS Vaccine Initiative HIV Vaccine Program	Not yet open for recruitm ent	Clinicaltrials .gov
A Phase I, Open Label, CT to Evaluate the Safety, Tolerability and Immunogenicity of a Multiclade Recombinant HIV-1 Adenoviral Vector Vaccine, VRC-HIVADV014-00-VP In Uninfected Adults	This study will compare the immune response and side effects of an experimental HIV vaccine given by two different methods of administration - by needle injection or by use of a needle-free device called the Biojector 2000 (Registered Trademark). The vaccine, called VRC-HIVADV014-00-VP, or rAd5, is made using an adenovirus that has been modified to contain DNA that codes for three HIV proteins. It cannot cause HIV or adenoviral infections.		National Institutes of Health Clinical Center, 9000 Rockville Pike; Bethesda, Maryland, United States, 20892	Recruitin g	Clinicaltrials .gov
VRC 012: A Phase I Clinical Trial of the Safety and Immunogenicity of an HIV-1 Adenoviral Vector Serotype 35 Vaccine: Dose Escalation as a Single Agent and Prime-Boost Schedules With an HIV-1 Adenoviral Vector Serotype 5 Vaccine in Uninfected Adults	The experimental vaccines in this study are the VRC-HIVADV027-00-VP (also called the rAd35-EnvA vaccine) and VRC-HIVADV038-00-VP (also called the rAd5-EnvA vaccine). The vaccines are made using an adenovirus (virus that normally causes respiratory infections and colds) that has been modified to contain DNA that codes for HIV proteins. The vaccines cannot cause HIV or adenoviral infections.		National Institutes of Health Clinical Center, 9000 Rockville Pike; Bethesda, Maryland, United States, 20892	Recruitin g	Clinicaltrials .gov

A Phase IIB Test-of-Concept, Randomized, Double-Blind, Placebo-Controlled, International Clinical Trial to Evaluate the Efficacy, Safety, and Immunogenicity of a Multiclade HIV-1 DNA Plasmid Vaccine, VRC-HIVDNA016-00-VP, Followed by a Multiclade Recombinant Adenoviral Vector Vaccine, VRC-HIVADV014-00-VP, in HIV Uninfected Persons	The purpose of this study is to determine the safety and effectiveness of and immune response to a series of multiclade DNA vaccine injections followed by a booster injection of a multiclade adenovirus vaccine against HIV-1 infection in healthy adults at risk for HIV infection in North and South America, the Caribbean, and Africa.	Scott M. Hammer, MD	Columbia University	Withdrawn prior to recruitment	Clinicaltrials.gov
A Phase I, Randomized, Placebo-Controlled, Double-Blind Trial to Evaluate the Safety and Immunogenicity of a Multiclade HIV-1 DNA Plasmid Vaccine Followed by Recombinant, Multiclade HIV-1 Adenoviral Vector Vaccine or the Multiclade HIV-1 Adenoviral Vector Vaccine Alone in Healthy Adult Volunteers Not Infected with HIV	This study will evaluate the safety and immunogenicity of an experimental adenovirus-vectored multiclade HIV vaccine, VRC-HIVADV014-00-VP, followed with either a similarly structured DNA plasmid HIV vaccine, VRC-HIVDNA016-00-VP, or a placebo. The DNA plasmids in both vaccines code for proteins from HIV subtypes A, B, and C, which together represent 90% of new HIV infections in the world. HIV uninfected volunteers will be recruited in Kenya and Rwanda.	Job Bwayo, MD, PhD; Etienne Karita, MD	Kenya AIDS Vaccine Initiative, University of Nairobi; Project San Francisco	Ongoing - no longer recruiting	Clinicaltrials.gov
Phase II Clinical Trial to Evaluate the Safety and Immunogenicity of a Multiclade HIV-1 DNA Plasmid Vaccine, VRC-HIVDNA016-00-VP, Followed By a Multiclade Recombinant Adenoviral Vector HIV-1 Vaccine Boost, VRC-HIVADV014-00-VP, in HIV-1 Uninfected Adults	This study will evaluate the safety and immunogenicity of an experimental multiclade HIV vaccine, VRC-HIVDNA016-00-VP, followed by a similarly structured adenovirus-vectored vaccine boost, VRC-HIVADV014-00-VP, in HIV uninfected adults. The DNA plasmids in both the vaccines code for proteins from HIV subtypes A, B, and C, which together represent 90% of new HIV infections in the world. Participants in this study will be recruited in North America, South America, and Africa.	Michael Keefer, MD; Gavin Churchyard, MBBCh, FCP, MMed, PhD	University of Rochester; Aurum Health Research Limited	Ongoing - no longer recruiting	Clinicaltrials.gov

VRC 011: A Phase I Clinical Trial of Intramuscular, Subcutaneous and Intradermal Administration of an HIV-1 Multiclade DNA Vaccine, VRC-HIVDNA016-00-VP, and an HIV-1 Multiclade Adenoviral Vector Vaccine,VRC-HIVADV014-00-VP, in Uninfected Adults	This Phase I, randomized, open-label exploratory study will evaluate the safety and tolerability and the immune responses when IM, subcutaneous (SC) or intradermal (ID) routes of administration are used for the priming vaccinations in a prime-boost schedule. The randomization will ensure that subjects with negative and positive screening adenovirus type 5 antibody (Ad5Ab) titers will be equally represented in each prime-boost schedule evaluated in the study.		National Institutes of Health Clinical Center, 9000 Rockville Pike; Bethesda, Maryland, United States, 20892	Ongoing - no longer recruiting	Clinicaltrials.gov
A Phase I Clinical Trial of a Prime-Boost HIV-1 Vaccination Schedule: Multiclade DNA Vaccine, VRC-HIVDNA016-00-VP, Followed by Multiclade Adenoviral Vector Vaccine, VRC-HIVADV014-00-VP, in Uninfected Adults	In this study equal numbers of subjects with high and low Ad5Ab titers will be randomized to receive DNA vaccinations by either needle and syringe (N/S) or by Biojector and then to receive either 1010 PU or 1011 PU rAd booster vaccination in a factorial design. The primary objective is to evaluate the safety and tolerability in humans of the prime-boost vaccination regimen. Secondary objectives are related to evaluation of the immunogenicity of the DNA vaccine when administered by N/S or Biojector, the immunogenicity of the Ad vaccine at two different doses in subjects with high and low pre-enrollment titers of Ad5Ab, the development of adenovirus serotype 5 neutralizing antibody and the social impact of participating in an HIV-1 vaccine trial.		National Institutes of Health Clinical Center, 9000 Rockville Pike; Bethesda, Maryland, United States, 20892	Completed	Clinicaltrials.gov
Phase I Clinical Trial to Evaluate the Safety and Immunogenicity of a Booster Dose of a Recombinant Multiclade HIV-1 Adenoviral Vector Vaccine, VRC-HIVADV014-00-VP, in Uninfected Subjects Who Where Previously Immunized With VRC-HIVDNA016-00-VP	The primary objective is to evaluate the safety and tolerability of a VRC-HIVADV014-00-VP booster vaccination in uninfected subjects who previously received 3 injections of VRC-HIVDNA016-00-VP. The secondary objectives include immunogenicity evaluations, adenovirus serotype 5 (Ad5) antibody titers, and social impacts. Exploratory evaluations include epitope mapping and other immunogenicity evaluations		National Institutes of Health Clinical Center, 9000 Rockville Pike; Bethesda, Maryland, United States, 20892	Completed	Clinicaltrials.gov

Phase I Clinical Trial to Evaluate the Safety and Immunogenicity of a Booster Dose of a Recombinant Multiclade HIV-1 Adenoviral Vector Vaccine, VRC-HIVADV014-00-VP, in Uninfected Subjects Who Were Previously Immunized With VRC-HIVDNA009-00-VP in VRC 004	The primary objective is to evaluate the safety and tolerability of a VRC-HIVADV014-00-VP booster vaccination in uninfected subjects who previously received 3 injections of VRC-HIVDNA009-00-VP more than one year prior to the study vaccination. The secondary objectives include immunogenicity evaluations and adenovirus serotype 5 (Ad5) antibody titers, and social impacts.		National Institutes of Health Clinical Center, 9000 Rockville Pike; Bethesda, Maryland, United States, 20892	Completed	Clinicaltrials.gov
Phase I Clinical Trial to Evaluate the Safety and Immunogenicity of a Recombinant Multiclade HIV-1 Adenoviral Vector Vaccine, VRC-HIVADV014-00-VP, in Uninfected Adult Volunteers	The primary objective is to evaluate the safety and tolerability of VRC-HIVADV014-00-VP in uninfected subjects and the secondary objectives include immunogenicity evaluations and adenovirus serotype 5 (Ad5) antibody titers through Week 4 and social impacts at Week 24.		National Institutes of Health Clinical Center, 9000 Rockville Pike; Bethesda, Maryland, United States, 20892	Completed	Clinicaltrials.gov
A Phase I Clinical Trial to Evaluate the Safety and Immunogenicity of a Prime-Boost HIV-1 Vaccination Schedule of a 6-Plasmid Multiclade HIV-1 DNA Vaccine, VRC-HIVDNA016-00-VP, Followed by a Recombinant Multiclade Adenoviral Vector HIV Vaccine	This study will determine the safety and side effects of two experimental HIV vaccines and see if vaccination can enhance the pre-existing HIV-specific immune response in HIV-infected individuals on anti-retroviral therapy . The vaccines are VRC-HIVDNA016-00-VP (called the "DNA vaccine") and VRC-HIVADV014-00-VP (called the "rAd vaccine"). The DNA vaccine codes for four HIV proteins. The rAd vaccine is made using an adenovirus (a common virus that causes upper respiratory infections, such as the common cold) that has been modified to contain DNA that codes for three HIV proteins. These vaccines will be given in a "prime-boost" schedule and cannot cause HIV or adenoviral infections		National Institutes of Health Clinical Center, 9000 Rockville Pike; Bethesda, Maryland, United States, 20892	Completed	Clinicaltrials.gov
Phase I Dose-Escalation Clinical Trial to Evaluate the Safety and Immunogenicity of a Multiclade, Multivalent Recombinant Adenoviral Vector HIV Vaccine, VRC-HIVADV014-00-VP, in Healthy, HIV-1	The purpose of this study is to determine the safety and immunogenicity of VRC-HIVADV014-00-VP in HIV uninfected adults. In this study, HIV uninfected individuals with low levels of pre-existing adenovirus neutralizing antibodies will receive different doses of the preventive vaccine	Laurence Peiperl, MD	San Francisco Department of Public Health	Ongoing - no longer recruiting	Clinicaltrials.gov

Uninfected Adult Participants Who Have Low Titers of Pre-Existing Ad5 Neutralizing Antibodies	to determine its safety, tolerability, and immunogenicity.				
Phase I/II Clinical Trial to Evaluate the Safety and Immunogenicity of a Multiclade HIV-1 DNA Plasmid Vaccine, VRC-HIVDNA016-00-VP, Boosted by a Multiclade HIV-1 Recombinant Adenovirus-5 Vector Vaccine, VRC-HIVADV014-00-VP, in HIV Uninfected Adult Volunteers	This study will evaluate the safety and immunogenicity of an experimental adenovirus-vectored multiclade HIV vaccine, VRC-HIVADV014-00-VP, followed with or without a similarly structured DNA plasmid HIV vaccine, VRC-HIVDNA016-00-VP. The DNA in both vaccines codes for proteins from HIV subtypes A, B, and C, which together represent 90% of new HIV infections in the world.	Merlin Robb, MD	U.S. Military HIV Research Program	Ongoing - no longer recruiting	Clinicaltrials.gov
Phase II Double-Blind, Randomized, Placebo-Controlled Study to Evaluate the Antiretroviral Effect of Immunization With the MRK Ad5 HIV-1 Gag Vaccine in HIV-1 Infected Individuals Who Interrupt Antiretroviral Therapy	This study will evaluate the ability of immunization with the MRK Ad5 HIV-1 gag vaccine to control HIV replication in individuals undergoing treatment interruption. The study will enroll individuals whose HIV replication has been successfully suppressed with ART for at least 2 years.	Robert T. Schooley, MD	University of Colorado at Denver and Health Sciences Center	Ongoing - no longer recruiting	Clinicaltrials.gov
Phase I Clinical Trial to Evaluate the Safety of a Multiclade Recombinant Adenoviral Vector HIV-1 Vaccine Administered to Healthy, HIV-1 Uninfected, Adult Participants Who Received DNA Plasmid Vaccine or Placebo in the HVTN 052	The purpose of this study is to determine the safety and immunogenicity of a VRC-HIVADV014-00-VP vaccine boost given to healthy, HIV uninfected individuals who participated in HVTN 052, which evaluated the VRC-HIVDNA009-00-VP DNA plasmid vaccine. In that study, participants received either 3 injections of vaccine, 2 injections of vaccine and 1 injection of placebo, or 3 injections of placebo over a 2-month period.	Larry Peiperl, MD; Julie McElrath, MD, PhD	San Francisco Department of Public Health / University of California - San Francisco; Fred Hutchinson Cancer Research Center / University of Washington	Ongoing - no longer recruiting	Clinicaltrials.gov
HVTN 502/Merck 023 (Step) (n=3000); Nonreplicating adenoviral vectors (clade B Gag-Pol-Nef); MRKAd5 trivalent			Merck		http://chi.ucsf.edu/vaccines
HVTN 503 (n=801); Closed to accrual; Nonreplicating adenoviral vectors			Merck		http://chi.ucsf.edu/vaccines

(clade B Gag-Pol-Nef)					
HVTN 050/Merck 018 (n=435); Nonreplicating adenoviral vector (clade B Gag)			Merck		http://chi.ucsf.edu/vaccines
Nonreplicating adenoviral vectors, type 35 (clade A Env)			NIH VRC		http://chi.ucsf.edu/vaccines
HVTN 054 (n=48); Nonreplicating adenoviral vectors (clade B Gag-Pol; clade A,B,C Env)			NIH VRC		http://chi.ucsf.edu/vaccines
HVTN 068 (n=66); Nonreplicating adenoviral vectors (clade B Gag-Pol; clade A,B,C Env)			NIH VRC		http://chi.ucsf.edu/vaccines

APPENDIX H: Author's *Curriculum Vitae*

Mr. Bumrae Cho

99 Clinton St. Unit E9, Concord, NH 03301
Home: 603-219-0226 / Cell: 603-545-5927 / *E-mail*: bcho@piercelaw.edu

Intellectual Property Experience

2009 Oct.- **McKenna Long & Aldridge LLP,** Washington, DC.
Associate

2008 Aug-Dec. **PIPRA (The Public Intellectual Property Resource for Agriculture)**, Davis, CA.
Project Leader of International Technology Transfer Institution Clinic at Franklin Pierce Law Center for Patent Landscape Research Project for HIV Adenovirus Vaccine

2008 May.-Aug. **McKenna Long & Aldridge LLP,** Washington, DC.
Summer Associate
● Won the firmwide business development competition (Summer Associate Challenge)

2008 Jan.-May **Franklin Pierce Law Center,** Concord, NH.
Teaching Assistant for 'IP Research Tools' class
● Assisted with supervision of a team of international students to create report and database dealing with "*Patent Landscape Research Project for HIV DNA Vaccine*"

2007 May-Dec. **PIPRA (The Public Intellectual Property Resource for Agriculture)**, Davis, CA.
Patent Landscape Research Project for specific transgenic plant technology
● EP, PCT, US, Kenyan, Ugandan, Peruvian Patent search
● Analyzed data and created charts
● Wrote research report

2007 Jul.-Aug. **Genzyme Corporation**, Cambridge, MA.
Summer Intern
● Organized INDA data and created reports in relation to RDP58
● Analyzed pre-clinical and clinical data (phase II and III)

2001-2006 **NewKorea International Patent & Law Office**, Seoul, Korea
General Manager of Int'l Dept.; General Manager of Chemical & Biotech Dept.
● Drafted over 300 Korean biotech and chemical patent specifications and office action responses

● Drafted over 200 US biotech and chemical patent specifications and office action responses
● Conducted complex patent searches and analytics using multiple database platforms
● Elaborated over 500 PCT and foreign patent filings for 80-plus countries
● Drafted over 50 Korean patent litigation briefs related to biotechnology
● Drafted over 30 legal opinions for pharmaceutical companies (FTO and patent infringement)
● Developed clients in EU, US, JP, CN and TW: succeeded in invitation of eight times more patent cases than before within 2 years

2000-2001 **L&K Patent Firm**, Seoul, Korea
Legal Assistant,
● Elaborated over 300 PCT and foreign patent applications

Education

Franklin Pierce Law Center, Concord, U.S.A.
J.D./LL.M. in Intellectual Property Law, 2009
(Completed courses in *Patent Law, Patent Practice I&II, Technology Licensing, Law Office Management, Copyright Law, Fundamentals of IP, Law & Biotechnology, Current issues of CAFC, International Comparative Trademark Law, Patent Mining, and IP Research Tools*)

Yonsei University, The Graduate School of Law, Seoul, Korea
LL.M., Intellectual Property Law, 2003

Yonsei University, College of Engineering, Seoul, Korea
B.S., Food and Biotechnology, 1996

Publication

Cho, B, Kenyon, J, and Pence, N. *"Educational Report of the Patent Landscape for the Use of Specific Cry Protein Genes from Bacillus Thuringiensis Sp. in Sweetpotato,"* Franklin Pierce Law Center, December 2007.

Cho, B. *"A Study of Self-Designation of the International Application,"* Yonsei University, The Graduate School of Law, LL.M. dissertation, 2003.

Yu Hui (Lisa) Sung

58 Rumford St.
Concord NH, 03301
Phone: 626-927-6008
Email: Ysung@piercelaw.edu
Lisalssung@gmail.com

Education

Aug. 2006- Present	Franklin Pierce Law Center, Concord NH Master in IP (MIP) (one semester); MIP-JD joint program (will graduate Dec. 2009)
1995-1998	National Chiao Tung University, HsinChu, Taiwan ROC M.S. Applied Chemistry (major in Biochemistry and Protein Expression)
1991-1995	National Chiao Tung University, HsinChu, Taiwan ROC B.S. Applied Chemistry

Work Experience

June 2008 to Aug. 2008	Wilson, Sonsini, Goodrich & Rosati Professional Corporation (Palo Alto office) -- Summer Law Clerk (a) Conducted legal searches for claim construction issues (b) Prepared discovery statements and responses. (c) Reviewed prior arts and prepare a summary for relevant prior arts.
June 2007 to Aug. 2007	Paul, Hastings, Janofsky & Walker LLP (Los Angeles office) -- Summer Law Clerk (a) Reviewed patents and file wrappers. (b) Searched prior arts by US/JP classifications and preparing memo for the results. (c) Drafted discovery requests.
April 2004 To Aug. 2006	AU Optronics Corporation -- Assistant Manager, Technology Office Handled all aspects of US litigation support including: (a) Preparing, collecting and responding to discovery for all patent infringement lawsuits in the US, including one International Trade Commission case and two Federal District Court cases. (b) Interviewed witnesses and prepared summaries. (c) Assisted in preparing expert reports, claim construction briefs, summary judgment motions and trial briefs. (d) Serve as company's designated F.R.C.P. 30(b)(6) witness for numerous subjects.
April 2002 To April 2004	BenQ Corporation -- Patent Engineer (i) Negotiation: (a) Attended negotiation meetings with patentees. (b) Responded to warning letters. (c) Assisted in preparing legal opinions. (ii) Patent prosecution: (a) Interviewed RD engineers and assisted in prior art searches. (b) Revised patent applications drafted by law firms.
Sep. 1999 To April 2002	Acer Display Technology Inc. -- Patent Engineer (a) Built up Patent system in the company. (b) Drafted invention disclosures. (c) Revised patent application drafts prepared by outside law firms for filing in 4 different countries (US, Taiwan, China, and Japan).
July 1998 To Sep. 1999	Deep & Far Attorney-at-law-- Patent Engineer (a) Interviewed clients. (b) Drafted US patent applications. (c) Prepared Office Action responses.

Language Skills:

Chinese - Mandarin (Fluent)	English (Fluent)

Publication and On-going project

1. HIV vaccine technology patents landscape project (Jan. 2008 to Dec. 2008):
   Two professors and several students in Franklin Pierce Law Center are working with the Public Intellectual Property Resource for Agriculture (PIPRA, http://www.pipra.org/) to build an on-line information resource database contains a distilled subset of HIV vaccine technology patents and applications to allow scientists, policy makers and other interested parties to facilitate informed decisions to accelerate research, development, production and deployment of HIV vaccines to developing countries. We also publish a limited access report for the landscaping result each semester.

2. Purification, Characterization and Mechanistic Study of β-Glucosidase from *Flavobacterium meningosepticum* (ATCC 13253) Yaw-Kuen Li, Shi-Her Chu and Yu-Hui Sung, ***Journal of the Chinese Chemical Society, Volume 45, No. 5, October 1998***

MICHELLE WINDOM
mwindom@piercelaw.edu

EDUCATION

Franklin Pierce Law Center, Concord, NH
Candidate for Juris Doctor, 2009
Member, Pierce Law Review
Member, Student Bar Association Finance Committee 1L Representative
Member, Student Intellectual Property Organization

Franklin Pierce Law Center, Concord, NH
Masters of Intellectual Property, 2006
Member, Student Bar Association Finance Committee MIP Representative
Member, Student Intellectual Property Organization

Tulane University, New Orleans, LA
Masters of Engineering, Biomedical Engineering, 2004

Louisiana State University, Baton Rouge, LA
Bachelor of Science, Biological Engineering, 2002
Member, Biological Engineering Society
Member, Zeta Tau Alpha Sorority

EXPERIENCE

Fall 2009 — Oliff & Berridge, PLC
Associate

Summer 2008 — **Oliff & Berridge, PLC**
Summer Associate
- Conducting and attending Examiner interviews
- Drafting patent application and preparing document for publication
- Preparing responses to PTO office actions

Summer 2007 — **Duane Morris LLP** (Philadelphia, PA)
Summer Associate
- Drafting legal memos and briefs
- Preparing responses to PTO office actions
- Legal research

Summer 2006 — **Tulane University Office of Technology Transfer**
Intern
- Patent searching
- Inventor interviews to determine patentability

ALEXANDRE FERRE

37 Alice Drive, Unit 96 **email : aferre@piercelaw.edu**
Concord, NH 03303 **Tel : (603)892 2156**

EDUCATION

Franklin Pierce Law Center, *Concord, NH*
Candidate for Juris Doctor, 2010

Virginia Commonwealth University *(VCU) Richmond, VA*
Bachelor of Science in Biochemistry and Minor in Biology, Cum Laude 2007

PAST EXPERIENCE

Professor Jon Cavicchi, Franklin Pierce Law Center, NH Summer/Fall 2008
International Technology Transfer Institute Patent Landscape Analysis Clinic (ITTI) – Team member
The ITTI Clinic provides instruction in professional skills related to the various responsibilities patent lawyers encounter when preparing patent landscape analysis search reports in biotechnological fields. Legal skills gained: participation in interdisciplinary teams working at the intersection of law and technology, approaches to interviewing and counseling the organizations the ITTI Clinic serves and preventative lawyering.

Dr. Stan Kowalski, Franklin Pierce Law Center, NH Spring 2009
International Technology Transfer Institute Patent Landscape Analysis Clinic (ITTI) – Team leader
A team leader's responsibilities include supervision of team members for the duration of the semester to make sure the project was completed on time and for quality control.

Professor Tom Field, Jr., Franklin Pierce Law Center, NH Spring 2009
Teaching Assistant – Fundamentals of Intellectual Property
Responsibilities include mastery of the material sufficient to hold extra sessions outside of class, supervising the students while they take their quizzes and being a liaison between the students and the professor.

Dr. Qibing Zhou, VCU assistant professor**,** Richmond, VA Fall 2005
Lab Assistant
Volunteered in an organic chemistry lab to work on synthesis of potential anti-cancer drugs. Focused firstly on the effects of natural polyterpene quinone methides derivatives on DNA and secondly on the development of a latent DNA alkylating agent that can be activated through target recognitions.

Mr. Jason Cotrell, VCU co-director of the Campus Learning Center 2005-2006
Tutor and Supplemental Instruction instructor
Tutored and taught courses that students were having difficulty with. Responsibilities included paying attention to individual learning needs, grading assignments and other teach assistant responsibilities.

PATENT TOOLS

Extremely proficient with patent searching tools such as Delphion, Aureka, Dialog, Total Patent, USPTO.gov. Proficiency with some patent analytics program (Aureka, Total Patent, MicroPatent)

LANGUAGES AND COMPUTER SKILLS

Fluent in French and English
Conversational in Spanish and Chinese
Extremely proficient with MS Office products

PROFESSIONAL AFFILIATIONS

AIPLA member since 2007

Constance Ann Rogers

115 S. State Street
Concord, NH 03301
(919) 414–9055
Crogers1@piercelaw.edu

EDUCATION

Franklin Pierce Law Center Concord, NH
Doctor of Jurisprudence/ Master of Laws in Intellectual Property Candidate
May 2009
Willem C. Vis International Commercial Arbitration Moot, Team Member 2007–2008

Tsinghua University Beijing, China
Intellectual Property Summer Institute June–July 2007

North Carolina State University Raleigh, NC
Master of Science, Biochemistry May 2004
Bachelor of Science, Biochemistry May 2002

LEGAL EXPERIENCE

International Technology Transfer Institute Concord, NH
HIV Patent Landscape Project Aug–Dec 2008
Worked on building a database to provide scientists, policy makers and other interested parties with ready access to a distilled subset of HIV vaccine technology patents and patent applications. Searched for patents using Delphion.

International Trade Commission Washington, D.C.
Law Clerk May-August 2008
Worked as a law clerk conducting legal research, drafting legal memoranda, and assisting with litigation.

Franklin Pierce Law Center Concord, NH
Contracts Teaching Assistant Aug–Dec 2007

Legal Assistance of New Hampshire Manchester, NH
Volunteer Summer Law Student May-June 2007
Work included conducting legal research, interpreting statutes, writing memos, and interviewing clients.

BIOCHEMISTRY RESEARCH

Department of Biochemistry and Biophysics, University of North Carolina
Chapel Hill, NC
Research Technician Level III April 2004–July 2006
Research involved the creation of platinated DNA oligomers for NMR Spectroscopy; Included expression, purification, and preparation of protein samples for NMR Spectroscopy; Responsible for the majority of the cloning and mutagenesis work, media, buffer, and reagent preparation

Department of Biochemistry, North Carolina State University
Raleigh, NC
Research Technician Level II Aug 2004–March 2004
Assisted the daily operations of the lab including, but not limited to, expression, purification, and preparation of protein samples for NMR Spectroscopy; Wrote lab protocols and project progress reports

ACTIVITIES AND PROFESSIONAL SOCIETIES

- **Durham Crisis Response Center** 2000-2001, 2005-2006
  Answered and supervised the domestic violence and sexual assault crisis line for Durham County.
- American Intellectual Property Law Association (AIPLA)
- International Intellectual Property Organization (IIPO), Secretary 2007-2008
- Lambda Legal Alliance 2006-2008
- Phi Alpha Delta Legal Fraternity, Marshall 2006-2008
- Student Intellectual Property Law Association (SIPLA) 2006-2008

CYRIL K. CHAN

31 Woburn Street • Andover, MA 01810 • cchan@piercelaw.edu

EDUCATION

Franklin Pierce Law Center, Concord, NH

Juris Doctor

Expected, May 2010

- *IDEA: The Intellectual Property Law Review*, Articles Editor
- IP Newsletter: *Germeshausen Center Newsletter*, Senior Editor
- Patent Landscape Analysis Clinic, International Technology Transfer Institute

University of Illinois at Urbana-Champaign, Urbana, IL

Bachelor of Science in Materials Science & Engineering

May 2007

- Concentrated in Polymer Engineering and in Biomaterials
- Senior design project: Cationic Liposomes for Gene Delivery
- Relevant course work: Plastic Engineering, Polymer Science, Design of Biomaterials, Biomedical Instrumentation, Biomolecular Materials Science, Organic Chemistry

Bachelor of Arts in English

May 2007

- Graduated with Distinction, English Honors Program
- Senior thesis: *The use of language and narrative shifts in the works of Chang-rae Lee*

PROFESSIONAL EXPERIENCE

Summer Associate Summer 2009

Sughrue Mion, PLLC, Washington, D.C.

Legal Intern June 2008 – August 2008

United States Patent and Trademark Office, Alexandria, VA

Office of Patent Legal Administration, Office of the Deputy Commissioner for Patent Examination Policy

- Worked closely with legal advisors in the implementation of patent law.
- Reviewed, edited, and presented proposed rule packages.
- Drafted decisions to various petitions regarding *ex parte* and *inter partes* reexamination proceedings (e.g. petitions for merger or suspension of proceedings, revival of proceedings, waiver of rules, entry of late papers).
- Determined eligibility for PTE under Hatch-Waxman (35 U.S.C. 156).
- Provided legal and policy guidance to members of the public and the patent bar.

Patent Examiner Intern Summers 2006 and 2007

United States Patent and Trademark Office, Alexandria, VA

Chemical and Materials Engineering Unit

- Prosecuted patent applications, including analyzing patentability and drafting office actions such as rejections, restrictions, allowances, and

amendments.

- Examined applications in various fields, including plastic and ceramic processing, glass manufacturing, and tobacco.
- Performed prior art searches using examiner tools.

Ee Ming Tracey Yap

(310) 923-4933 eyap@piercelaw.edu

Education

Franklin Pierce Law Center, Concord, NH
Juris Doctor Candidate, May 2009

Franklin Pierce Law Review, Senior Articles Editor
Daniel Webster Scholar Honors Program Participant: Counsel clients and appear before local judges. Will be sworn into NH bar May 2009.

University of California, Los Angeles, Los Angeles, CA
Bachelor of Arts in English (Patent Bar eligible), June 2005

Publications

Eric Ka-Wai Hui, Ee Ming Yap, Dong Sung An, Irvin S.Y. Chen and Debi P. Nayak, *Inhibition of Influenza Virus Matrix (M1) Protein Expression and Virus Replication by U6 Promoter-Driven and Lentivirus-Mediated Delivery of siRNA*, 85 J. General Virology. 1867–75 (2004).

Relevant Coursework:

Physics – Mechanics, Sound and Light and Hydrodynamics
Chemistry – Structures and Equilibria, Thermodynamics and Kinetics, General and Organic Chemistry Lab, Organic Reactions, Structures and Enzymes and Metabolism

Experience

Oliff and Berridge, PLC Alexandria, VA
Associate Fall 2009

U.S. District Court of New Hampshire, Chief Judge McAuliffe's Chambers
Concord, NH
Extern January 2009-August 2009

Franklin Pierce Law Center Concord, NH
Legal Writing Teaching Assistant August 2007-current
Lead individual and group sessions on the fundamentals of legal writing and legal analysis.

Oliff and Berridge, PLC Alexandria, VA
Summer Associate May 2008-August 2008
Conducted over a dozen personal Examiner interviews at USPTO; wrote Amendments and Requests for Reconsiderations, amended claims for electrical and mechanical engineering

applications; drafted interrogatories, responses, and stipulation motions for ongoing patent litigation; drafted and sent cease and desist letters.

Ostrolenk, Faber, Gerb & Soffen, LLP, New York City, NY
Summer Associate May 2007-August 2007
Drafted amendments and arguments in response to office actions on several types of semiconductor packages.
Drafted abstract and specification to a provisional application about a multi-chip module with copper wire bonds.

International Rectifier Corporation, El Segundo, CA
Legal Consultant August 2005-August 2006
Composed legal memoranda regarding common law interpretations of ambiguities in patent statutes. Conducted prior art searches for patent disclosures pending filing.

Anthrax Microbiology, Immunology and Molecular Genetics Lab,
University of California, Los Angeles, CA
Laboratory Assistant March 2003-July 2005
Prepared high concentration of DNA and protein purified from Luria Broth (LB) and Terrific Broth (TB) cultures, buffers, agarose and protein gels, and cell culture media.

Influenza Microbiology, Immunology and Molecular Genetics Lab,
University of California, Los Angeles, CA
***Student Research Assistant*, Honors Thesis** July 2002-July 2005
Coordinated and designed experiments aimed at suppressing expression of M1 protein. Cultured 293T and Madine Darby Canine Kidney Cells (MDCK). Labeled RNA polymerase III promoters with immuno-florescence proteins.
Developed lab's protocol for competent E. coli Cells for transformation with plasmid DNA. Transfected host cells to identify plaque regions that detect slowed virus growth.

Todd Aaron Pratt

49 Centre Street ♦ Concord, NH 03301 ♦ (603) 219-3891 ♦ tpratt82@yahoo.com

Education

Franklin Pierce Law Center, Concord, NH

Juris Doctor anticipated May 2009

- Patent Bar Eligible, with a focus in Biotechnology.
- Participant in Frederick Douglass Moot Court Competition
- Communication's Director for SIPLA and the J. Reuben Clark Law Society; Member of LES and BLSA

Southern Oregon University, Ashland, OR

Bachelor of Science - Biology, Biomedical, June 2006

- Beta Beta Beta Biological Honor Society

Legal Experience

Oliff & Berridge, PLC, Alexandria, VA 2009 Spring Extern

- I will be assigned to attorneys and will work on patent prosecution.

One Communications Corp., Manchester, NH Summer 2008

- Working as in-house counsel intern, with a focus on ensuring adequate protection of the IP Portfolio and contract work

Schwegman, Lundberg & Woessner, L.L.P., Minnesota Dec '07 - Current

- Working in a satellite office with the claim processing and claim mapping teams, and helping write Office Action responses

Social Security Administration, Manchester, NH 2007

Office of Disability Adjudication and Review, *Opinion Writer*

- Assigned files and wrote opinions for subsequent judicial review

Skills and Interests

- I have strong organizational, interpersonal, and communication skills, that resulted from my educational endeavors and a two year Christian mission in southern Texas.
- Proficiency in WESTLAW, LEXIS, and the Spanish language.
- Interests in running, skiing, wakeboarding, and working on an old 1974 VW Bug. I also enjoy visiting the outdoors with my family whenever possible.

TRISTAN CARRIER

99 Clinton Street Unit 216
Concord, NH 03301
207-314-6863
TCarrier@piercelaw.edu

EDUCATION:

Franklin Pierce Law Center, Concord, NH
Juris Doctor Candidate, May 2010
GPA: 3.11/4.00
Participant, Giles Sutherland Rich Moot Court Competition (Patent Law), Spring 2009
Academic Success Office, Tutor (Civil Procedure & Legal Writing)
Licensing Executives Society (LES) – Vice President

Boston University, College of Engineering, Boston, MA

Bachelor of Science: Biomedical Engineering, 2007
Senior Project: *An Algorithm to Identify Bird Species from their Vocalizations*

- Utilized digital signal processing (DSP) techniques and cross correlation to analyze bio-acoustical signals for identification characteristics.

EXPERIENCE:

Schwegman, Lundberg, & Woessner, P.A., Concord, NH **November 2008-Present**
Patent Mapping Intern

- Provide patent portfolio reporting and strategic analysis services for SLW clients
- Coordinate projects with Schwegman satellite attorneys whom oversee assignments in Concord, NH
- Utilize Schwegman's exclusive patent mapping software which involves: key-word categorizing; ranking & rating based on scope, detectability & design around protection of patents; technical categorizing & portfolio management

Davis, Bujold & Daniels, P.L.L.C., Concord, NH **October 2008-Present**
Law Clerk

- Preparing responses to PTO Office Actions

International Technology Transfer Institute, Pierce Law **Fall 2008**
Patent Landscape Analysis Clinic

- Collaboration with Public Intellectual Property Resource for Agriculture (PIPRA)
- Extensive Patent Research and Data Analysis
- Project Purpose: To compile a database that will provide scientists, policy makers and other interested parties with ready access to a distilled subset of HIV vaccine technology patents and patent applications, so as to facilitate informed decisions in order to accelerate research, development, production and deployment of HIV vaccines to developing countries.

Office of Technology Transfer, Boston University **Summer 2008**
Licensing Analyst

- Assisted with negotiating a term sheet for a start-up company
- Performed Prior Art Searches
  - Ex: "TiB_2 Whiskers as Hydrogen Storage Materials"
  - Ex: "Genetic Approach to Split-Drug Therapy of HIV-infected Cells"
- Assisted with drafting and negotiating licensing agreements
  - Ex: "Nanoimprinting of Photonic Structures on Biocompatible Materials"
  - Ex: "Rodent Diet to Deter Coprophagia"
- Conducted Technology Evaluations

Mills & Onello, LLP, Boston, MA **Summer 2007**

Law Clerk

- Created claims outlines from invention specifications
- Assisted with prior art searches and Information Disclosure Statements

INTERESTS:

Snowboarding, Golf, Rugby, Running, Attending Sporting Events

APPENDIX I: MicroPatent Summary Report for Relevant Patents

(see following pages)

MicroPatent Report

Report Summary:

Name of Session/Report: patent summary2
Report Created: 2008-12-04 - 19:30 GMT
Number of records selected: 296

Table of Contents

1. US7410954B2 A61K UNIV IOWA RES FOUND
ADENOVIRUS SEROTYPE 30 (AD30)
2. US7326692B2 C12N UNIV CHICAGO
INDUCTION OF IMMUNITY USING INHIBITORS OF GRANZYMES
3. US7344873B2 C12N MERCK CO INC
METHODS OF ADENOVIRUS PRODUCTION
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7. US7264958B1 B01J TRANSGENE SA
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MicroPatent Report

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ACNE VACCINE

199. US20020085999A1 C07K USA SECRETARY OF AGRICULTURE A
MAREK'S DISEASE VIRUS GENES AND THEIR USE IN VACCINES FOR PROTECTION AGAINST MAREK'S DISEASE

200. US20020037280A1 C12N
RECOMBINANT, MODIFIED ADENOVIRAL VECTORS FOR TUMOR SPECIFIC GENE EXPRESSION AND USES THEREOF

201. US20020058045A1 A61K NAT INST OF HEALTH SCIENCES
ADENOVIRUS VECTOR

202. US20020072120A1 C12N
HELPER VIRUSES FOR THE PREPARATION OF RECOMBINANT VIRAL VECTORS

203. US20020064859A1 C12N
ADENOVIRUS VECTORS COMPRISING INTRONS

204. US20020061517A1 C12Q
ADENOVIRUS CARRYING GAG GENE HIV VACCINE

205. US20020051966A1 C12N
EFFICIENT GENERATION OF ADENOVIRUS-BASED LIBRARIES BY POSITIVE SELECTION OF ADENOVIRAL RECOMBINANTS THROUGH ECTOPIC EXPRESSION OF THE ADENOVIRUS PROTEASE

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206. US20020034519A1 C12N
MODIFIED BOVINE ADENOVIRUS HAVING ALTERED TROPISM

207. US20020006395A1 C07K
DEFECTIVE ADENOVIRUSES INCLUDING A THERAPEUTIC GENE AND AN IMMUNOPROTECTIVE GENE

208. US20010049136A1 C12N
DEFECTIVE ADENOVIRUSES AND CORRESPONDING COMPLEMENTATION LINES

209. US20020028497A1 B01J
METHOD FOR PRODUCING RECOMBINANT ADENOVIRUS

210. US20020019051A1 C12N
CHIMERIC ADENOVIRAL VECTORS

211. US20010046965A1 C07K
ADENOVIRUS E1-COMPLEMENTING CELL LINES

212. US20010010933A1 C07K GENVEC INC
USE OF TRANS-ACTIVATION AND CIS-ACTIVATION TO MODULATE THE PERSISTENCE OF EXPRESSION OF A TRANSGENE IN AN AT LEAST E4-DEFICIENT ADENOVIRUS

213. US20010026938A1 C12N
ADENOVIRUS MUTANTS WITH DELETED PROTEASE GENE, COMPLEMENTING CELL LINES, AND CORRESPONDING VECTORS FOR GENE TRANSFER AND POSITIVE SELECTION OF RECOMBINANT ADENOVIRAL VECTORS

214. US20010006974A1 A61K
COMBINATION THERAPY FOR LYMPHOPROLIFERATIVE DISEASES

215. EP1224310B1 C12N AVENTIS PHARMA SA
RECOMBINANT ADENOVIRUSES PREPARATION AND ADENOVIRUS BANKS

216. EP1785488A1 A61K CRUCELL HOLLAND BV
ADENOVIRAL VECTORS WITH TWO SEPARATE EXPRESSION CASSETTES

217. EP1201761A1 C12N JAPAN SCIENCE TECH CORP
METHOD OF CONSTRUCTING RECOMBINANT ADENOVIRUS VECTOR

218. EP1201761A4 C12N JAPAN SCIENCE TECH CORP
METHOD OF CONSTRUCTING RECOMBINANT ADENOVIRUS VECTOR

219. EP1054064A1 C12N INTROGENE BV
ADENOVIRUS DERIVED GENE DELIVERY VEHICLES COMPRISING AT LEAST ONE ELEMENT OF ADENOVIRUS TYPE 35

220. EP1000628A1 A61P FOND MONDIALE RECH PREV SIDA
USE OF ANTIGENIC COMPLEXES OF HIV ENVELOPE AND HLA CLASS I ANTIGENS AS HIV VACCINE

221. WO2008025015A2 G06F GOVERNMENT OF THE USA AS REPRE
EPITOPE-TRANSPLANT SCAFFOLDS AND THEIR USE

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222. WO2008025015A3 G06F GOVERNMENT OF THE USA AS REPRE
EPITOPE-PROTEIN SCAFFOLDS AND THEIR USE

223. WO2006120034A1 A61K GLAXO GROUP LTD
VACCINE COMPOSITION

224. WO2006120034A8 A61K GLAXO GROUP LTD
VACCINE COMPOSITION

225. WO2007136763A2 A61K SANOFI PASTEUR INC
IMMUNOLOGICAL COMPOSITION

226. WO2007071997A2 IntC GLAXO GROUP LTD
METHOD OF ELICITING IMMUNE RESPONSE

227. WO2007071997A3 A61P GLAXO GROUP LTD
METHOD OF ELICITING IMMUNE RESPONSE

228. WO2007104792A2 C12N CRUCELL HOLLAND BV
RECOMBINANT ADENOVIRUSES BASED ON SEROTYPE 26 AND 48, AND USE THEREOF

229. WO2007104792A3 A61K CRUCELL HOLLAND BV
RECOMBINANT ADENOVIRUSES BASED ON SEROTYPE 26 AND 48, AND USE THEREOF

230. WO2007094653A1 C12N VERENIGING VOOR CHRISTELIJK HO
ADENOVIRUS PARTICLES HAVING A CHIMERIC ADENOVIRUS SPIKE PROTEIN, USE THEREOF AND METHODS FOR PRODUCING SUCH PARTICLES.

231. WO2007059473A2 C12N INTROGEN THERAPEUTICS INC
METHODS FOR THE PRODUCTION AND PURIFICATION OF ADENOVIRAL VECTORS

232. WO2007059473A3 C12N INTROGEN THERAPEUTICS INC
METHODS FOR THE PRODUCTION AND PURIFICATION OF ADENOVIRAL VECTORS

233. WO2006086284A2 C12Q MERCK CO INC
ADENOVIRUS SEROTYPE 26 VECTORS, NUCLEIC ACID AND VIRUSES PRODUCED THEREBY

234. WO2006108707A1 C12N CRUCELL HOLLAND BV
VIRUS PURIFICATION USING ULTRAFILTRATION

235. WO2006086357A2 C12N MERCK CO INC
ADENOVIRUS SEROTYPE 36 VECTORS, NUCLEIC ACID AND VIRUSES PRODUCED THEREBY

236. WO2006086357A3 C12N MERCK CO INC
ADENOVIRUS SEROTYPE 36 VECTORS, NUCLEIC ACID AND VIRUSES PRODUCED THEREBY

237. WO2005086658A3 C12N ALFA WASSERMANN INC
PROCESSES FOR ADENOVIRUS PURIFICATION USING CONTINUOUS FLOW CENTRIFUGATION

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238. WO2006033672A2 C12N TRUSTEES OF THE UNIVERSITY OF
IMMUNIZATION REGIMEN WITH E4-DELETED ADENOVIRUS PRIME AND E1-DELETED ADENOVIRUS BOOST

239. WO2006033672A3 C12N TRUSTEES OF THE UNIVERSITY OF
IMMUNIZATION REGIMEN WITH E4-DELETED ADENOVIRUS PRIME AND E1-DELETED ADENOVIRUS BOOST

240. WO2005094415A2 C12N WISTAR INST
RECOMBINANT VECTORS AND METHODS FOR INDUCING AN IMMUNE RESPONSE

241. WO2005094415A3 C12N WISTAR INST
RECOMBINANT VECTORS AND METHODS FOR INDUCING AN IMMUNE RESPONSE

242. WO2005071093A2 C12N ANGELETTI P IST RICHERCHE BIO
CHIMPANZEE ADENOVIRUS VACCINE CARRIERS

243. WO2005071093A3 C12N ANGELETTI P IST RICHERCHE BIO
CHIMPANZEE ADENOVIRUS VACCINE CARRIERS

244. WO2005075506A1 C12N SCRIPPS RESEARCH INST
IDENTIFICATION OF ENDOGENOUS TRIMERIZATION DOMAINS IN THE ADENOVIRUS FIBER PROTEIN THAT ALLOW DETARGETING AND RETARGETING OF VIRAL VECTORS

245. WO2005027840A2 A61K CHIRON CORP
COMBINATION APPROACHES FOR GENERATING IMMUNE RESPONSES

246. WO2005027835A2 A61K MERCK CO INC
THERAPEUTIC IMMUNIZATION OF HIV-INFECTED INDIVIDUALS

247. WO2005027835A3 A01N MERCK CO INC
THERAPEUTIC IMMUNIZATION OF HIV-INFECTED INDIVIDUALS

248. WO2004027073A1 C12N CRUCELL HOLLAND BV
MODIFIED ADENOVIRAL VECTORS FOR USE IN VACCINES AND GENE THERAPY

249. WO2004044155A2 A61K BETH ISRAEL HOSPITAL
MIP-1α AND GM-CSF AS ADJUVANTS OF IMMUNE RESPONSE

250. WO2004044155A3 A61K BETH ISRAEL HOSPITAL
MIP-1α AND GM-CSF AS ADJUVANTS OF IMMUNE RESPONSE

251. WO2004044155A8 A61K BETH ISRAEL HOSPITAL
MIP-1ALPHA AND GM-CSF AS ADJUVANTS OF IMMUNE RESPONSE

252. WO2003084479A2 A61K MERCK CO INC
LARGE SCALE METHODS OF PRODUCING ADENOVIRUS AND ADENOVIRUS SEED STOCKS

253. WO2003084479A3 C12N MERCK CO INC
LARGE SCALE METHODS OF PRODUCING ADENOVIRUS AND ADENOVIRUS SEED STOCKS

254. WO2002031170A1 C12N MERCK CO INC
METHOD FOR CIRCULARIZING ADENOVIRAL NUCLEIC ACID VIA HOMOLOGOUS RECOMBINATION

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255. WO2002032943A2 C07K US GOVERNMENT
MODIFICATIONS OF HIV ENV, GAG, AND POL ENHANCE IMMUNOGENICITY FOR GENETIC IMMUNIZATION

256. WO2002032943A3 C07K US GOVERNMENT
MODIFICATIONS OF HIV ENV, GAG, AND POL ENHANCE IMMUNOGENICITY FOR GENETIC IMMUNIZATION

257. WO2002032943A9 C07K US GOVERNMENT
MODIFICATIONS OF HIV ENV, GAG, AND POL ENHANCE IMMUNOGENICITY FOR GENETIC IMMUNIZATION

258. WO2002040693A1 C12N CRUCELL HOLLAND BV
ADENOVIRAL REPLICONS

259. WO2001098513A2 C12N VERENIGING VOOR CHRISTELIJK WE
METHODS AND MEANS FOR THE COMPLEMENTATION OF VIRAL PROTEIN EXPRESSION IN STABLE CELL LINES

260. WO2001098513A3 C12N VERENIGING VOOR CHRISTELIJK WE
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261. WO2001066137A1 A61K MERCK CO INC
ADENOVIRUS FORMULATIONS

262. WO2001044280A2 C12Q GENOVO INC
METHODS AND COMPOSITIONS FOR THE MANUFACTURE OF REPLICATION INCOMPETENT ADENOVIRUS

263. WO2001044280A3 C12Q GENOVO INC
METHODS AND COMPOSITIONS FOR THE MANUFACTURE OF REPLICATION INCOMPETENT ADENOVIRUS

264. WO2001081607A2 C12N CRUCELL HOLLAND BV
ADENOVIRUS VECTORS WITH KNOBLESS FIBERS, AND THEIR USES

265. WO2001081607A3 C12N CRUCELL HOLLAND BV
ADENOVIRUS VECTORS WITH KNOBLESS FIBERS, AND THEIR USES

266. WO2001015511A2 C40B UNIV PITTSBURGH
IDENTIFICATION OF PEPTIDES THAT FACILITATE UPTAKE AND CYTOPLASMIC AND/OR NUCLEAR TRANSPORT OF PROTEINS, DNA AND VIRUSES

267. WO2001015511A3 C40B UNIV PITTSBURGH
IDENTIFICATION OF PEPTIDES THAT FACILITATE UPTAKE AND CYTOPLASMIC AND/OR NUCLEAR TRANSPORT OF PROTEINS, DNA AND VIRUSES

268. WO2001002548A2 C12N GLAXO GROUP LTD
PROPAGATION METHOD

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269. WO2001002548A3 C12N GLAXO GROUP LTD
METHODS FOR THE PROPAGATION OF LYTIC ORGANISMS

270. WO2000063403A2 C12N INTROGENE BV
RECOMBINANT PROTEIN PRODUCTION IN A HUMAN CELL

271. WO2000063403A3 C12N INTROGENE BV
RECOMBINANT PROTEIN PRODUCTION IN A HUMAN CELL USING SEQUENCES ENCODING ADENOVIRUS E1 PROTEIN

272. WO2000075353A1 C12N UNIV PENNSYLVANIA
COMPOSITIONS AND METHODS USEFUL FOR PRODUCTION OF RECOMBINANT VIRUSES WHICH REQUIRE HELPER VIRUSES

273. WO2000073480A1 C12N GENOVO INC
COMPOSITIONS AND METHODS FOR PRODUCTION OF RECOMBINANT VIRUS USING A CARRIER VECTOR DERIVED FROM A NONMAMMALIAN VIRUS

274. WO2000072887A1 C12N SINAI SCHOOL MEDICINE
A NOVEL PACKAGING CELL LINE FOR THE RESCUE, PRODUCTION AND TITRATION OF HIGH-CAPACITY ADENOVIRUS AMPLICON VECTORS

275. WO2000072887A9 C12N SINAI SCHOOL MEDICINE
A NOVEL PACKAGING CELL LINE FOR THE RESCUE, PRODUCTION AND TITRATION OF HIGH-CAPACITY ADENOVIRUS AMPLICON VECTORS

276. WO2000046360A1 A61K MERCK CO INC
IMPROVED HELPER DEPENDENT VECTOR SYSTEM FOR GENE THERAPY

277. WO2000042208A1 C12N NOVARTIS AG
ADENOVIRUS VECTORS, PACKAGING CELL LINES, COMPOSITIONS, AND METHODS FOR PREPARATION AND USE

278. WO2000042208A8 C12N SCRIPPS RESEARCH INST
ADENOVIRUS VECTORS, PACKAGING CELL LINES, COMPOSITIONS, AND METHODS FOR PREPARATION AND USE

279. WO2000034494A1 A61K US HEALTH
A RECOMBINANT VECTOR EXPRESSING MULTIPLE COSTIMULATORY MOLECULES AND USES THEREOF

280. WO2000011140A1 A61K WISTAR INST
METHODS OF AUGMENTING MUCOSAL IMMUNITY THROUGH SYSTEMIC PRIMING AND MUCOSAL BOOSTING

281. WO2000004185A1 C12N MERCK CO INC
ADENOVIRAL BASED PROMOTER ASSAY

282. WO1999064577A1 C12N MERCK CO INC
NOVEL ADENOVIRAL VECTORS FOR GENE THERAPY

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283. **WO1999055894A1** C12N OKLAHOMA MED RES FOUND
CONSTRUCTION OF RETROVIRAL PRODUCER CELLS FROM ADENOVIRAL AND RETROVIRAL VECTORS

284. **WO1999055894A9** C12N OKLAHOMA MED RES FOUND
CONSTRUCTION OF RETROVIRAL PRODUCER CELLS FROM ADENOVIRAL AND RETROVIRAL VECTORS

285. **WO1999054441A1** G01N GENVEC INC
EFFICIENT PURIFICATION OF ADENOVIRUS

286. **WO1999054441A8** G01N GENVEC INC
EFFICIENT PURIFICATION OF ADENOVIRUS

287. **WO1999016466A2** A61K BETH ISRAEL HOSPITAL
VACCINE COMPOSITIONS AND METHODS OF ENHANCING VACCINE EFFICACY

288. **WO1999016466A3** A61K BETH ISRAEL HOSPITAL
VACCINE COMPOSITIONS AND METHODS OF ENHANCING VACCINE EFFICACY

289. **WO1999009194A1** C12N VETERINAIRES ET ALIMENTAIRES C
RECOMBINANT CELO AVIAN ADENOVIRUS AND USE AS VACCINATING VECTOR

290. **WO1997038723A1** C12N IMMUSOL INC
TARGETED VIRAL VECTORS

291. **WO1997031115A2** C12N MERCK CO INC
SYNTHETIC HIV GENES

292. **WO1997031115A3** C12N MERCK CO INC
SYNTHETIC HIV GENES

293. **WO1996022378A1** C12N RHONE POULENC RORER SA
CELLS FOR THE PRODUCTION OF RECOMBINANT ADENOVIRUSES

294. **WO1995024485A2** A61P MERCK CO INC
COORDINATE (IN VIVO) GENE EXPRESSION

295. **WO1995024485A3** A61P MERCK CO INC
COORDINATE IN VIVO GENE EXPRESSION

296. **WO1995016772A1** C12N CORNELL RES FOUNDATION INC
ADENOVIRUS GENE EXPRESSION SYSTEM

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ADENOVIRUS SEROTYPE 30 (AD30)

[71] Applicant: UNIV IOWA RES FOUND

[75] Inventors: Davidson, Beverly L.; Law, Lane K.

[21] Application No.: NA

[22] Filed: 20030715

[43] Published: 20080812

[30] Priority: US US2001758008A 20010109 ...

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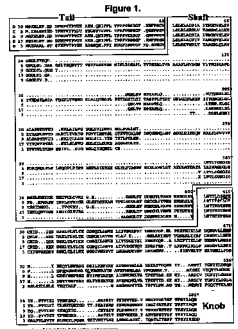

[57] Abstract:

The present invention provides an adenovirus serotype 30 (Ad30) fiber amino acid sequence. The present invention also provides polynucleotides and expression vectors encoding an Ad30 fiber and viral particles and cells containing such expression vectors. The present invention further provides methods of treating genetic diseases or cancers in a mammal using the polynucleotides, polypeptides, expression vectors, viral particles and cells of the present invention.

[52] US Class: 514044 4240932 4241921 4242011 4242331

[51] Int'l Class: A61K0039295 C12N001534 A61K003900 C12N000508 C12N0015861 C07K0014075 A01N006300 A01N004304 C12N000701 A61K0039235 A61K004800 A61K003800 A61K0039175

[52] ECLA: C07K0014075 C12N0015861C K61K003800 K61K004800 M07K020700 M07K031900 M12N081060A1

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INDUCTION OF IMMUNITY USING INHIBITORS OF GRANZYMES

[71] Applicant: UNIV CHICAGO

[75] Inventors: Ashton Rickardt, Philip G.; Opferman, Joseph T.

[21] Application No.: NA

[22] Filed: 20011114

[43] Published: 20080205

[30] Priority: US US2001993363A 20011114

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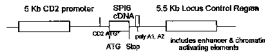

FIG. 1

[57] Abstract:

The present invention provides methods for enhancing host immunity to a virus and/or a cancer and methods for enhancing the cytotoxic T-cell (CTL) mediated immune responses by providing granzyme B inhibitors to a subject. One objective of the invention is to induce long-term protective immunity to a subject in need thereof This is accomplished by providing granzyme inhibitors to the subject which increase the number of memory-CTLs and thereby prevent or alleviate viral infections and/or treat. Providing granzyme inhibitors is also effective in the prevention of cancers. Some examples of granzyme inhibitors contemplated within the present invention include the endogenous serpins such as SPI6 and PI9, other suicide substrates of granzyme B, granzyme B antibodies, etc. Also provided are methods for expression of nucleic acids encoding granzyme inhibitors in cytotoxic T-lymphocytes (CTLs).

[52] US Class: 514044 4240931 4240932 42409321 4353201 435325 435455

[51] Int'l Class: C12N001563 A61K003855 C12N001574 A61K004748 A61K003170 A61K004800 C12N000506 A61K003512

[52] ECLA: A61K003170 A61K003855 A61K004748T4B28 C12N000506B11C K61K003512 M12N051000

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METHODS OF ADENOVIRUS PRODUCTION

[71] Applicant: MERCK CO INC

[75] Inventors: Xie, Liangzhi; Goochee, Charles F.

[21] Application No.: NA

[22] Filed: 20040923

[43] Published: 20080318

[30] Priority: US US2002368654P 20020329 ...

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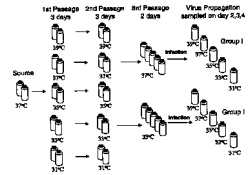

FIGURE 1

[57] Abstract:

A simple yet effective method of increasing production of a thermo-stable virus, such as adenovirus and picornavirus, is presented. The method entails a temperature shift strategy whereby the culture of host cells are shifted to a sub-optimal temperature for a period of time prior to virus infection or cells are grown at a sub-optimal level for the entire cell expansion process including one or more than one passages of cell growth from cryopreserved cells, followed by a shift back to a more optimal temperature at or near the time of virus infection of the respective host cells. Adaptation of such a temperature shift strategy present a simple yet effective method to substantially increase recoverable virus within a respective host cell/virus production scheme without the need to further manipulate other culture and/or media conditions within an established host cell/virus production scheme.

[52] US Class: 4352351 4242331 435325

[51] Int'l Class: C12N000702 A61K0039235 C12N0015861 A61K003923 C12N000700 C12Q000170

[52] ECLA: C12N000700 M12N074003

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RECOMBINANT PORCINE ADENOVIRUS VECTOR

[71] Applicant: VECTOGEN PTY LTD

[75] Inventors: Johnson, Michael Anthony; Hammond, Jeffrey Michael; McCoy, Richard J.; . . .

[21] Application No.: NA

[22] Filed: 20000505

[43] Published: 20080129

[30] Priority: AU AU19978560A 19970814 ...

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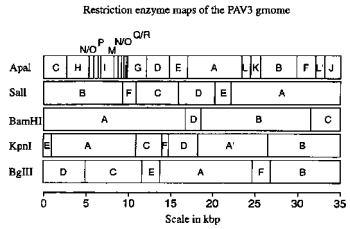
Fig 1.



[57] Abstract:

This invention relates to a recombinant vector including a recombinant porcine adenovirus, stably incorporating and capable of expression of at least one heterologous nucleotide sequence. The nucleotide sequence is preferably one which encodes an antigenic determinant of Hog Cholera Virus or Pseudorabies virus. The further invention relates to a method of production of recombinant vectors, to methods of preparation of vaccines based on the vectors, to administration strategies and to methods of protecting pigs from disease.

[52] US Class: 4241991 4242331 4352351 4353201 435456 435471

[51] Int'l Class: A61P003112 C12N000701 A61K000956 A61P003704 C07K0014535 C12N0015861 A61K000912 C07K001418 C12N001509 A61K0039235 C12N000510 A61K0039295 A61K003900

[52] ECLA: C07K001418F C07K0014535 C12N0015861 K61K003900 M12N022104

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METHODS OF ADENOVIRUS PURIFICATION

[71] Applicant: MERCK CO INC

[75] Inventors: Konz, Jr., John O.; Lee, Ann L.; To, Chi Shung Brian; Goerke, Aaron R

[21] Application No.: NA

[22] Filed: 20041025

[43] Published: 20080205

[30] Priority: US US2002380332P 20020514 ...

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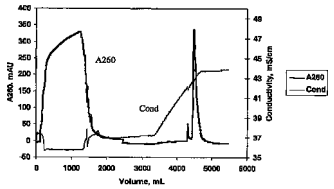

FIGURE 1

[57] Abstract:

A process for purifying virus particles, especially recombinant adenovirus vector particles, is presented. The process relies on various combinations of cell lysis, detergent-based precipitation of host cell contaminants away from the virus, depth filtration or centrifugation, ultrafiltration, nuclease digestion and chromatography to robustly and economically produce highly purified product. This process results in contaminating DNA levels which are consistently below detectable levels.

[52] US Class: 435239 4242331

[51] Int'l Class: A61K0039235 C12N000702

[52] ECLA: C12N000702 C12N0015861 M12N071019

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STABLE ADENOVIRAL VECTORS AND METHODS FOR PROPAGATION THEREOF

[71] Applicant: CRUCELL HOLLAND BV

[75] Inventors: Vogels, Ronald;
Havenga, Menzo Jans Emco;
Zuijdgeest, David Adrianus . . .

[21] Application No.: NA

[22] Filed: 20041025

[43] Published: 20071023

[30] Priority: WO WO2002NL281A 20020425 ...

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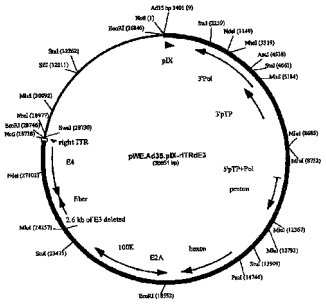
Fig. 1



[57] Abstract:

The present invention provides methods and means to increase the stability and/or the packaging capacity of recombinant adenoviruses, by overexpression of pIX in an adenoviral packaging cell, by retaining at least a part of the E1B 55K region in the recombinant adenoviral vector or by regulating pIX with a heterologous promoter. The invention further relates to methods and means for the production of such adenoviruses on complementing cell lines, wherein the early region 4 open reading frame 6 (E4-orf6) encoding nucleic acid is present in the adenovirus and wherein the E4-orf6 gene product is compatible with one or more products of the E1 gene products in the complementing cell, such that the adenoviral vector can be efficiently produced by the complementing cell.

[52] US Class: 4240932 4353201 435455 435456 5360241

[51] Int'l Class: C12N001501 C12N001500 C12N0015861 C07H002104 A01N006300

[52] ECLA: C12N0015861 K61K0039525C M12N084020

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METHOD FOR OBTAINING A PURIFIED VIRAL PREPARATION

[71] Applicant: TRANSGENE SA

[75] Inventors: Koehl, Michel;
Gaillac, David

[21] Application No.: NA

[22] Filed: 20011210

[43] Published: 20070904

[30] Priority: FR FR19992167A 19990222 ...

Go to Fulltext

[No drawing]

[57] Abstract:

The invention concerns a method for purifying a crude viral preparation containing viral, in particular adenoviral, particles of interest. The invention is characterised in that it comprises a step of adsorption on a fluidised bed. The invention also concerns a protocol for producing viral particles for use in gene therapy comprising such a purifying process.

[52] US Class: 435239 4242041 4242331 435004 435005 4350071

[51] Int'l Class: B01J000818 B01D001508 C12N001509 A61K0039235 C12N000702

[52] ECLA: C12N000702 M12N071019

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US7232889B2 MicroPatent Report

PRO300 ANTIBODIES

[71] Applicant: GENENTECH INC

[75] Inventors: Goddard, Audrey; Godowski, Paul J.; Grimaldi, J. Christopher; Gurney, . . .

[21] Application No.: NA

[22] Filed: 20020501

[43] Published: 20070619

[30] Priority: US US199882797P 19980422 ...

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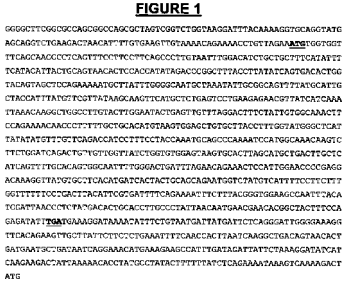
FIGURE 1



[57] Abstract:

The present invention is directed to novel polypeptides and to nucleic acid molecules encoding those polypeptides. Also provided herein are vectors and host cells comprising those nucleic acid sequences, chimeric polypeptide molecules comprising the polypeptides of the present invention fused to heterologous polypeptide sequences, antibodies which bind to the polypeptides of the present invention and to methods for producing the polypeptides of the present invention.

[52] US Class: 5303879 5303871 5303877 5303881 53038815 5303911 5303913

[51] Int'l Class: C07K001600

[52] ECLA: C07K001447

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US7109025B1 MicroPatent Report

VIRAL VECTORS AND VIRAL VACCINES BASED ON RECOMBINANT PORCINE ADENOVIRUSES

[71] Applicant: ENVT TOULOUSE

[75] Inventors: Eloit, Marc; Klonjkowski, Bernard Georges

[21] Application No.: NA

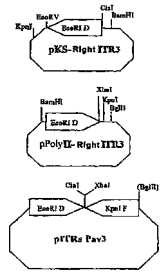
[22] Filed: 20010810

[43] Published: 20060919

[30] Priority: FR FR19991813A 19990211 ...

Go to Fulltext

FIG. 1



[57] Abstract:

An in vivo replicative and recombined porcine adenovirus characterized in that it comprises a heterologous nucleotide sequence inserted into the porcine adenovirus in conditions enabling the latter to be replicated in vivo and to express the inserted heterologous nucleotide sequence, and in that the adenovirus genome comes from a 3 or 5 serotype (PAV-3 or PAV-5) adenovirus. Insertion occurs in a non-essential zone of the E3 region, preferably with deletion of said zone. The invention also relates to a recombined porcine vaccine comprising one such porcine adenovirus. The invention further relates to a serotype 3 or 5 porcine adenovirus vector that is replicative in vivo and is deleted in a non-essential region of the genome thereof. The invention also relates to a DNA fragment comprising all or part of the referenced SEQ ID NO.5 nucleotide sequence.

[52] US Class: 4353201 4352351 4241841 4242021 4242041 4242331

[51] Int'l Class: C12N000701 A61K003939 C12N001534 A61K0039235 C12N0015861 A61P003112 C12N001509 C12N001500 C12N000700

[52] ECLA: C12N0015861

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RECOMBINANT ADENOVIRAL VECTORS EXPRESSING CHIMERIC FIBER PROTEINS FOR CELL SPECIFIC INFECTION AND GENOME INTEGRATION

[71] Applicant: UNIV WASHINGTON

[75] Inventors: Lieber, André; Shayakhmetov, Dmitry M; Farrer, Denise R; . . .

[21] Application No.: NA

[22] Filed: 20011130

[43] Published: 20060822

[30] Priority: US US19991372l3P 19990601 ...

Go to Fulltext

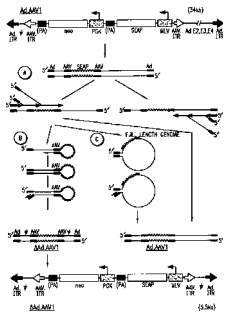

FIG. 1

[57] Abstract:

The present invention provides for novel chimeric Ad-vectors carrying transgene, or portions of transgenes for stable and efficient gene transfer into diverse cell types or tissues in a CAR-and/or $\alpha_u\beta_{3/5}$-independent manner. Also provided are methods for producing such vectors and the use thereof for gene therapy to target a specific cell type or tissue.

[52] US Class: 4240932 42409321 4350691 4353201 435455 435456 5360232 5360241

[51] Int'l Class: C12N001586 C12N001563 C12P002106 C12N001500 A01N006300

[52] ECLA: C12N0015861C C12N0015861T C12N0015864A M12N081040 M12N081060A1 M12N081080

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GENE TRANSFER METHOD

[71] Applicant: TAKARA BIO INC

[75] Inventors: Ueno, Takashi; Matsumura, Hajime; Tanaka, Keiji; Iwasaki, Tomoko; . . .

[21] Application No.: NA

[22] Filed: 20020429

[43] Published: 20060207

[30] Priority: JP JP1999308839A 19991029 ...

Go to Fulltext

Fig. 1

No viral infection

AxCANCre

AxCALNLRep78

AxITRZ

AxCANCre+AxCALNLRep78

AxCANCre+AxITRZ

AxCALNLRep78+AxITRZ

AxCANCre+AxCALNLRep78+AxITRZ

[57] Abstract:

A method of transferring a foreign gene into cells, characterized by involving: the step of transferring into the cells with the use of an adenovirus vector, a first nucleic acid, which has a sequence provided with adeno-associated virus-origin ITRs in both sides of the target foreign gene to be transferred, and a second nucleic acid, which has an adeno-associated virus-origin rep gene and a promoter for expressing this gene and carries a stuffer sequence inserted thereinto sandwiched in two recombinase recognition sequences and located between the rep gene and the promoter; and the step of expressing the Rep protein under the action of recombinase in the cells obtained in the above step to thereby integrate the target foreign gene into the chromosomal DNA.

[52] US Class: 4353201 4240932 435325 435455 435456 435457 435462 435466

[51] Int'l Class: C12N0015861 C12N000701 C12N0015864 A61K004800 C12N000516

[52] ECLA: C12N0015861 M12N080030

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GENE DELIVERY VECTORS WITH CELL TYPE SPECIFICITY FOR MESENCHYMAL STEM CELLS

[71] Applicant: CRUCELL HOLLAND BV

[75] Inventors: Havenga, Menzo
Jans Emco; Bout, Abraham;
Vogels, Ronald

[21] Application No.: NA

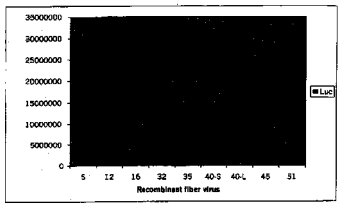
[22] Filed: 20011113

[43] Published: 20050614

[30] Priority: US US2001303734P 20010706 ...

Go to Fulltext

FIG. 1



[57] Abstract:

Methods and associated materials for transducing mesenchymal stem cells with a desired nucleic acid. Mesenchymal stem cells are a recently discovered kind of stem cell for which suitable transfer vehicles are still desired. Typical gene delivery vehicles such as the adenoviruses or adeno associated viruses have no particular tropism for mesenchymal stem cells. Also disclosed is gene therapy using adenoviruses provided with tropism for mesenchymal stem cells.

[52] US Class: 4240932 42409321 4350691 4353201 435325 435455 435456 514044

[51] Int'l Class: C12N001563 C12N000508 C12N0015861 C12N000500 C12N000700 A61K004800 A01N006300 C12N001500

[52] ECLA:

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MEANS AND METHODS FOR FIBROBLAST-LIKE OR MACROPHAGE-LIKE CELL TRANSDUCTION

[71] Applicant: CRUCELL HOLLAND BV

[75] Inventors: Vogels, Ronald;
Schouten, Govert J. ; Bout,
Abraham; Havenga, Menzo . . .

[21] Application No.: NA

[22] Filed: 20000303

[43] Published: 20050322

[30] Priority: US US1999122732P 19990304 ...

Go to Fulltext

[No drawing]

[57] Abstract:

The invention provides a nucleic acid delivery vehicle with or having been provided with at least a tissue tropism for fibroblast-like or macrophage-like cells, preferably synoviocytes. In one aspect the nucleic acid delivery vehicle is a virus capsid or a functional part, derivative and/or analogue thereof. Preferably, the virus capsid is an adenovirus capsid. Preferably, the adenovirus is a subgroup B adenovirus, preferably adenovirus 16. Preferably, the tissue tropism is provided by at least a tissue tropism determining part of an adenovirus fiber protein or a functional derivative and/or analogue thereof. The invention further presents methods for the treatment of diseases, preferably joint related diseases.

[52] US Class: 514044 4240931 4353201 5360231

[51] Int'l Class: C12N0015861 A61K003845 A61K004800

[52] ECLA: A61K003845 C12N0015861T K61K004800 M12N081060A1

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ADENOVIRUS E4 PROTEIN VARIANTS FOR VIRUS PRODUCTION

[71] Applicant: UNIV WAKE FOREST

[75] Inventors: Orlando, Joseph S.; Ornelles, David A.

[21] Application No.: NA

[22] Filed: 20010629

[43] Published: 20050118

[30] Priority: US US2001895940A 20010629

[No drawing]

Go to Fulltext

[57] Abstract:

A method of packaging a recombinant viral vector is carried out by: (a) providing a packaging cell, the packaging cell containing and expressing a nucleic acid encoding a mutant adenovirus E4orf6 protein, the E4orf6 protein containing at least one mutation that renders the protein non-toxic to the host cell; (b) transfecting or infecting the packaging cell with a nucleic acid that encodes a recombinant viral vector (e.g., an adenovirus vector or an adeno-associated virus vector), where the vector lacks a functional gene encoding E4orf6 protein; (c) culturing the transfected cells; and then (d) collecting packaged recombinant viral vector from the cultured cells. Nucleic acids, vectors and packaging cells used for carrying out the methods, as well as proteins utilized in the methods, are also described.

[52] US Class: 435456 4350691 4352351 4353201 435325 435366 435369 435455 435457 5360231 53602372

[51] Int'l Class: C12N0015861 C12N000510 C12N000508 C07K0014075

[52] ECLA: C07K0014075 C12N000510T C12N0015861

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IMMUNOMODULATION BY GENETIC MODIFICATION OF DENDRITIC CELLS AND B CELLS

[71] Applicant: UAB RESEARCH FOUNDATION

[75] Inventors: Curiel, David T.; Tillman, Bryan Walter

[21] Application No.: NA

[22] Filed: 20000612

[43] Published: 20050111

[30] Priority: US US1998102257P 19980929 ...

[No drawing]

Go to Fulltext

[57] Abstract:

The present invention provides a CD40-targeted gene delivery system and a CD40-targeted recombinant adenoviral vector for genetic manipulation of dendritic cells and B cells. Also provided are methods of using this enhanced gene delivery to immune system cells and therefore, enhancing dendritic cell-based immunotherapy.

[52] US Class: 514044 4240931 4240932 42409321 4353201 435325 435455 5360231

[51] Int'l Class: C12N000506 C07K001628 C12N0015861 C07K001608 A61K004800

[52] ECLA: A61K004800 C07K001608A C07K001628B10 C07K001628R C12N000506B11B C12N000506B11D C12N0015861T K61K0039505 K61K0039515B K61K0039515C K61K004800 M07K020700 M07K0316300 M07K0316550 M07K031900 M12N0501220 M12N0501230 M12N051000 M12N081085D M12N081085G

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REPLICATION DEFICIENT ADENOVIRUS VECTORS AND METHODS OF MAKING AND USING THEM

[71] Applicant: UNIV MICHIGAN

[75] Inventors: Imperiale, Michael J.

[21] Application No.: NA

[22] Filed: 20000121

[43] Published: 20050315

[30] Priority: US US2000488867A 20000121

[No drawing]

Go to Fulltext

[57] Abstract:

The invention provides novel replication deficient adenovirus vectors and methods for making and using these viruses. The invention also provides vector systems and kits using a serotype specific strategy for making adenoviral vector preparations substantially free of replication competent "helper" virus. The helper virus-free preparations provide novel pharmaceutical compositions substantially free of helper virus for use in gene transfer and gene therapy.

[52] US Class: 4350914 4240932 4353201 435325 435369 435455 435456 435457 435471 435475

[51] Int'l Class: C12N0015861 C12N000701 C12N000510 A61K004800

[52] ECLA: C12N000510T C12N0015861 K61K004800

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HUMAN AND MOUSE UROPLAKIN II GENE TRANSCRIPTIONAL REGULATORY ELEMENTS

[71] Applicant: CELL GENESYS INC

[75] Inventors: Yu, De Chao; Zhang, Hong; Henderson, Daniel R.

[21] Application No.: NA

[22] Filed: 20010321

[43] Published: 20050208

[30] Priority: US US2000191861P 20000324 ...

[No drawing]

Go to Fulltext

[57] Abstract:

The invention provides new urothelial cell specific transcriptional regulatory sequences derived from human uroplakin II (hUPII), as well as polynucleotide constructs such as adenoviral vectors and methods of using hUPII-derived TREs. Additionally, the invention provides adenoviral vectors comprising a gene, preferably an adenovirus gene, under transcriptional control of a urothelial cell-specific transcriptional regulatory element (TRE). These vectors display urothelial cell-specific cytotoxicity, which is especially useful in the context of bladder cancer, in which destruction of these cells is desirable. The invention further provides compositions and host cells comprising the vectors, as well as method of using the adenoviral vectors.

[52] US Class: 4353201 435006 4350691 4350697 4352351 435455 514044 5360231 5360234 5360241

[51] Int'l Class: C12N0015861 C07K001447 A61K004800

[52] ECLA: C07K001447A1 C12N0015861 C12N0015861T K61K004800 M12N083000C M12N083085 M12N084020 M12N084020A

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ADENOVIRUS GENE EXPRESSION SYSTEM

[71] Applicant: CORNELL RES FOUNDATION INC

[75] Inventors: Falck Pedersen, Erik S.

[21] Application No.: NA

[22] Filed: 19960524

[43] Published: 20041130

[30] Priority: US US1993166925A 19931214 ...

Go to Fulltext

[No drawing]

[57] Abstract:

The invention is directed to an adenoviral vector comprising (a) at least one insertion site for cloning a heterologous gene, and, in an orientation opposite to the direction of transcription of the adenoviral region into which it is inserted, (b) a heterologous promoter positioned upstream from the insertion site, (c) a eukaryotic splice acceptor and splice donor site positioned between the promoter and the insertion site; and (c) a polyadenylation sequence positioned downstream of the insertion site. The invention also provides a host cell infected with such a vector, a method of producing a selected protein, and a method of delivering a heterologous gene to an animal heart.

[52] US Class: 4240932 4240931 4350691 4353201 435325 435456 514044 5360231 5360241

[51] Int'l Class: C12N0015861 C07K001472 C07K001457

[52] ECLA: C07K001457 C07K001472B C12N0015861 M07K020700 M12N083038 M12N083044

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COMPOSITIONS AND METHODS FOR INCREASING PACKAGING AND YIELD OF RECOMBINANT ADENOVIRUSES USING MULTIPLE PACKAGING SIGNALS

[71] Applicant: TRUSTEES OF THE UNIVERSITY OF

[75] Inventors: Gao, Guangping; Wilson, James M.

[21] Application No.: NA

[22] Filed: 20020530

[43] Published: 20041123

[30] Priority: US US1999169025P 19991203 ...

Go to Fulltext

[No drawing]

[57] Abstract:

A recombinant adenoviral vector which has multiple adenovirus packaging domains is provided. This vector has advantages over conventional adenoviral vectors in packaging plasmid vectors into adenoviral capsids. Methods of making and using this vector are described.

[52] US Class: 4240932 4240931 4240936 4350691 4353201 435325 435455 435456 435457

[51] Int'l Class: C12N0015861 A61K004800

[52] ECLA: C12N0015861 K61K004800

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PREPARATION AND USE OF VIRAL VECTORS FOR MIXED ENVELOPE PROTEIN VACCINES AGAINST HUMAN IMMUNODEFICIENCY VIRUSES

[71] Applicant: ST JUDE CHILDRENS RES HOSPITAL

[75] Inventors: Hurwitz, Julia; Coleclough, Christopher; Owens, Randall; Slobod, . . .

[21] Application No.: NA

[22] Filed: 20000510

[43] Published: 20040420

[30] Priority: US US1996590288A 19960123 ...

Go to Fulltext



[57] Abstract:

Polyenv vaccines are provided that comprise mixtures of at least 4 to about 10,000 different recombinant viruses that each express a different HIV env variant or a portion thereof containing both constant and variable regions, as well as methods of making and using such polyenv vaccines and viruses, including the use of the polyenv vaccine, in live, attenuated or inactivated form, for prophylaxis or treatment of HIV infection. The viral vaccines of the invention are optimally combined with a recombinant HIV env booster, or a recombinant HIV env gene DNA priming or boosting vaccine.

[52] US Class: 4353201 4241601 4241991 4242081 4242301 514044 5360231 5360232

[51] Int'l Class: C07K001416 A61K003921 C12N0015863 A61K003900 A61K003812

[52] ECLA: A61K003921 C07K001416D C12N0015863V K61K003812 K61K003900 M07K020700 M07K022100 M07K022104 M07K022112 M07K022120

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RECOMBINANT ADENOVIRAL VECTORS

[71] Applicant: TRANSGENE SA

[75] Inventors: Rooke, Ronald

[21] Application No.: NA

[22] Filed: 20011004

[43] Published: 20040217

[30] Priority: EP EP2000440267A 20001006 ...

Go to Fulltext

[No drawing]

[57] Abstract:

The present invention concerns a recombinant adenoviral vector derived from an adenovirus genome in which at least a part of the E3 region is deleted or is non functional, wherein said adenoviral vector retains E3 sequences encoding a functional 14.7K protein, a functional 14.5K protein, and/or a functional 10.4K protein. The present invention further relates to the use of a polynucleotide comprising at least one or more gene(s) of an E3 region of an adenovirus, taken individually or in combination, to protect from an inflammatory reaction in a host cell, tissue or organism. The present invention additionally concerns a viral particle, a host cell and a composition comprising said recombinant adenoviral vector or said polynucleotide, as well as their use for therapeutic or prophylactic purpose.

[52] US Class: 4353201 4242331

[51] Int'l Class: C12N0015861 C07K0014075 A61K004800 A61K003900

[52] ECLA: C07K0014075 C12N0015861 K61K003900 K61K0039525C K61K003953 K61K004800 M07K020700 M12N083042 M12N083044 M12N084020A

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METHODS AND COMPOSITIONS FOR THE LARGE SCALE PRODUCTION OF RECOMBINANT ADENO-ASSOCIATED VIRUS

[71] Applicant: UAB RESEARCH FOUNDATION

[75] Inventors: Dong, Jianyun; Frizzell, Raymond A.

[21] Application No.: NA

[22] Filed: 19930831

[43] Published: 20040203

[30] Priority: US US1993114595A 19930831

Go to Fulltext

[No drawing]

[57] Abstract:

This invention provides novel methods and compositions for use in the efficient and large-scale production of recombinant adeno-associated virus (AAV). Described herein are new producer cell lines, recombinant adenovirus or herpes virus vectors and AAV constructs. Also disclosed are particularly advantageous methods of using such materials to produce recombinant AAV virions using only the efficient process of viral infection, without requiring transfection steps. The AAV produced may be used in a variety of embodiments including, for example, for transferring exogenous genes into human cell lines and for use in human gene therapy regimens.

[52] US Class: 435457 4350691 4352351 4353201 435325 435366 435455 435456

[51] Int'l Class: C12N0015864 C12N0015861 C12N0015869 C12N000704 C07K001447

[52] ECLA: C07K001447A4 C12N000704A C12N0015861 C12N0015864A C12N0015869

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HYBRID VECTORS FOR GENE THERAPY

[71] Applicant: UNIV CALIFORNIA

[75] Inventors: Kasahara, Noriyuki; Higo, Collin; Soifer, Harris; Mitani, Kohnosuke

[21] Application No.: NA

[22] Filed: 20000118

[43] Published: 20030610

[30] Priority: US US1999116150P 19990115 ...

Go to Fulltext

[No drawing]

[57] Abstract:

The invention discloses hybrid vectors for delivering genes or other nucleic acids into mammalian cells. The hybrid vectors of the invention contain both a helper dependent adenoviral portion and a second portion derived from either a replication incompetent retrovirus or from a transposon. Such vectors provide efficient transduction of quiescent cells and provide for stable integration of the gene to be delivered.

[52] US Class: 4353201 4240931 4240932 4240936 4350691 4352351 435455 435456 435457

[51] Int'l Class: C12N0015861 A61K004800

[52] ECLA: C12N0015861 C12N0015861C K61K004800 M12N080030 M12N080090 M12N083044 M12N084020

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PERMANENT AMNIOCYTIC CELL LINE, ITS PRODUCTION AND USE FOR THE PRODUCTION OF GENE TRANSFER VECTORS

[71] Applicant: KOCHANEK STEFAN; SCHIEDNER GUDRUN

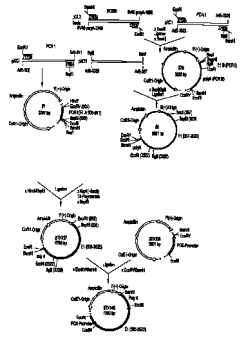
[75] Inventors: Kochanek, Stefan; Schiedner, Gudrun

[21] Application No.: NA

[22] Filed: 20001116

[43] Published: 20030506

[30] Priority: US US1999167439P 19991123 ...



Go to Fulltext

[57] Abstract:

The invention relates to a permanent amniocytic cell line comprising at least one nucleic acid which brings about expression of the gene products of the adenovirus E1A and E1B regions. The present invention further relates to the production of a permanent amniocytic cell line and to its use for producing gene transfer vectors and/or adenovirus mutants. Further aspects are the use of amniocytes and of the adenoviral gene products of the E1A and E1B regions for producing permanent amniocytic cell lines.

[52] US Class: 435325 4242331 4350691 4350701 4353201 435366 435372

[51] Int'l Class: C12N000506

[52] ECLA: C12N000506B2L M12N051002

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MODIFIED ADENOVIRAL FIBER AND TARGET ADENOVIRUSES

[71] Applicant: TRANSGENE SA; CENTRE NAT RECH SCIENT

[75] Inventors: Legrand, Valérie; Mehtali, Majid; Boulanger, Pierre

[21] Application No.: NA

[22] Filed: 19991004

[43] Published: 20030527

[30] Priority: FR FR19973987A 19970402 ...

Go to Fulltext

[No drawing]

[57] Abstract:

The invention relates to an adenovirus fiber modified by the mutation of one or more residues. The residues are directed towards the natural cell receptor in the three-dimensional structure of said adenovirus. The invention further relates to a DNA fragment, and expression vector, and a cell line expressing said fiber, and also concerns an adenovirus, the process for producing this type of adenovirus, and a infectable host cell, as well as their therapeutic application and a corresponding pharmaceutical composition.

[52] US Class: 4353201 4240932 4350914 514044

[51] Int'l Class: A61K003855 C12N000700 A61K003827 A61K0039395 C07K0014075 C12N001534 A61K003800 A61K004800 A61K003828 A61K003576 C12N001509 C12N0015861 C12N000510 A61K003843

[52] ECLA: C07K0014075 C12N0015861 K61K003800 M07K020500 M07K020700 M07K021300 M07K022104 M07K031900 M12N071019 M12N071019B

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METHODS FOR PRODUCING AN IMMUNE RESPONSE AGAINST HIV-1

[71] Applicant: DAVIS ALAN R; HUNG PAUL P; LUBECK MICHAEL D; NATUK ROBERT J; CHANDA . . .

[75] Inventors: Davis, Alan R.; Hung, Paul P.; Lubeck, Michael D.; Natuk, Robert J. . . .

[21] Application No.: NA

[22] Filed: 20000718

[43] Published: 20030128

[30] Priority: US US1992926491A 19920807 ...

Go to Fulltext

[No drawing]

[57] Abstract:

This invention provides a method of protecting a primate from an infectious organism by stimulating the production of antibodies or cell mediated immunity to the infectious organism which comprises administering to said primate intranasally, intramuscularly, or subcutaneously, live recombinant adenoviruses in which the virion structural protein is unchanged from that in the native adenovirus from which the recombinant adenovirus is produced, and which contain the gene coding for the antigen corresponding to said antibodies or inducing said cell mediated immunity. Preferably, the infectious organism is HIV and the primate is a human.

[52] US Class: 4353201 4240931 4240936 4241991 4242081 4242331 4350691

[51] Int'l Class: C12N001548 C12N001507 C12N0015861 C07K001416 A61K003900

[52] ECLA: C07K001416 C07K001416B C07K001416D C12N0015861 K61K003900 M07K020700

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COMPLEMENTING CELL LINES

[71] Applicant: CRUCELL HOLLAND BV

[75] Inventors: Vogels, Ronald; Havenga, Menzo; Mehtali, Majid

[21] Application No.: NA

[22] Filed: 20001115

[43] Published: 20021210

[30] Priority: US US1999134764P 19990518 ...

Go to Fulltext

[No drawing]

[57] Abstract:

A packaging cell line capable of complemention recombinant adenoviruses based on serotypes from subgroup B, preferably adenovirus type 35. The cell line is preferably human embryonic kidney cells and primary human amniocytes) which are transformed by adenovirus E1 sequences either operatively linked on one DNA molecule or located on two separate DNA molecules, the sequences being operatively linked to regulatory sequences enabling transcription and translation of encoded proteins.

[52] US Class: 435325 4350691 4352351 435455

[51] Int'l Class: C12N001535 C12N000700 C12N001563 C12N001574 C12N000510 C12N001570 C12N001500 C12N000502 A61K004800 C12N0015861 C12N001509

[52] ECLA: C12N0015861 C12N000510T M12N083000

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METHODS AND COMPOSITIONS FOR PRODUCING VIRAL PARTICLES

[71] Applicant: AVENTIS PHARMA SA; GENOPOIETIC

[75] Inventors: Torrent, Christophe; Yeh, Patrice; Perricaudet, Michel; . . .

[21] Application No.: NA

[22] Filed: 20010125

[43] Published: 20021203

[30] Priority: FR FR19986258A 19980518 ...

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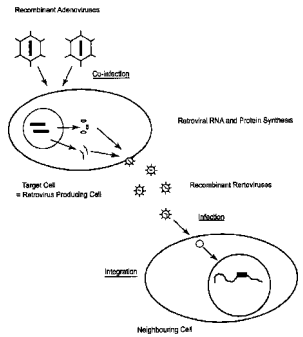

[57] Abstract:

The invention concerns methods and constructs for producing retroviral particles, in vitro, ex vivo or in vivo. It also concerns the use of said methods and constructs for transferring nucleic acids into cells. More particularly, the invention concerns a composition comprising the whole set of genetic elements required for constituting a retroviral particle, incorporated in one or several recombinant adenoviruses defective for all or part of the regions E1 and E4 at least (adenoviral/retroviral chimeric vectors).

[52] US Class: 4350691 435006 4350697 5303873 5360234 53602372

[51] Int'l Class: C12N000700 C12N000510 C12N0015861 C07K001415 C12N001509 C12N0015867

[52] ECLA: C07K001415 C12N0015861 C12N0015867 M07K022104 M12N084020

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BOVINE CELLS EXPRESSING ADENOVIRUS ESSENTIAL FUNCTIONS FOR PROPAGATION OF RECOMBINANT ADENOVIRAL VECTORS

[71] Applicant: UNIV SASKATCHEWAN

[75] Inventors: Tikoo, Suresh Kumar; Babiuk, Lorne A.; Reddy, Police Seshidhar

[21] Application No.: NA

[22] Filed: 19991101

[43] Published: 20021001

[30] Priority: US US1998155219P 19981102 ...

Go to Fulltext

[No drawing]

[57] Abstract:

The invention provides cell lines capable of supporting the replication of a defective recombinant virus vector. In one aspect, bovine cell lines expressing adenovirus E1 functions are provided. The cell lines are useful for the propagation of adenovirus vectors with mutations and/or deletions in E1 and other essential regions of the adenovirus genome.

[52] US Class: 435325 4240931 4240932 4241991 4242331 424813 4352351 4353201 5360231 53602372

[51] Int'l Class: C12N0015861 C12N000701 C12N000510 C12N000502

[52] ECLA: C12N000510T C12N0015861

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VIRAL VECTORS FOR USE IN MONITORING HIV DRUG RESISTANCE

[71] Applicant: MUSC FOUND FOR RES DEV

[75] Inventors: Dong, Jian yun

[21] Application No.: NA

[22] Filed: 20000426

[43] Published: 20020625

[30] Priority: US US1999117136P 19990125 ...

[No drawing]

Go to Fulltext

[57] Abstract:

Recombinant expression vectors and methods are provided for detecting HIV and monitoring HIV drug resistance. The method comprises: taking a culture of cells; adding a recombinant viral vector into the culture to transduce the cells, the recombinant viral vector comprising a reporter sequence comprising a reporter gene whose expression is regulated by a protein specific to HIV viruses which is expressed from a genome of an HIV virus upon infection of a cell in the culture that is transduced by the recombinant viral vector, and a receptor sequence comprising CD 4 and one or more coreceptor genes, expression of the coreceptor genes facilitating productive infection of the transduced cell and enabling HIV virus which has infected the transduced cell to replicate and infect non-infected cells in the culture of the cells transduced by the recombinant viral vector; infecting the transduced cells with a sample containing HIV; adding one or more anti-HIV agents to the cell culture; and detecting a change in a level of expression of the reporter gene in cells.

[52] US Class: 4240932 4240936 4242081 4242331 435005 4351733 4352351 4353201 514044 53602372

[51] Int'l Class: C12N001512 G01N003315 C12N000516 C12P002106 C07H002104 G01N0033569 A01N006300 C12Q000168 G01N003350 C12N001587 C12N001570 C12N000510 C12N000500 C12N001500 C12N001563 C12N001574 C12N001585 C12N001300 C12N000502 C12Q000170 C12N001509 C12N000506 C12R000193

[52] ECLA: C12Q000168M6 G01N0033569K2 M12Q000170B2B

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CELL LINES AND CONSTRUCTS USEFUL IN PRODUCTION OF E1-DELETED ADENOVIRUSES IN ABSENCE OF REPLICATION COMPETENT ADENOVIRUS

[71] Applicant: TRUSTEES OF THE UNIVERSITY OF

[75] Inventors: Gao, Guangping; Wilson, James M.

[21] Application No.: NA

[22] Filed: 20000911

[43] Published: 20020402

[30] Priority: US US1999156644P 19990929 ...

[No drawing]

Go to Fulltext

[57] Abstract:

Novel cell lines useful for trans-complementing E1-deleted adenoviral vectors are described. The cell lines are capable of providing high yields of E1-deleted adenoviral vectors in the absence of replication-competent adenovirus over multiple passages.

[52] US Class: 435239 4350703 4352351 435367 435455 435456 435464 435465 435476

[51] Int'l Class: C12N000510 C07K0014075 C12N0015861 C12P002104 A61K004800

[52] ECLA: C07K0014075 C12N000510T C12N0015861 K61K004800 M07K020700 M12N022104

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RECOMBINANT ADENOVIRAL VECTORS COMPRISING A SPLICING SEQUENCE

[71] Applicant: TRANSGENE SA

[75] Inventors: Mehtali, Majid; Leroy, Pierre; Michou, Anne . . .

[21] Application No.: NA

[22] Filed: 19991202

[43] Published: 20020604

[30] Priority: FR FR19976757A 19970602 ...

Go to Fulltext

[No drawing]

[57] Abstract:

The invention concerns a recombinant adenoviral vector driving from an adenovirus genome at least by deleting all or part of the E1 region, the adenoviral vector comprising an expression cassette of a gene of interest placed under the control of elements necessary for its expression in a host cell or a host organism, the elements required for its expression including at least a splicing sequence. The invention is characterized in that the splicing sequence is derived from a eukaryotic nuclear gene selected among the ovalbumen genes, β or β-globine, collagen and factor VIII of mammals or a synthetic splicing sequence. The invention also concerns a host cell and an infectious viral particle comprising such a vector, a method for preparing such a particle and their therapeutic or prophylactic use. The invention further concerns a pharmaceutical composition containing the adenoviral vector, the host cell or the viral particle.

[52] US Class: 514044 4240932 4353201 435325 435455 5360231 5360241

[51] Int'l Class: A61P004300 A61K004800 C12N001509 C12N000510 C12N0015861

[52] ECLA: C12N0015861 K61K004800 M12N022104 M12N083042 M12N083044

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CHICKEN EMBRYO LETHAL ORPHAN (CELO) VIRUS

[71] Applicant: BOEHRINGER INGELHEIM INT

[75] Inventors: Baker, Adam; Cotten, Matthew; Chiocca, Susanna; Kurzbauer, Robert; . . .

[21] Application No.: NA

[22] Filed: 19990112

[43] Published: 20020101

[30] Priority: DE DE19615803A 19960420 ...

Go to Fulltext

[No drawing]

[57] Abstract:

A CELO virus obtained by in vitro manipulation of a plasmid-cloned CELO virus DNA is suitable for the production of vectors for gene therapy and as a vaccine against infectious diseases in humans and animals, particularly birds.

[52] US Class: 4241991 4241841 4241851 4241861 4242041 4242331 4352351 5360231 53602372

[51] Int'l Class: C12N001534 C12N000510 A61K003900 A61K003100 C12N001509 C07K0014075 A61K004800 C12N000701 C12N0015861 C12N000700 A61P003100 C12N001500 A61P003500 C12R000192

[52] ECLA: C07K0014075 C12N0015861 K61K003900 K61K0039525 M07K020300 M07K020700 M07K022104 M12N071019B

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METHOD FOR PREPARING PERMUTED, CHIMERIC NUCLEIC ACID LIBRARIES

[71] Applicant: UNIV CALIFORNIA

[75] Inventors: Stull, Robert A.; Pallavicini, Maria; Green, Gary

[21] Application No.: NA

[22] Filed: 19980527

[43] Published: 20011127

[30] Priority: US US199885686A 19980527

Go to Fulltext

[No drawing]

[57] Abstract:

The present invention relates to permuted, chimeric nucleic acid libraries and methods of preparing such permuted, chimeric nucleic acid libraries.

[52] US Class: 506016 435004 435005 435006 435489 506017 506026 5360231 5360234

[51] Int'l Class: C12N001566 C12N001510

[52] ECLA: C12N001510C100 C12N001510B2 C12N001566

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BOVINE ADENOVIRUS TYPE 3 GENOME AND VECTOR SYSTEMS DERIVED THEREFROM

[71] Applicant: UNIV SASKATCHEWAN

[75] Inventors: Tikoo, Suresh Kumar; Babiuk, Lorne A.; Reddy, Police Seshidhar; . . .

[21] Application No.: NA

[22] Filed: 19980623

[43] Published: 20011120

[30] Priority: US US1997880234A 19970623 ...

Go to Fulltext

[No drawing]

[57] Abstract:

The present invention provides the complete nucleotide sequence of a bovine adenovirus. The invention further provides bovine adenovirus vectors and expression systems which can be used, among other things, for insertion of foreign sequences, for provision of DNA control sequences including transcriptional and translational regulatory sequences, for diagnostic purposes to detect the presence of viral nucleic acids or proteins encoded by these regions in a subject or biological sample, for provision of immunogenic polypeptides or fragments thereof, for vaccines and for gene therapy. Cell lines comprising the vectors of the invention, and methods for making bovine adenovirus vectors are also provided.

[52] US Class: 435471 4240932 4241991 4352351 4353201 435472 435475 435477

[51] Int'l Class: A61P003704 A61K003846 C12N000702 A61K003576 A61K0031711 C12N0015861 C12N001509 C12N000701 C07K001608 A61K003844 A61K003800 A61K004800 C07K0014075 C12Q000168 C12N000510 C12N000121 A61K003822 C12P002102 A61P003100 A61K003843 C12R000119 C12R000191 C12R000193 A61K003900

[52] ECLA: C07K0014075 C12N0015861 K61K003900 K61K003951 M07K020300 M07K020500 M07K020700 M07K021500 M07K022104

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VIABLE CONTAMINANT PARTICLE FREE ADENOVIRUSES, THEIR PREPARTION AND USE

[71] Applicant: RHONE POULENC RORER SA

[75] Inventors: Yeh, Patrice; Perricaudet, Michel; Orsini, . . .

[21] Application No.: NA

[22] Filed: 19970422

[43] Published: 20011106

[30] Priority: FR FR199413355A 19941028 ...

Go to Fulltext

[No drawing]

[57] Abstract:

Novel adenovirus-derived viral vectors, the preparation thereof, and their use in gene therapy, are disclosed. In particular, recombinant adenoviruses including an adenovirus genome wherein (i) the E1 region is inactivated, (ii) the genomic organization is modified, and (iii) optional recombination with the producing line genome generates non-viable viral particles, are disclosed.

[52] US Class: 4353201 4240932 42409321 435455 435456 514044

[51] Int'l Class: A61K004800 A61K003576 C12N001509 C12N0015861 C07K0014075 C12N000700 C12N000701 C12R000191

[52] ECLA: C07K0014075 C12N0015861 K61K004800 M07K020700 M07K022104 M12N083000A1

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RNA EXPORT ELEMENT AND METHODS OF USE

[71] Applicant: SALK INST

[75] Inventors: Hope, Thomas J.; Zufferey, Romain; Trono, Didier; Donello, John . . .

[21] Application No.: NA

[22] Filed: 20000620

[43] Published: 20010911

[30] Priority: US US1997936476A 19970918 ...

Go to Fulltext

[No drawing]

[57] Abstract:

A cis-acting posttranscriptional regulatory element (PRE) useful for efficient RNA export of RNA is provided. The element, termed WPRE, is originally derived from woodchuck hepatitis virus. The invention also provides a method for enhancing the expression of transgenes by insertion of the WPRE nucleic acid sequences in operably linkage with the transgene.

[52] US Class: 4350691 435375

[51] Int'l Class: C12N001582 C12N000502 C07K001402 C12Q000168

[52] ECLA: C07K001402 C12N001582B C12Q000168 C12Q000168P M07K020300 M07K020500 M07K020700

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RECOMBINANT AVIAN ADENOVIRUS VECTOR

[71] Applicant: COMMW SCIENT IND RES ORG

[75] Inventors: Johnson, Michael A. ; Prideaux, Christopher T.; McCoy, Richard J.; . . .

[21] Application No.: NA

[22] Filed: 19990318

[43] Published: 20011002

[30] Priority: AU AU19938297A 19930414 ...

Go to Fulltext

[No drawing]

[57] Abstract:

This invention relates to a recombinant vector comprising a recombinant avian adenovirus incorporating, and capable of expression of at least one heterologous nucleotide sequence. The nucleotide sequence is preferably one which encodes an antigenic determinate of infectious bursal disease virus. The invention further relates to a method of production of recombinant vectors, to methods of preparation of vaccines based on the vectors, to administration strategies and to methods of protecting poultry from disease.

[52] US Class: 4241991 4241841 4241851 4241861 4242041 4242331 4352351 4353201 5360231 53602372

[51] Int'l Class: C12N0015861 C07K0014075 A61K003900

[52] ECLA: C07K0014075 C12N0015861 K61K003900 M07K020700 M12N071019B

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SYSTEM FOR GENERATING RECOMBINANT VIRUSES

[71] Applicant: GLAXO WELLCOME INC

[75] Inventors: Richards, Cynthia Ann; Weiner, Michael Phillip

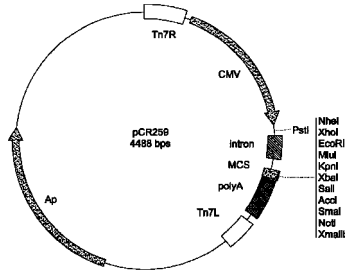
[21] Application No.: NA

[22] Filed: 19990510

[43] Published: 20010918

[30] Priority: US US199884936P 19980511 ...

Go to Fulltext



[57] Abstract:

The present invention provides a system for simple generation of recombinant animal viruses. The system includes a virus homing vector and can further comprise a transfer vector. These components are used in a system that reduces the number of cloning steps and provides for easier preparation of a number of recombinant viruses.

[52] US Class: 4350914 43525233 43525421 4353201 435325 5360231 5360241

[51] Int'l Class: C12N001590 C12N000502 C12N000121 C12N000119 C12N0015867 C12N001585 C12N001586 C12N0015861

[52] ECLA: C12N0015864A C12N001585 C12N0015861 C12N0015867 C12N001590B M12N080020B M12N080090 M12N083042 M12N084020

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REPLICATION-DEFECTIVE ADENOVIRUS HUMAN TYPE 5 RECOMBINANT AS A VACCINE CARRIER

[71] Applicant: WISTAR INST;
TRUSTEES OF THE UNIVERSITY OF

[75] Inventors: Ertl, Hildegund C. J.; Wilson, James M.

[21] Application No.: NA

[22] Filed: 19990702

[43] Published: 20010911

[30] Priority: US US1995461837A 19950605 ...

Go to Fulltext

[No drawing]

[57] Abstract:

A replication defective recombinant adenovirus is provided which contains a complete deletion of its E1 gene and at least a partial deletion of its E3 gene, said virus containing in the site of the E1 deletion a sequence comprising a non-adenovirus promoter directing the replication and expression of DNA encoding a heterologous protein from a disease-causing agent, which, when administered to a mammal in said recombinant virus, elicits a substantially complete protective immune response against the agent. Pharmaceutical and veterinary products containing the recombinant adenovirus are provided.

[52] US Class: 4241991 4242041 4242331 4352351 4353201 53602372

[51] Int'l Class: C12N0015861 C12N000700 A61K0039235 A61K0039205 A61K003912 C07K0014025 A61P003118 C12N001500 C12N000701 A61P003704 C12N001509 C07H002104

[52] ECLA: C07K0014025 C12N0015861 K61K003953 M07K022104

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METHODS TO INHIBIT REPLICATION OF INFECTIVE VIRUS

[71] Applicant: UNIV JOHNS HOPKINS MED

[75] Inventors: Dropuli#263;, Boro; Pitha, Paula M.

[21] Application No.: NA

[22] Filed: 19990216

[43] Published: 20010515

[30] Priority: US US199532800P 19951128 ...

Go to Fulltext

[No drawing]

[57] Abstract:

The present invention provides a conditionally replicating viral vector, methods of making, modifying, propagating and selectively packaging, and using such a vector, isolated molecules of specified nucleotide and amino acid sequences relevant to such vectors, a pharmaceutical composition and a host cell comprising such a vector, the use of such a host cell to screen drugs. The methods include the prophylactic and therapeutic treatment of viral infection, in particular HIV infection, and, thus, are also directed to viral vaccines and the treatment of cancer, in particular cancer of viral etiology. Other methods include the use of such conditionally replicating viral vectors in gene therapy and other applications.

[52] US Class: 435375 4353201 435457 435458 514044

[51] Int'l Class: C12N001511 C12N000508 C12N0015867 A61K004800

[52] ECLA: C12N001511B1A C12N0015867 K61K004800 M07K021300 M07K021304 M12N022124

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METHOD FOR PREPARING A RECOMBINANT ADENOVIRUS GENOME

[71] Applicant: RHONE POULENC RORER SA

[75] Inventors: Crouzet, Joël; Naudin, Laurent; Yeh, Patrice; Orsini, Cécile; . . .

[21] Application No.: NA

[22] Filed: 19970808

[43] Published: 20010717

[30] Priority: FR FR19951632A 19950213 ...

Go to Fulltext

[No drawing]

[57] Abstract:

A novel method for preparing recombinant adenoviruses and the use of such adenoviruses in gene therapy are disclosed. Plasmids used in the construction of said adenoviruses are also disclosed.

[52] US Class: 4350911 4350691 4352351 4352523 4353201

[51] Int'l Class: C12N001534 A61K004800 A61K003576 C12N001509 C12N001500 C12N000121 C12N0015861 C12N001570 C12N000700 C12N000701 C12R000192 C12R000119

[52] ECLA: C12N000700 C12N001570 C12N0015861

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HELPER-FREE, TOTALLY DEFECTIVE ADENOVIRUS FOR GENE THERAPY

[71] Applicant: UNIV CALIFORNIA

[75] Inventors: Hardy, Stephen F.

[21] Application No.: NA

[22] Filed: 19970307

[43] Published: 20010508

[30] Priority: US US199613220P 19960307 ...

Go to Fulltext

[No drawing]

[57] Abstract:

A method for producing in vivo packaged recombinant adenovirus vectors is provided. The recombinant Ad vectors do not contain any Adenovirus genes and are therefore useful for gene therapy. The recombinant Adenovirus vectors are packaged in vivo using a helper virus which is itself very inefficiently packaged, providing a recombinant viral preparation with very little or no contamination with helper virus. In particular, the method makes use of a helper virus in which the packaging site can be easily excised in vivo by recombination mediated by a recombinase. The helper virus is also useful for the in vivo construction of new recombinant adenovirus vectors containing substitutions in the E1 or other adenoviral region.

[52] US Class: 435455 4353201 435456 435457

[51] Int'l Class: C12N0015861 C12N000704

[52] ECLA: C12N000704A C12N0015861 M12N080030 M12N083038

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USE OF TRANS-ACTIVATION AND CIS-ACTIVATION TO MODULATE THE PERSISTENCE OF EXPRESSION OF A TRANSGENE IN AN AT LEAST E4-DEFICIENT ADENOVIRUS

[71] Applicant: GENVEC INC

[75] Inventors: Brough, Douglas E.; Kovesdi, Imre

[21] Application No.: NA

[22] Filed: 19981204

[43] Published: 20010501

[30] Priority: US US1998205014A 19981204

Go to Fulltext

[No drawing]

[57] Abstract:

The present invention provides a method of modulating the persistence of expression of a trans gene in an at least E4Δ adenoidal vector in a cell. In one embodiment, the method comprises contacting the cell with an at least E4Δ adenoidal vector comprising (i) a transgene and (ii) a gene encoding a trans-acting factor, which is not from the E4 region of an adenovirus and which modulates the persistence of expression of the transgene. In another embodiment, the method comprises contacting the cell simultaneously or sequentially with (i) an at least E4Δ adenoidal vector comprising a transgene and (ii) a viral vector comprising a gene encoding a trans-acting factor, which is not from the E4 region of an adenovirus and which modulates the persistence of expression of the transgene. In addition, the present invention provides a recombinant at least E4Δ adenoviral vector for use in the method and a composition comprising the vector and a carrier therefor. Also provided by the present invention is a system for modulation of a recombinant at least E4Δ adenoviral vector for use in the method and a composition comprising the system and a carrier there for.

[52] US Class: 4353201

[51] Int'l Class: C07K0014075 A61K003800 A61K003576 C12N001509 C07K0014035 A61K004800 C12N001563 C12N001535 A61P003100 C12N0015861 A61P003500

[52] ECLA: C07K0014035 C07K0014075 C12N001563 C12N0015861 M07K020700

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VIRAL VECTORS AND LINE FOR GENE THERAPY

[71] Applicant: TRANSGENE SA

[75] Inventors: Mehtali, Majid; Lusky, Monika; Rittner, Karola

[21] Application No.: NA

[22] Filed: 19970331

[43] Published: 20010320

[30] Priority: FR FR19958946A 19950724 ...

Go to Fulltext

[No drawing]

[57] Abstract:

Novel viral vectors in which the expression of viral genes is regulated in such a way that it is functional in a complementation cell and non-functional in a host cell, as well as viral particles and host cells containing said novel vectors, are disclosed. A complementation cell including a viral gene expression regulator, and a method for preparing infectious viral particles, are also disclosed. Finally, a pharmaceutical composition containing said vectors, and the therapeutical use thereof, are disclosed.

[52] US Class: 435456 4353201 435325 435366 435369 435370

[51] Int'l Class: A61K004800 A61K003576 C12N001509 C12N0015861 C12N000510 C12N000700 C12N000701

[52] ECLA: C12N0015861 M12N022104 M12N083000A2A M12N084020

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METHOD FOR TOLERIZING A MAMMALIAN PATIENT TO ADMINISTRATION OF GENE THERAPY VIRUS VECTORS

[71] Applicant: UNIV PENNSYLVANIA

[75] Inventors: Wilson, James M.; Chen, Youhai

[21] Application No.: NA

[22] Filed: 19970710

[43] Published: 20010403

[30] Priority: US US199625549P 19960906 ...

Go to Fulltext

[No drawing]

[57] Abstract:

A method for tolerizing a mammalian subject to administration of a live virus carrying a gene for delivery to a cell of the subject is disclosed. The method entails administering to the subject a suitable amount of an inactivated virus prior to administration of the live virus. The prior administration of the inactivated virus suppresses anti-virus cytotoxic T cells, permitting longer transgene persistence once the live virus is administered, and permitting effective readministration of live virus.

[52] US Class: 514044 42409321 4240936 4241991 4242041 4242051 4242331 4353201 435375

[51] Int'l Class: A61P003706 A61K004800 A61K003576

[52] ECLA: A61K004800

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DEFECTIVE RECOMBINANT ADENOVIRUSES WITH INACTIVATED IVA2 GENE

[71] Applicant: RHONE POULENC RORER SA

[75] Inventors: Yeh, Patrice; Perricaudet, Michel; Orsini, Cécile; Vigne, Emmanuelle

[21] Application No.: NA

[22] Filed: 19970321

[43] Published: 20010313

[30] Priority: FR FR199411511A 19940927 ...

Go to Fulltext

[No drawing]

[57] Abstract:

The present invention relates to new viral vectors derived from adenoviruses, their preparation and utilization in gene therapy. It relates particularly to defective recombinant adenoviruses wherein the Iva2 gene at least is inactivated.

[52] US Class: 4353201 42409321 435325 435455 435456 514044

[51] Int'l Class: C12N000701 A61P000500 A61K003800 A61K003574 C12N001509 A61K004800 A61K003821 C07K0014075 C12N0015861 A61P003700 A61K003822 C12N000700 A61K003843

[52] ECLA: C07K0014075 C12N0015861 K61K004800 M07K020700 M12N080010E

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ADENOVIRUS VECTORS FOR GENE THERAPY

[71] Applicant: ADVEC INC

[75] Inventors: Graham, Frank L.; Bett, Andrew; Prevec, Ludvik; Haddara, Wael M.

[21] Application No.: NA

[22] Filed: 19940531

[43] Published: 20001031

[30] Priority: US US199380727A 19930624 ...

Go to Fulltext

[No drawing]

[57] Abstract:

The invention comprises a series of adenovirus-based vectors having deletions in the E1 and/or E3 regions, and also insertions of pBR322 sequences, which can be used to deliver nucleic acid inserts into host cells, tissues or organisms that then can express the insert. The invention includes the use of the vectors in introducing genes into cells, in making vaccines and in gene therapy.

[52] US Class: 43509142 4350914 4353201 435455 435456 53602372 5360241

[51] Int'l Class: C12N0015861

[52] ECLA: C12N0015861 K01K021700 M12N080030

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METHOD FOR THE PREPARATION OF A VIRAL VECTOR BY INTERMOLECULAR HOMOLOGOUS RECOMBINATION

[71] Applicant: TRANSGENE SA

[75] Inventors: Chartier, Cecile; Degryse, Eric

[21] Application No.: NA

[22] Filed: 19960801

[43] Published: 20000829

[30] Priority: FR FR199414470A 19941201 ...

Go to Fulltext

[No drawing]

[57] Abstract:

A recombinant adenoviral vector containing an exogenous DNA sequence insertion is prepared in a prokaryotic cell using homologous intermolecular recombination. The exogenous DNA sequence codes for a polypeptide of therapeutic interest for applications in gene therapy. The adenoviral vector may lack all or part of at least one region essential for replication.

[52] US Class: 4353201 4242331 4350914 43509141 4352351 4352521 4352523 43525233 4352528 514044 530350

[51] Int'l Class: A61P004300 A61K004800 C12N001586 A61K003800 A61K003576 C12N0015861 C12N001509 C12N001510 C12N000121 A61K0039395 A61K003827 A61P003112 C07H002104 C12N000701 C12N000700 A61P000700 A61K003843 A61P003122 A61K003855

[52] ECLA: C12N000700 C12N001510 C12N001586 C12N0015861 K61K004800 M12N071019

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RECOMBINANT CANINE ADENOVIRUSES, METHOD FOR MAKING AND USES THEREOF

[71] Applicant: MERIAL SAS
[75] Inventors: Fischer, Laurent
[21] Application No.: NA
[22] Filed: 19960703
[43] Published: 20000718
[30] Priority: US US1996675566A 19960703

[No drawing]

Go to Fulltext

[57] Abstract:

Disclosed and claimed are recombinant adenoviruses, methods of making them, uses for them (including in immunological, immunogenic, vaccine or therapeutic compositions, or, as a vector for cloning, replicating or expressing DNA and methods of using the compositions and vector), expression products from them, and uses for the expression products. More particularly, disclosed and claimed are recombinant canine adenoviruses (CAV) and methods of making them, uses for them, expression products from them, and uses for the expression products, including recombinant CAV2 viruses. Additionally, disclosed and claimed are truncated promoters, expression cassettes containing the promoters, and recombinant viruses and plasmids containing the promoters or expression cassettes.

[52] US Class: 4242331 4242041 4242051 4352351

[51] Int'l Class: C12N0015861 C07K001413 A61K003900

[52] ECLA: C07K001413 C12N0015861 K61K003900 M07K020700 M07K022104 M12N081060 M12N081060A1 M12N081060D1 M12N083000 M12N083060

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HELPER VIRUSES FOR PREPARING RECOMBINANT VIRAL VECTORS

[71] Applicant: TRANSGENE SA
[75] Inventors: Lusky, Monika;
Mehtali, Majid
[21] Application No.: NA
[22] Filed: 19980130
[43] Published: 20000523
[30] Priority: FR FR19959289A 19950731 ...

[No drawing]

Go to Fulltext

[57] Abstract:

Novel helper vectors are provided for complementing defective recombinant viral vectors, characterized in that they are provided with recombination sequences recognized by a recombinase. A complementation cell expressing the recombinase, and a method for preparing recombinant viral vectors as infectious viral particles for transferring and expressing genes of interest in a host organism or cell, are also provided. The invention is particularly suitable for use in gene therapy, especially in humans.

[52] US Class: 43509141 4350914 43509142 4353201 435325 435366 435369 435455 435456 435457 5360232 5360234 5360235 5360237

[51] Int'l Class: C12N0015861 A61K004800 A61K003576 C12N001509 C12N001556 C12N000510 C12P002100 C12N000700 C12N000701 C12R000191

[52] ECLA: C12N0015861 M12N022104 M12N080030

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CHIMPANZEE ADENOVIRUS VECTORS

[71] Applicant: UNIV PENNSYLVANIA

[75] Inventors: Wilson, James M.; Farina, Steven F.; Fisher, Krishna J.

[21] Application No.: NA

[22] Filed: 19970904

[43] Published: 20000704

[30] Priority: US US199624700P 19960906 ...

Go to Fulltext

[No drawing]

[57] Abstract:

A recombinant vector comprises chimpanzee adenovirus sequences and a heterologous gene under the control of regulatory sequences. A cell line which expresses chimpanzee adenovirus gene(s) is also disclosed. Methods of using the vectors and cell lines are provided.

[52] US Class: 4350691 4240932 4240936 4353201 435325 435366 435455 435456 53602372

[51] Int'l Class: C12N0015861 C07K0014075

[52] ECLA: C07K0014075 C12N0015861C M07K020700

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ADENOVIRUS VECTORS

[71] Applicant: UNIV MICHIGAN

[75] Inventors: Chamberlain, Jeffrey S.; Hartigan O'Connor, Dennis J.

[21] Application No.: NA

[22] Filed: 19990518

[43] Published: 20000502

[30] Priority: US US1996735609A 19961023 ...

Go to Fulltext

[No drawing]

[57] Abstract:

The present invention provides improved adenovirus vectors and packaging cell lines. One type of improved adenoviral vector comprises deletions within the E2b region of the adenoviral genome. These E2b-deleted virus are used in conjunction with novel cell lines that constitutively express E2b gene products. The present invention further provides adenoviral vectors deleted for all viral coding regions. These "gutted" vectors permit the transfer of large genes to cells as demonstrated herein by the transfer of the dystrophin gene to the muscle of mice. The E2b-deleted vectors and the gutted vectors provide improved adenoviral vectors useful for a wide variety of gene therapy applications.

[52] US Class: 435456 435325 435369

[51] Int'l Class: C12N000508 C07K001447 C12N0015861 A61K004800

[52] ECLA: C07K001447A2A C12N0015861 K61K004800 M07K020700 M07K022104 M12N022104 M12N080030 M12N083000C M12N083030

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ADENOVIRUS VECTORS GENERATED FROM HELPER VIRUSES AND HELPER-DEPENDENT VECTORS

[71] Applicant: MERCK CO INC

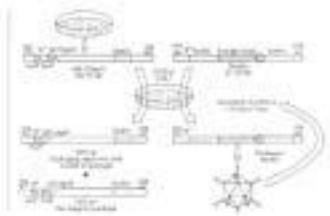
[75] Inventors: Graham, Frank L.;
Parks, Robin; Chen, Liane

[21] Application No.: NA

[22] Filed: 19960925

[43] Published: 20000627

[30] Priority: US US199380727A 19930624 ...



Go to Fulltext

[57] Abstract:

The present invention provides an improved helper-dependent vector system for production of high capacity adenoviral cloning vectors. The invention makes use of the DNA size packaging constraints imposed on a pIX-defective Ad virion that prevent such virions from packaging DNA larger than approximately 35 kb. This constraint can be used to develop helper viruses that do not package their DNA. In one embodiment, the invention combines this methodology with the Cre-loxP helper-dependent system to decrease the quantity of contaminating helper virus in vector preparations. In another embodiment the invention is used for vector growth.

[52] US Class: 4352351 4353201 435440 435455 435457

[51] Int'l Class: C12N0015861 C12N001583

[52] ECLA: C12N0015861 K01K021700 M12N020700 M12N022104 M12N080030 M12N083000A1 M12N083038

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VIRAL PRODUCTION PROCESS

[71] Applicant: CANJI INC

[75] Inventors: Giroux, Daniel D.;
Goudreau, Ann M.;
Ramachandra, Muralidhara; . . .

[21] Application No.: NA

[22] Filed: 19980504

[43] Published: 19991130

[30] Priority: US US199873076A 19980504

Go to Fulltext

[No drawing]

[57] Abstract:

The present invention is directed to a method of producing recombinant viral vectors at high titers incorporating a variety of important advancements over the art. The method of the present invention incorporates multiple features which provide enhanced production of viruses, particularly those viruses encoding exogenous transgenes. The specifically illustrated method describes a method for the high titer serum-free media production of recombinant replication defective adenoviruses containing an exogenous transgene. The invention provides methods of preparing microcarriers, methods for seeding bioreactors at high cell density, increasing the infectivity of the producer cells to the virus, methods to increase product yield through synchronization of the cell cycle of the producer cells, and methods to minimize the deleterious effects of exogenous transgenes. The invention further provides producer cells prepared by the process of the invention. The invention further provides viruses produced by the process.

[52] US Class: 435403 435041 435174 435177 4352351 435239 4352891 435325 435366 435369 435395 435948

[51] Int'l Class: C12N000700 C12N000510 C12N001509 C12N000701

[52] ECLA: C12N000700 M12N022104 M12N053100 M12N071019 M12N079902A61

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PACKAGING SYSTEMS FOR HUMAN RECOMBINANT ADENOVIRUS TO BE USED IN GENE THERAPY

[71] Applicant: INTROGENE BV

[75] Inventors: Bout, Abraham; Hoeben, Robert Cornelis

[21] Application No.: NA

[22] Filed: 19970715

[43] Published: 20000307

[30] Priority: EP EP1995201611A 19950615 ...

[No drawing]

Go to Fulltext

[57] Abstract:

The invention provides improved methods and products based on adenoviral materials which can advantageously be used in for instance gene therapy. In one aspect an adenoviral vector is provided which has no overlap with a suitable packaging cell line which is another aspect of invention. This combination excludes the possibility of homologous recombination, thereby excluding the possibility of the formation of replication competent adenovirus. In another aspect an adenovirus based helper construct which by its size is incapable of being encapsidated. This helper virus can be transferred into any suitable host cell making it a packaging cell. Further a number of useful mutations to adenoviral based materials and combinations of such mutations are disclosed, which all have in common the safety of the methods and the products, in particular avoiding the production of replication competent adenovirus and/or interference with the immune system. Further a method of intracellular amplification is provided.

[52] US Class: 435325 42409321 4350691 4353201 435455 514044 5360231

[51] Int'l Class: A61K004800 A61K003576 C12N001509 C12N000510 C12N000700 C12N0015861

[52] ECLA: C12N000510T C12N0015861 K61K004800 M07K022104

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ADENOVIRUS AND METHODS OF USE THEREOF

[71] Applicant: UNIV PENNSYLVANIA

[75] Inventors: Wilson, James M.; Fisher, Krishna J.; Chen, Shu Jen; Weitzman, Matthew

[21] Application No.: NA

[22] Filed: 19970825

[43] Published: 19991214

[30] Priority: US US1994331381A 19941028 ...

[No drawing]

Go to Fulltext

[57] Abstract:

A recombinant adenovirus and a method for producing the virus are provided which utilize a recombinant shuttle vector comprising adenovirus DNA sequence for the 5' and 3' cis-elements necessary for replication and virion encapsidation in the absence of sequence encoding viral genes and a selected minigene linked thereto, and a helper adenovirus comprising sufficient adenovirus gene sequences necessary for a productive viral infection. Desirably, the helper gene is crippled by modifications to its 5' packaging sequences, which facilitates purification of the viral particle from the helper virus.

[52] US Class: 435005 435006 4350914 435239 4353201 435325 435366 435367 435368 435369 530300

[51] Int'l Class: A61K004800 A61K003576 C12N001509 C12N000700 C12N0015861

[52] ECLA: C12N0015861 K61K004800 M12N071019 M12N081060A1 M12N083044

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STOCKS OF RECOMBINANT, REPLICATION-DEFICIENT ADENOVIRUS FREE OF REPLICATION-COMPETENT ADENOVIRUS

[71] Applicant: GENVEC INC

[75] Inventors: Kovesdi, Imre; Brough, Douglas E.; McVey, Duncan L.; Bruder, Joseph T. . . .

[21] Application No.: NA

[22] Filed: 19961126

[43] Published: 19991130

[30] Priority: US US1994258416A 19940610 ...

Go to Fulltext

[No drawing]

[57] Abstract:

The present invention provides multiply deficient adenoviral vectors and complementing cell lines. Also provided are recombinants of the multiply deficient adenoviral vectors and a therapeutic method, particularly relating to gene therapy, vaccination, and the like, involving the use of such recombinants.

[52] US Class: 4350914 4353201 435325 435366 435456

[51] Int'l Class: C12N000510 A61K003576 C12N001509 C07K001447 A61K004800 C12N0015861 C12N001500 A61P004300 C12Q000168 C07K0014075 C12R000192 A61K003800

[52] ECLA: C07K0014075 C07K001447A4 C12N000510T C12N0015861 K61K003800 K61K0039525C K61K004800 M07K020700 M12N081060 M12N081060F1 M12N083000A1 M12N083044 M12N083085 M12N084020 M12N084020A

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IMMORTAL AVIAN CELL LINE TO GROW AVIAN AND ANIMAL VIRUSES TO PRODUCE VACCINES

[71] Applicant: UNIV MICHIGAN

[75] Inventors: Reilly, John David; Taylor, Daniel C.; Maes, Roger; Coussens, Paul M.

[21] Application No.: NA

[22] Filed: 19971110

[43] Published: 19991123

[30] Priority: US US1995549045A 19951027 ...

Go to Fulltext

[No drawing]

[57] Abstract:

Method of propagating viruses that replicate in embryonated eggs or in primary cultures of chicken embryo cells on an immortal, virus-free, contact-inhibited, and non-oncogenic chicken embryo cell line. The method supports replication of avian viruses of the Birnaviridae, Coronaviridae, Herpesviridae, Orthomyxoviridae, Paramyxoviridae, Picornaviridae, Polyomaviridae, Poxviridae, and Reoviridae families. The immortal cell line of the present invention supports replication of swine influenza virus, for instance. The cell line is useful for virus isolation diagnostic assays and for propagating virus suitable for live or killed vaccines.

[52] US Class: 435005 4242291 435349

[51] Int'l Class: A61K0039255 A61K003912 C07K0014055 C12Q000104 G01N0033569 A61K003900

[52] ECLA: G01N0033569K A61K0039245 A61K0039255 C07K0014055 C12Q000104 K61K003900

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GENE TRANSFER VECTOR, RECOMBINANT ADENOVIRUS PARTICLES CONTAINING THE SAME, METHOD FOR PRODUCING THE SAME AND METHOD OF USE OF THE SAME

[71] Applicant: BAYLOR COLLEGE MEDICINE

[75] Inventors: Kochanek, Stefan; Schiedner, Gudrun

[21] Application No.: NA

[22] Filed: 19980416

[43] Published: 19991109

[30] Priority: US US199860828A 19980416

Go to Fulltext

[No drawing]

[57] Abstract:

A gene transfer vector comprising adenovirus inverted terminal repeats, at least one adenovirus packaging signal, and an adenoviral VAI gene and/or VAII gene; recombinant adenovirus particles containing the same; a method for producing the same and a method of use of the same to introduce and express a foreign gene in adenovirus target cells, is disclosed.

[52] US Class: 4350691 4353201 435456 435457 5360235 53602372 5360241

[51] Int'l Class: C12N0015861

[52] ECLA: C12N0015861

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ADENOVIRUS E1-COMPLEMENTING CELL LINES

[71] Applicant: MASSIE; BERNARD

[75] Inventors: Massie, Bernard

[21] Application No.: NA

[22] Filed: 19960426

[43] Published: 19990406

[30] Priority: US US1996638149A 19960426 ...

Go to Fulltext

[No drawing]

[57] Abstract:

The present invention relates to adenovirus (Ad) E1-complementing cell lines which significantly reduce the presence of replication competent Ad (RCA) and can serve for the large scale production of infectious E1-deleted adenoviral particles that may be used for the treatment human patients as for example in gene therapy. As well the invention relates to a method for the large scale production of recombinant infectious adenoviral particles harboring an exogenous sequence of interest and to a RCA-free stock of infectious adenoviral particles. The invention further relates to a recombinant vector for transfecting an eukaryotic cell line in order to construct Ad E1-complementing cell lines which significantly reduce the presence of RCA and to a method therefor.

[52] US Class: 435456 4352351 435371

[51] Int'l Class: C12N0015861 C12N000510

[52] ECLA: C12N000510T C12N0015861 M12N083042

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PREPARATION AND USE OF VIRAL VECTORS FOR MIXED ENVELOPE PROTEIN IMMUNOGENIC COMPOSITION AGAINST HUMAN IMMUNODEFICIENCY VIRUSES

[71] Applicant: ST JUDE CHILDRENS RES HOSPITAL

[75] Inventors: Hurwitz, Julia; Slobod, Karen

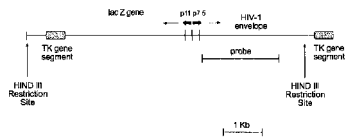
[21] Application No.: NA

[22] Filed: 19970123

[43] Published: 19981208

[30] Priority: US US1996590288A 19960123 ...

Go to Fulltext



[57] Abstract:

Polyenv immunogenic composition are provided that comprise mixtures of at least 4 different recombinant viruses that each express a different HIV env variant or a portion thereof containing both constant and variable regions, as well as methods of making and using such polyenv immunogenic composition and viruses. The immunogenic composition of the invention are optimally combined with a recombinant HIV env booster, or a recombinant HIV env gene DNA priming or boosting vaccine.

[52] US Class: 4242021 4241991 4242081 514044 53602372

[51] Int'l Class: C12N000700 A61P003118 A61K003576 A61K003100 C12N001509 A61P003100 A61P003702 C12N0015863 A61P003700 C07K001416 A61K003921 A61K003812 A61K003900

[52] ECLA: A61K003921 C07K001416D C12N0015863V K61K003812 K61K003900 K61K0039525C K61K003953 K61K003954 K61K0039545 M07K020700 M07K022100 M07K022104 M07K022112 M07K022120

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ADENOVIRAL VECTORS FOR GENE THERAPY CONTAINING DELETIONS IN THE ADENOVIRAL GENOME

[71] Applicant: GENZYME CORP

[75] Inventors: Gregory, Richard J. ; Armentano, Donna; Couture, Larry A.; Smith, Alan E.

[21] Application No.: NA

[22] Filed: 19970716

[43] Published: 19990316

[30] Priority: US US1992985478A 19921203 ...

Go to Fulltext

[No drawing]

[57] Abstract:

Adenoviral vectors which contain deletions of the early regions and/or late genes provide efficient delivery and expression of foreign nucleic acids of interest to patients. These vectors have a particular use in the treatment of cystic fibrosis patients. Furthermore, PAV vectors provide for a second generation of adenoviral vectors that contain the 5' ITR's, the packaging signal and the E1A enhancer. Other adenoviral vectors contain a deletion of the E1 region or a deletion of E4 but retain orf3 or orf6, and can either retain or delete the E3 region.

[52] US Class: 4353201 435456 435457

[51] Int'l Class: C07K001447 C12N0015861 A61K004800 A61K003800

[52] ECLA: C07K001447A4 C12N0015861 K61K003800 K61K004800 M07K020700 M12N084020A

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RECOMBINANT VACCINE

[71] Applicant: COMMW SCIENT IND RES ORG; UNIV AUSTRALIAN

[75] Inventors: Ramshaw, Ian Allister; Boyle, David Bernard; Coupar, Barbara . . .

[21] Application No.: NA

[22] Filed: 19901109

[43] Published: 19990202

[30] Priority: AU AU19867212A 19860801 ...

Go to Fulltext

[No drawing]

[57] Abstract:

A recombinant vaccine comprises a vaccine vector which incorporates a first nucleotide sequence capable of being expressed as all or a part of an antigenic polypeptide, together with a second nucleotide sequence capable of being expressed as all or a part of a lymphokine effective in enhancing the immune response to the antigenic polypeptide. The vaccine vectors include poxvirus, herpes virus or adenovirus, and the lymphokine may be an interleukin, tumour necrosis factor or gamma-interferon. The vaccine vector may express an antigenic polypeptide which is foreign to the host vector.

[52] US Class: 4241991 4240932 4353201 435456

[51] Int'l Class: C12N001562 C07K001407 C07K001457 C07K001452 C12N0015863 C12N001585 C07K0014525 C07K001454 A61K003900 A61K003800

[52] ECLA: C07K001407 C07K001452 C07K0014525 C07K001454 C07K001457 C12N001562 C12N001585 C12N0015863 K61K003800 K61K003900 M07K020700 M07K031900 M07K031940

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COMPLEMENTARY ADENOVIRAL SYSTEMS AND CELL LINES

[71] Applicant: GENVEC INC

[75] Inventors: Kovesdi, Imre; Brough, Douglas E.; McVey, Duncan L.; Bruder, Joseph T. . . .

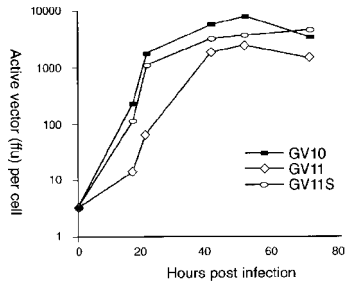
[21] Application No.: NA

[22] Filed: 19951214

[43] Published: 19981222

[30] Priority: US US1994258416A 19940610 ...

Go to Fulltext



[57] Abstract:

The present invention provides multiply replication deficient adenoviral vectors having a spacer in at least one replication deficient adenoviral region, as well as complementing cell lines therefor. Also provided are means of constructing the multiply replication deficient adenoviral vectors and methods of use thereof, e.g., in gene therapy.

[52] US Class: 43509141 4353201 435325 435366 5360242

[51] Int'l Class: C12N000510 A61K003576 C12N001509 C07K001447 A61K004800 C12N0015861 C12N001500 A61P004300 C12Q000168 C07K0014075 C12R000192 A61K003800

[52] ECLA: C07K0014075 C07K001447A4 C12N000510T C12N0015861 K61K003800 K61K0039525C K61K004800 M07K020700 M12N081060 M12N081060F1 M12N083000A1 M12N083044 M12N083085 M12N084020 M12N084020A

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RECOMBINANT PROTEIN PRODUCTION IN BOVINE ADENOVIRUS EXPRESSION VECTOR SYSTEM

[71] Applicant: VETERINARY INFECTIOUS DISEASE

[75] Inventors: Mittal, Suresh K.; Graham, Frank L.; Prevec, Ludvik; Babiuk, Lorne A.

[21] Application No.: NA

[22] Filed: 19931209

[43] Published: 19981013

[30] Priority: US US1993164292A 19931209

Go to Fulltext

[No drawing]

[57] Abstract:

The present invention relates novel live bovine adenovirus (BAV) expression vector systems in which part or all of one or both of the early region 1 (E1) and early region 3 (E3) genes are deleted and replaced by a foreign gene or fragment thereof and novel recombinant mammalian cell lines stably transformed with BAV E1 sequences, and therefore, express E1 gene products capable of allowing replication therein of a bovine adenovirus having an E1 deletion replaced by a heterologous nucleotide sequence encoding a foreign gene or fragment thereof and their use in production of (antigenic) polypeptides or fragments thereof for the purpose of live recombinant virus or subunit vaccine or for other therapies.

[52] US Class: 4241991 4242331 4352351 4353201

[51] Int'l Class: C12N000701 C07K0014075 C12N0015861 A61K004800

[52] ECLA: C07K0014075 C12N0015861 K61K004800 M07K020700

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NON-GROUP C ADENOVIRAL VECTORS

[71] Applicant: CORNELL RES FOUNDATION INC

[75] Inventors: Falck Pedersen, Erik S.; Crystal, Ronald G.; Mastrangeli, Andrea; . . .

[21] Application No.: NA

[22] Filed: 19951002

[43] Published: 19981117

[30] Priority: US US1995537402A 19951002

Go to Fulltext

[No drawing]

[57] Abstract:

The present invention provides replication-deficient non-group C adenoviral vectors. Also provided is a therapeutic method, particularly relating to gene therapy, vaccination, and the like, involving the use of such vectors incorporating a foreign nucleic acid.

[52] US Class: 435006 4352351 4353201 435325 435456 514044

[51] Int'l Class: C12N001500 A61K004800 C12N001509 C12N0015861 C12Q000168 C12R000192

[52] ECLA: C12N0015861 K61K004800

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CHIMERIC ADENOVIRAL FIBER PROTEIN AND METHODS OF USING SAME

[71] Applicant: CORNELL RES FOUNDATION INC; GENVEC INC

[75] Inventors: Wickham, Thomas J.; Falck Pedersen, Erik; Roelvink, Petrus W.; Bruder, . . .

[21] Application No.: NA

[22] Filed: 19950221

[43] Published: 19980623

[30] Priority: US US1995395381A 19950221

Go to Fulltext

[No drawing]

[57] Abstract:

A recombinant adenovirus comprising a chimeric fiber protein and a therapeutic gene, a method of gene therapy involving the use of such an adenovirus, and an adenoviral transfer vector for the generation of such a recombinant adenovirus are provided.

[52] US Class: 4353201 4350691 4350697 53038822 5360242

[51] Int'l Class: A61K004800 A61K003576 C12N001509 C12N0015861 C07K0014075 C07K001900 C12N000700

[52] ECLA: C07K0014075 C12N0015861 K61K004800 M07K020700 M07K022104 M07K031900 M12N081040A M12N081060A1 M12N083000 M12N083060

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RECOMBINANT ADENOVIRUS AND PROCESS FOR PRODUCING THE SAME

[71] Applicant: SUMITOMO PHARMA

[75] Inventors: Saito, Izumu; Kanegae, Yumi

[21] Application No.: NA

[22] Filed: 19940908

[43] Published: 19980324

[30] Priority: JP JP199466813A 19940309 ...

Go to Fulltext

[No drawing]

[57] Abstract:

Disclosed are a recombinant adenovirus bearing a DNA sequence encoding a desired foreign polypeptide, and a hybrid promoter (CAG promoter) comprising a cytomegalovirus enhancer, a chicken β-actin promoter, a rabbit β-globin splicing acceptor and a polyA sequence, a process for production thereof, as well as use thereof for in genetic treatment. The recombinant adenovirus effectively expresses the foreign polypeptide in a wide range of animal cells.

[52] US Class: 43509142 4353201 435369 435465

[51] Int'l Class: C12N0015861

[52] ECLA: C12N0015861

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ADENOVIRUS VECTORS FOR GENE THERAPY

[71] Applicant: GENZYME CORP

[75] Inventors: Armentano, Donna; Romanczuk, Helen; Wadsworth, Samuel Charles

[21] Application No.: NA

[22] Filed: 19950324

[43] Published: 19980113

[30] Priority: US US1995409874A 19950324

Go to Fulltext

[No drawing]

[57] Abstract:

The present invention relates to novel adenovirus vectors for use in gene therapy which are designed to prevent the generation of replication-competent adenovirus (RCA) during in vitro propagation and clinical use. The invention also provides methods for the production of the novel virus vectors. These vectors maximize safety for clinical applications in which adenovirus vectors are used to transfer genes into recipient cells for gene therapy.

[52] US Class: 42409321 4240932 4353201 514044

[51] Int'l Class: C12N0015861 C07K001447 A61K004800

[52] ECLA: C07K001447A4 C12N0015861 K61K004800 M07K020700

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ADENOVIRAL-MEDIATED CELL TARGETING COMMANDED BY THE ADENOVIRUS PENTON BASE PROTEIN

[71] Applicant: GENVEC INC

[75] Inventors: Wickham, Thomas J.; Kovesdi, Imre; Roelvink, Petrus W. ; Brough, Douglas . . .

[21] Application No.: NA

[22] Filed: 19960417

[43] Published: 19980127

[30] Priority: US US1994303162A 19940908 ...

Go to Fulltext

[No drawing]

[57] Abstract:

A method of introducing an adenovirus into a cell that comprises a particular cell surface binding site, as well as a chimeric adenovirus penton base protein and recombinant adenoviral vector comprising the chimeric adenovirus penton base protein for use in the method, are provided.

[52] US Class: 435456 4352351 4353201 530350

[51] Int'l Class: C12P002104 C12N000701 A61K003800 A61K003576 C12N001509 C12N000700 A61K004800 C12N0015866 C12N0015861 C07K0014075 C12N001587 C07K0014705

[52] ECLA: C07K0014075 C07K0014705D C12N000700 C12N0015861 C12N0015866 C12N001587 K61K004800 M07K020700 M07K022104 M07K022108 M07K031900 M12N071019 M12N081040 M12N081040A M12N081060 M12N081060A1 M12N081085D M12N081085D1 M12N081085G

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PENTON BASE PROTEIN AND METHODS OF USING SAME

[71] Applicant: GENVEC INC

[75] Inventors: Wickham, Thomas J.; Kovesdi, Imre; Brough, Douglas E.; McVey, Duncan L. . . .

[21] Application No.: NA

[22] Filed: 19940908

[43] Published: 19960924

[30] Priority: US US1994303162A 19940908

Go to Fulltext

[No drawing]

[57] Abstract:

A recombinant adenovirus comprising a chimeric penton base protein, which includes a nonpenton base sequence, and a therapeutic gene, a method of gene therapy involving the use of such adenovirus, and adenoviral transfer vectors for the generation of such recombinant adenovirus are provided.

[52] US Class: 514044 4350697 4352351 4353201

[51] Int'l Class: C12P002104 C12N000701 A61K003800 A61K003576 C12N001509 C12N000700 A61K004800 C12N0015866 C12N0015861 C07K0014075 C12N001587 C07K0014705

[52] ECLA: C07K0014075 C07K0014705D C12N000700 C12N0015861 C12N0015866 C12N001587 K61K004800 M07K020700 M07K022104 M07K022108 M07K031900 M12N071019 M12N081040 M12N081040A M12N081060 M12N081060A1 M12N081085D M12N081085D1 M12N081085G

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DETECTION OF HUMAN ADENOVIRUS

[71] Applicant: RES CORP TECHNOLOGIES INC

[75] Inventors: Pieniazek, Norman J.; Slemenda, Susan B.; Pieniazek, Danuta; Velarde, . . .

[21] Application No.: NA

[22] Filed: 19900409

[43] Published: 19920421

[30] Priority: US US1989442027A 19891127 ...

Go to Fulltext

[No drawing]

[57] Abstract:

The present invention relates to DNA and proteins of human adenovirus Type 41 and their use in detection of said virus. More specifically, the present invention relates to the isolation of a 41.4 kd short fiber protein and a 60.6 kd long fiber protein of adenovirus type 41 (Ad41), as well as proteins derived from the Ad41 E3 region, thereby providing virus-derived antigens and active derivatives and parts thereof, useful in the development of diagnostic assays, DNA probes and vaccines for said virus or other related viruses belonging to the human enteric adenovirus family. In addition, the present invention is directed to recombinant DNA molecules containing the human enteric adenovirus Type 41 Tak long fiber protein gene, the Ad41 short fiber protein gene and the Ad41 E3 gene (encoding the Ad41 proteins RL-1 to RL-6) thereby providing a source of recombinant viral components useful in the development of said diagnostic assays, DNA probes and vaccines for human adenoviruses. The present invention is also directed to first antibodies specific to the above-identified Ad41 viral components and to second antibodies specific to the first antibodies. These second antibodies are also useful in the development of diagnostic assays for Ad41 and other adenoviruses.

[52] US Class: 53602372 435005 530350 5360243 53602432

[51] Int'l Class: C07K0014075 A61K003800

[52] ECLA: C07K0014075 K61K003800 M07K020500 M07K020700

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VACCINE AGAINST PANDEMIC STRAINS OF INFLUENZA VIRUSES

[71] **Applicant:** N/A

[75] **Inventors:** Sambhara, Suryaprakash; Katz, Jacqueline; Hoelscher, Mary; . . .

[21] **Application No.:** NA

[22] **Filed:** 20071010

[43] **Published:** 20080807

[30] **Priority:** US US2005670826P 20050411 ...

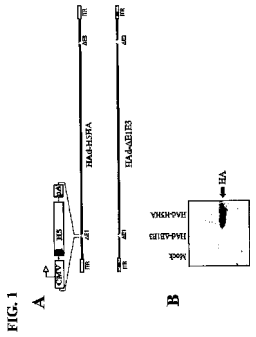

FIG. 1

Go to Fulltext

[57] **Abstract:**

The present disclosure provides compositions and methods for eliciting an immune response against avian or pandemic influenza. The compositions include adenovirus vectors comprising avian influenza antigens, recombinant adenovirus and immunogenic compositions comprising such recombinant vectors and adenovirus. Methods for eliciting an immune response against avian or pandemic influenza involving administering such adenovirus vectors or recombinant adenovirus are also provided.

[52] **US Class:** 4242331 4353201 435326

[51] **Int'l Class:** C12N0015861 C12N000510 A61K0039235

[52] **ECLA:** A61K0039145 C07K001411 C12N000510T C12N0015861 K61K0039525C K61K003953 M07K022104 M12N080010E

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NOVEL METHODS FOR PRODUCING ADENOVIRAL VECTOR PREPARATIONS WITH REDUCED REPLICATION-COMPETENT ADENOVIRUS CONTAMINATION AND NOVEL ADENOVIRAL

[71] **Applicant:** BIOGEN IDEC INC

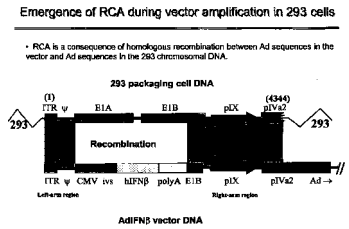
[75] **Inventors:** Wang, Xinzhong; Kaynor, George C.; Barsoum, James

[21] **Application No.:** NA

[22] **Filed:** 20080307

[43] **Published:** 20080814

[30] **Priority:** US US2004621782P 20041025 ...



Go to Fulltext

[57] **Abstract:**

This invention provides novel replication-defective adenoviral vectors comprising an adenoviral genome in which the protein IX gene, preferably under the control of its own promoter, is in an inverted orientation relative to the direction of transcription of the native protein IX gene at a location where the protein IX gene normally resides, for production of replication-competent adenovirus (RCA) free, or substantially RCA-free, adenovirus preparations. Said vector preferably encodes a gene of interest. The invention relates to viral particles, host cells and compositions comprising said adenoviral vector. This invention further relates a method for propagating adenovirus preparations, free, or substantially free, of replication-competent adenovirus (RCA) particles, from host cells comprising vectors of this invention, for use to treat a subject suffering from a disease or disorder or to prevent a subject from getting a disease or disorder, such as cancer. The invention also provides methods of treating such subjects and methods of prophylactically treating unaffected subjects. This invention further provides for vaccine compositions comprising the novel replication-defective adenoviral vectors of the present invention.

[52] **US Class:** 4242331 42409321 4353201 435325 435369 435456

[51] **Int'l Class:** C12N000500 A61K004800 A61K003900 C12N001500

[52] **ECLA:** C12N0015861 K61K003953 K61K004800 M12N083042 M12N084020A

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CELL STRAIN CAPABLE OF BEING CULTURED WITHOUT INGREDIENTS DERIVED FROM ANIMALS, METHOD OF PRODUCING THE SAME, METHOD OF PRODUCING VIRUS

[71] Applicant: N/A

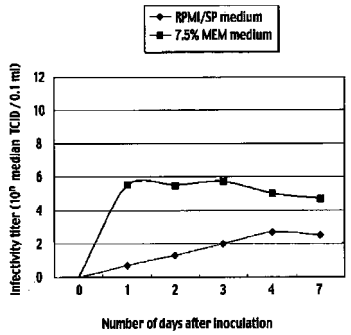
[75] Inventors: Mochizuki, Masami

[21] Application No.: NA

[22] Filed: 20070907

[43] Published: 20080612

[30] Priority: JP WO2005JP4240A 20050310 ...



Go to Fulltext

[57] Abstract:

[Abstract] The invention relates to a cell strain induced from MDCK cells as dog kidney-derived cells, and being able to be cultured without ingredients derived from animals. The cell strain is produced by adapting a MDCK cell to a medium without a serum but with a cell growth factor; and culturing the cell in a medium with an RPMI 1640 medium and a soybean-derived peptone but without ingredients derived from animals.

[52] US Class: 4242041 435005 4352351 435350 435384 435405

[51] Int'l Class: C12N000500 A61K003900 A61P003900 C12N000700 C12Q000170

[52] ECLA: C12N000506B12K C12N000702 M12N050099 M12N0501110

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HIV-1 CLADE A CONSENSUS SEQUENCES, ANTIGENS, AND TRANSGENES

[71] Applicant: N/A

[75] Inventors: Gupta, Kalpana; Jackson, Nicholas

[21] Application No.: NA

[22] Filed: 20070604

[43] Published: 20080417

[30] Priority: US US2006810816P 20060602 ...

Consensus Gag

MGARASVLSGGKLDAWEKIRLRPGGKKYRLKHLVWASRELERFALNPSLLETAEGCQQIM
EQLQPALKTGTEELRSLFNTVATLYCVHQRIDVKDTKEALDKIEEIQNKSKQK--TQQ--
AAADTGXSSKVS----
QNYPIVQNAQGQMIHQXLSPRTLNAWVKVIEEKAFSPEVIPMFSALSEGATPQDLNMMLNIVG
GHQAAMQMLKDTINEEAAEWDRLHPVHAGPIPPGQMREPRGSDIAGTTSTPQEQGAWMTC
NPPIPVGDIYKRWILGLNKIVRMYSPVSILDIKQGPKEPFRDYVDRFFKTLRAEQATQEVKGW
MTETLLVQNANPDCKSILRALGXGATLEEMMTACQGVGGPGHKARVLAEAMSQVQQTN-
IMM-QRGNFRGQKR-
IKCFNCGKEGHLARNCRAPRKKGCWKCGKEGHQMKDCTERQANFLGKIWPSSKGRPGNFP
QSRPEPTAPPAEHFGMGEEIASPPKQEQK--DREQXXPPLVSLKSLFGNDPLSQ

Go to Fulltext

[57] Abstract:

The present invention relates to consensus nucleotide and protein sequences for HIV-1 Clade A antigens, and to nucleotide and protein sequences for Clade A antigens from circulating HIV-1 field isolates wherein the antigen sequences are closely related to the these consensus sequences. In a preferred embodiment, the present invention relates to HIV-1 Clade A transgenes that are derived from such sequences, and that encode either HIV-1 Clade A Gag, Pol (RT and Int), and Nef (referred to as “GRIN”), HIV-1 Clade A Gag, RT, and Nef (referred to as (“GRN”), or HIV-1 Clade A Env. The invention also relates to vectors containing such transgenes, including in preferred embodiment, adenovirus vectors containing such transgenes. The invention also relates to immunogenic compositions comprising the HIV-1 Clade A antigens, nucleotide sequences, vectors, or transgenes of the invention, and to methods of generating an immune response against HIV in a subject by administering an effective amount of such immunogenic compositions.

[52] US Class: 4242081 435005 435236 514044 53602372

[51] Int'l Class: A61P003118 A61K003921 A61K003170 C07H002104 C12N000704 C12Q000170

[52] ECLA: C12Q000170B2B

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ACTIVATION AND INHIBITION OF THE IMMUNE SYSTEM

[71] Applicant: N/A

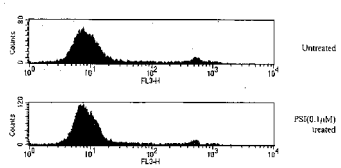
[75] Inventors: Foxwell, Brian; Feldmann, Marc

[21] Application No.: NA

[22] Filed: 20071206

[43] Published: 20080529

[30] Priority: GB GB199930616A 19991224 ...



Go to Fulltext

[57] Abstract:

Activation of the immune response by NF-kB inducers, induction of an anergic response by NF-kB inhibitors and the inhibition and activation of immune response by the administration of an activator or inhibitor of NF-kB is disclosed. Examples of NF-kB inhibitors include IkBα, PSI, a nucleotide sequence encoding IkBα anti-sense nucleic acid encoding an NF-kB sequence, such as Rel B, and anti-NF-kB antibodies. Examples of NF-kB inducers include NIK, MEKK, IKK2, TFRRF2, and Rel B. Also disclosed are vectors encoding inducers and inhibitors of NF-kB, for example adenoviral vectors.

[52] US Class: 4241301 4240932 4241841 4242771 435375 514012 514044 5360231 5360235

[51] Int'l Class: A61K003845 A61P003708 A61K003806 C12N000506 A61P003500 A61K00317088 C07H002104 C12N001509 A61P003700 A61K0039395 C07K001447 A61P003100 A61K004500 C07K001900 A61K003800 A61K0031711 A61K003816 A61K003900 A61P003704 A61P002528 A61K004800 A61K003512 C07K001618 A61P003702 A61K003817 A61K003576 A61K003811

[52] ECLA: A61K003806 A61K003817A2 A61K003817C A61K003845 A61K003900D6 K61K003811 K61K0039515B K61K003953

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SHIELDED ADENOVIRAL VECTORS AND METHODS OF USE

[71] Applicant: N/A

[75] Inventors: Kovesdi, Imre; Hedley, Susan, J.; Korokhov, . . .

[21] Application No.: NA

[22] Filed: 20071130

[43] Published: 20080515

[30] Priority: US US2005685960P 20050531 ...

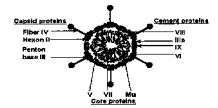

FIG. 1A

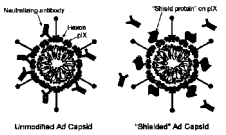

FIG. 1B FIG. 1C

Go to Fulltext

[57] Abstract:

The present invention encompasses replication deficient or a replication competent adenoviral vectors which may comprise moieties covering and shielding the vector from the effects of humoral immune responses, as well as a method of constructing and using such vectors. The preferred viral constructs may incorporate the shielding moieties into the pIX coat protein of the adenovirus vectors. The invention also provides recombinant viral vectors with both shielding and specific targeting abilities. Preferably, the viral vector may comprise a nucleic acid sequence, which codes for therapeutically important genes. Methods for treating of a host with an effective amount of adenovirus vector of the present invention are also provided.

[52] US Class: 4240932 435456 530350

[51] Int'l Class: C12N0015861 C07K0014075 A61K004800

[52] ECLA: C12N0015861T C12N0015861 M07K031930 M07K031931 M07K031933 M07K031974 M12N071019A M12N081085 M12N081085G M12N083000C K61K004800

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METHOD OF USING ADENOVIRAL VECTORS WITH INCREASED IMMUNOGENICITY IN VIVO

[71] Applicant: GOVERNMENT OF THE U S A AS REP; AND HUMAN SERVICES; GENVEC INC; . . .

[75] Inventors: Nabel, Gary, J.; Cheng, Cheng; Gall, Jason, G.D.; Wickham, Thomas, J.

[21] Application No.: NA

[22] Filed: 20070226

[43] Published: 20080320

[30] Priority: US US2004606273P 20040901 ...

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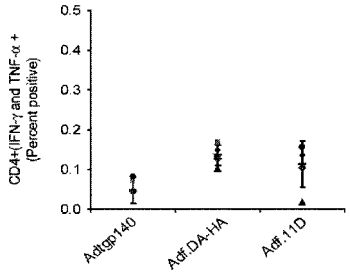

[57] Abstract:

The invention provides a method of inducing an immune response in a mammal. The method comprises administering to the mammal an adenoviral vector comprising (a) a subgroup C fiber protein wherein a native coxsackievirus and adenovirus receptor (CAR)-binding site is disrupted, (b) a subgroup C penton base protein wherein a native integrin-binding site is disrupted, and (c) a nucleic acid sequence encoding at least one antigen derived from an infectious agent other than an adenovirus which is expressed in the mammal to induce an immune response.

[52] US Class: 4241991 4353201

[51] Int'l Class: C12N001563 A61P003704 A61K003900

[52] ECLA: C12N0015861 K61K003900

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ADENOVIRAL VECTOR COMPOSITIONS

[71] Applicant: N/A

[75] Inventors: Emini, Emilio, A.; Shiver, John, W.; Casimiro, Danilo, R.; Bett, Andrew, . . .

[21] Application No.: NA

[22] Filed: 20070207

[43] Published: 20080313

[30] Priority: US US2004600328P 20040809 ...

Go to Fulltext

Sequence of the open reading frame for FL-gag (human codon optimized)

atgggtgcgagagcgtctgtgcgtctggtgtgagctggacaagtgggagaagatcagccgtgaggccgtgtggc
aagaagaagtacaagctaaagcaaatgtgtgggcctccaggtgcgtggagggttgctgtgcaacccgggcc
tgctggagcacctctgaggggtgcaggcagatcctgggccagctccagcctccctgcaaacagggctctgagga
gctgaggtcctgttacaacacagtggctacccttactgtgtgcaccagaagattgatgtgaaggacacccagg
aggccctgaagaagattgaggaggaggcagacaagttcaagtccaagaagaggcccagcgaggctgatgtggcac
aggcaactccagccaggtgtccagaactacccatgtgcagaacctccaggccagtggccacccagcc
catctcccccgggaccctgaatgccttgggtgaaggtggtgaggagaaggccttctcccctgaggtgatcccca
tgttctgccctgtctgagggtgccaccccccaggacctgaacacatgctgaacacagtggggggccatcag
gctgccatgcagatgctgaaggaggaacattaatgaggaggctgctgaggtggatcgctgcatcctgtgcacg
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ggagcagattggctggatgacctaacaacaccccccatccctgtgggggaaatctacaagaggtggatcatcctg
ggcctgaacaagattgtgagaatgtacttcccctccatcttcctggacatcaggcaggggccccaagaggccct
tcaggagtatgtggacaggttctacaagaccctgagggctgaggaggcctcccaggaggtgaagaatttggct
gacagaggaccctgctggtgcagaattgccaaccctgactgccagaccatcttgaaggccctggcccctggcatgt
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gctgaagtgtgtgcaaggtgtggccaccagatgaagaatgcaatgagggccaggccaacttcctggcaa
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(SEQ ID NO: 2)

[57] Abstract:

Applicants disclose herein novel methods, vectors, and vector compositions for improving the efficiency of adenoviral vectors in the delivery and expression of heterologous nucleic acid encoding a polypeptide(s) (e.g, a protein or antigen) of interest. Adenoviral infection is quite common in the general population, and a large percentage of people have neutralizing antibodies to the more prevalent adenoviral serotypes. Such pre-existing anti-adenoviral immunity can dampen or possibly abrogate the effectiveness of this virus for the delivery and expression of heterologous proteins or antigens. The method taught herein functions to offset pre-existing immunity through the delivery of the protein or antigen by a cocktail of at least two adenoviral serotypes. Utilizing a composition of at least two adenoviral serotypes in this manner has been found to increase the effectiveness of adenoviral administration. Adenoviral vectors of utility in the elicitation of an immune response against Human Immunodeficiency Virus (“HIV”) are also disclosed.

[52] US Class: 4241881 4240936 4352351 4353201 514044

[51] Int'l Class: A61K003900 A61K003500 A61K003170 A61P004300 C12N000700 C12N001500

[52] ECLA: C12N0015861 A61K003921 A61K004800H K61K003953 K61K0039545 K61K004800 M12N071019A M12N079902A61

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ADENOVIRUS FIBER SHAFT COMPOSITION AND METHODS OF USE

[71] **Applicant:** GENVEC INC; GOVERNMENT OF THE U S A REPRES

[75] **Inventors:** King, C., Richter; Gall, Jason, G. D.; Nabel, Gary, J.; Cheng, Cheng

[21] **Application No.:** NA

[22] **Filed:** 20070413

[43] **Published:** 20080103

[30] **Priority:** US US2004619912P 20041018 ...

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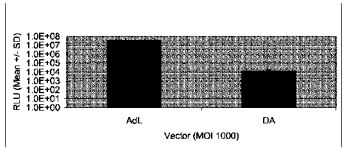

[57] Abstract:

The invention provides a gene transfer vector and a conjugate comprising at least three contiguous amino acids of a shaft region of a subgroup C adenovirus fiber protein. The invention also provides methods of using the gene transfer vector and the conjugate to induce an immune response in a mammal, and to deliver a protein or a non-proteinaceous molecule to a specific cell type.

[52] **US Class:** 4241921 42419611 4350691 4353201 514044

[51] **Int'l Class:** A61K0039385 A61K003900 A61K003800 A61P004300 C12N001500 C12P002106

[52] **ECLA:** A61K003816A A61K003816B M12N071019 M12N072006C M12N079902A61

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ADENOVIRAL AMPLICON AND PRODUCER CELLS FOR THE PRODUCTION OF REPLICATION-DEFECTIVE ADENOVIRAL VECTORS, METHODS OF PREPARATION AND USE THEREOF

[71] **Applicant:** N/A

[75] **Inventors:** Colloca, Stefano; Catalucci, Daniele

[21] **Application No.:** NA

[22] **Filed:** 20070501

[43] **Published:** 20071227

[30] **Priority:** US US2004624459P 20041102 ...

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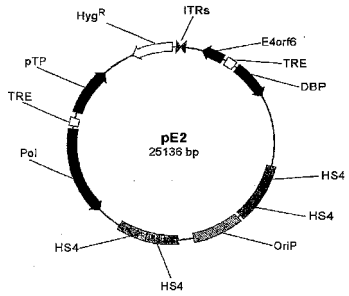

[57] Abstract:

The present invention relates to a plasmid that can be used for the development of efficient producer cell lines for the production of helper independent adenovirus vectors carrying multiple deletions of non-structural as well as structural genes. More specifically, the present invention provides producer cells which comprise a novel adenoviral amplicon that can be used to complement a multi-deleted adenoviral vectors and obtain high titer preparations. The amplicon is an episomal plasmid that expresses Ad5 E2 viral genes (i.e., polymerase, pre-terminal protein and DNA binding protein) and E4 orf6, the EBV the latent origin of replication (OriP) as well as adenoviral origins of replications in form of a covalent junction of left and right ITRs. This plasmid is capable of self-replication upon induction of Ad5 E2 gene expression. The invention further includes methods for the preparation of the disclosed producer cells and uses of the cells to produce viral vectors on a scale that is sufficient for therapeutic uses.

[52] **US Class:** 435455 435243 435363 435477 5360232

[51] **Int'l Class:** C12N000100 C07H002104 C12N001586 C12N000516 C12N001574

[52] **ECLA:** C12N0015861 C12N000510T M12N080010E M12N082060 M12N083000A2A

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CHIMERIC ADENOVIRAL VECTORS

[71] Applicant: WEST COAST BIOLOG
[75] Inventors: Tucker, Sean, N.
[21] Application No.: NA
[22] Filed: 20070228
[43] Published: 20071122
[30] Priority: US US2006778026P 20060228 ...

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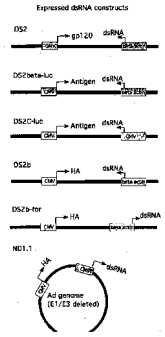

[57] Abstract:

The present invention provides chimeric adenoviral vectors and methods for using the vectors to elicit an immune response to an antigen of interest.

[52] US Class: 4240932 4353201 435456 514044 5360231
[51] Int'l Class: C07H002102 A61K003576 A61K004800 C07H002104 C12N0015867
[52] ECLA: A61K003939 A61K0039145 A61K003921 C07H002102 C12N0015861 K61K0039525C K61K003954 K61K003954A2 K61K0039555B7 M12N079902A61 M12N079904

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ADENOVIRAL EXPRESSION VECTORS

[71] Applicant: N/A
[75] Inventors: Mayall, Timothy, P.
[21] Application No.: NA
[22] Filed: 20061211
[43] Published: 20071025
[30] Priority: US US2005750012P 20051212 ...

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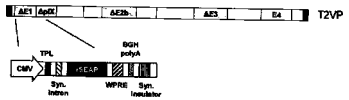

[57] Abstract:

The present invention provides a recombinant adenovirus vector characterized by the partial or total deletion of adenoviral E2B function and having an expression cassette containing a heterologous sequence encoding a protein of interest inserted into the E1 region. Such vectors are designed to reduce or eliminate the occurrence of replication competent adenovirus contamination. Additionally, the expression cassette of the vector may contain one or more regulatory elements capable of increasing the expression of the heterologous sequence and/or reducing the expression of viral proteins. Such a reduction in expression of viral proteins reduces the cytotoxicty and immunogenicity of the adenovirus vectors when administered in vivo. Transformed production host cells and a method of producing recombinant proteins and gene therapy also are included within the scope of this invention.

[52] US Class: 4353201 514044
[51] Int'l Class: C12N001500 A61K003170
[52] ECLA: C12N0015861 K61K004800

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US20070231303A1 MicroPatent Report

METHODS OF GENERATING CHIMERIC ADENOVIRUSES AND USES FOR SUCH CHIMERIC ADENOVIRUSES

[71] Applicant: TRUSTEES OF THE UNIVERSITY OF

[75] Inventors: Roy, Soumitra; Wilson, James, M.

[21] Application No.: NA

[22] Filed: 20030620

[43] Published: 20071004

[30] Priority: US US2003465302A 20030620

Go to Fulltext

[No drawing]

[57] Abstract:

A method for providing an adenovirus from a serotype which does not grow efficiently in a desired cell line with the ability to grow in that cell line is described. The method involves replacing the left and right termini of the adenovirus with the corresponding termini from an adenovirus which grow efficiently in the desired cell line. At a minimum, the left terminus spans the 5' inverted terminal repeat, the left terminus spans the E4 region and the 3' inverted terminal repeat. The resulting chimeric adenovirus contains the internal regions spanning the genes encoding the penton, hexon and fiber from the serotype which does not grow efficiently in the desired cell. Also provided are vectors constructed from novel simian adenovirus sequences and proteins, host cells containing same, and uses thereof.

[52] US Class: 4240932 4352351 435362 435456 530350 53602372

[51] Int'l Class: C07K0014075 C07H002102 A61K004800 C12N000506 C12N000700 C12N0015861

[52] ECLA: C12N0015861 M12N071019A M12N081060A1

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US20070248679A1 MicroPatent Report

VACCINE

[71] Applicant: GLAXO GROUP LTD

[75] Inventors: ERTL, PETER, Franz

[21] Application No.: NA

[22] Filed: 20070412

[43] Published: 20071025

[30] Priority: GB GB200225786A 20021105 ...

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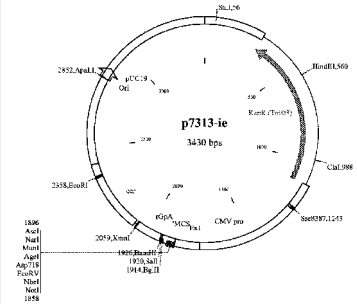

[57] Abstract:

The invention relates to polynucleotides for DNA vaccination which polynucleotides encode an HIV envelope protein or fragment or immunogenic derivative fused to an additional HIV protein selected from a non-structural protein or capsid protein or fragment or immunogenic derivative thereof. Preferably the HIV envelope molecule is gp120 and preferred fusions include one or more of HIV Nef, Gag, RT or Tat. Preferably the HIV envelope molecule is non-glycosylated in mammalian cells.

[52] US Class: 424489 4350691 4353201 514044 530350 53602372

[51] Int'l Class: C12N001548 A61K000914 A61K0031711 C07K001900 A61P003118 C12P002100 C12N001586 C07H002104 C07K001416 A61K003900

[52] ECLA: C07K001416B C07K001416D C07K001416F K61K003900 K61K003953 M07K020700 M07K031900

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VIRUS PURIFICATION METHODS

[71] Applicant: CRUCELL HOLLAND BV

[75] Inventors: Weggeman, Miranda;
Van Corven, Emile Joannes
Josephus, Maria

[21] Application No.: NA

[22] Filed: 20061030

[43] Published: 20070906

[30] Priority: EP EP200450190A 20040223 ...

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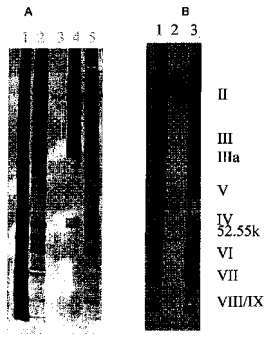

[57] Abstract:

The invention provides a method for the purification of a virus from a host cell, the method comprising the steps of: a) culturing host cells, b) infecting the host cells with a virus, c) treating the cell culture with nuclease, d) lysing the host cells to provide a lysate comprising the virus. The virus is preferably a recombinant adenovirus. The invention further provides a method for the purification of a recombinant virus expressing a heterologous protein that is capable of binding nucleic acid, comprising the steps of: a) culturing host cells, b) infecting the host cells with the recombinant virus, c) lysing the host cells to provide a lysate comprising the recombinant virus, d) subjecting the recombinant virus to anion exchange chromatography and size exclusion chromatography, characterized in that the virus-containing mixture is buffer exchanged at least once with a solution comprising at least 2 M NaCl, or another salt providing an equivalent ionic strength.

[52] US Class: 435006 4350691

[51] Int'l Class: C12P002106 C12Q000168

[52] ECLA: C12N000702 M12N0501700 M12N071019

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VECTORS AND VIRAL VECTORS, AND PACKAGING CELL LINES FOR PROPAGATING SAME

[71] Applicant: N/A

[75] Inventors: Liu, Dakai;
Rabbani, Elazar

[21] Application No.: NA

[22] Filed: 20030604

[43] Published: 20070726

[30] Priority: US US1997822963A 19970321 ...

Go to Fulltext

[No drawing]

[57] Abstract:

Provided are novel vectors and viral vectors capable of expressing exogenous gene or exogenous nucleic acid sequences in a target cell of interest, such as T cells, bone marrow cells, epithelial cells, liver cells and the like. The nucleic acid components of the vectors may include one or more native promoter/enhancer regions having modified sequence segments, one or more non-native promoter/enhancer or non-native promoter's gene or gene segment, and a native viral vector terminator or processing signal or segment thereof. The viral vectors comprise a virus or viral portion having on the surfaces or envelopes adsorption components, one for a packaging cell line and the other for delivery to a target cell. Other viral vectors provided by this invention have two components on their surfaces or envelopes, one of which is native to the virus and the other being non-native and capable of adsorbing to the target cell while being incapable of adsorbing to a native cell for the viral vector. Packaging cell lines for propagating the vectors and viral vectors are also provided, as are novel processes for propagating any of the disclosed vectors or viral vectors.

[52] US Class: 435456 4352351

[51] Int'l Class: C12N0015867 C12N000700 C12N001586

[52] ECLA: C12N0015867 C12N000700 M12N072006C M12N074003 M12N079902A67

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LIGAND-PSEUDORECEPTOR SYSTEM FOR GENERATION OF ADENOVIRAL VECTORS WITH ALTERED TROPISM

[71] Applicant: N/A

[75] Inventors: Massie, Bernard; Zeng, Yue; O'Connnor McCourt, Maureen

[21] Application No.: NA

[22] Filed: 20061122

[43] Published: 20070510

[30] Priority: US US2003514532P 20031024 ...

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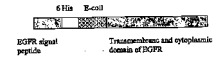

Fig. 1

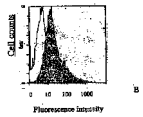

Fig. 2A



Fig. 2B

[57] Abstract:

In accordance with the present invention, there is provided a modified virus ablated of its natural receptors interactions with an unmodified or non-naturally occurring cell, said modified virus comprising a non-native polypeptide, said modified virus having an altered tropism conferred by said non-native peptide, and replicating only in cells that can interact with said non-native peptide, said virus being incapable of infecting a cell through a CAR-dependent entry pathway. There is also provided a modified cell line for replicating the modified virus. These two together can be advantageously put into practice in the field of medicine and more particularly in gene therapy.

[52] US Class: 4242041 435005 4352351 435456

[51] Int'l Class: C12N001586 C12N000700 A61K003912 C12Q000170

[52] ECLA: C12N0015861T M12N071019A M12N081080 M12N081085G

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GUTLESS ADENOVIRUS VECTOR AND THE CONSTRUCTION METHOD THEREOF

[71] Applicant: SHANGHAI INST BIOL SCIENCES

[75] Inventors: Liu, Xinyuan; Pei, Zifel; Li, Binghua; Gu, Jinfa; Zou, Weiguo; Sun, . . .

[21] Application No.: NA

[22] Filed: 20061113

[43] Published: 20070405

[30] Priority: CN CN2003128996A 20030530 ...

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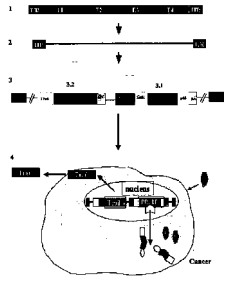

Fig.1.

[57] Abstract:

The present invention disclosed a kind of gutless adenovirus vector and the construction method thereof. Two structural independent but functional related cassettes, the trans-activator (TA) and anti-tumor cassette, are both carried by the gutless vector. hTERT promoter restricts the expression of TA only in tumor cells, and RU486, associated with TA, regulates the expression of interesting gene: when needed, add the RU486 and the gene expression is on, and when not needed, remove the RU486 and the gene expression is off. Tumor-specificity and small molecule regulation of the vector spare the toxicity to the normal tissue caused by the foreign gene product and endow the gene's long lifetime expression in vivo. The vector of the present invention shows many advantages over traditional adenovirus vectors in targeting, gene regulation and expression lifetime.

[52] US Class: 4240932 435456 977802

[51] Int'l Class: A61P003500 A61K004800 C12N000701 C12N0015861 A61K003800

[52] ECLA: C12N0015861 K61K003800 K61K004800 M12N080030 M12N083000C M12N083038 M12N083085

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US20070042977A1 MicroPatent Report

VACCINE

[71] Applicant: N/A

[75] Inventors: Ertl, Peter, Franz

[21] Application No.: NA

[22] Filed: 20060519

[43] Published: 20070222

[30] Priority: GB GB200225788A 20021105 ...

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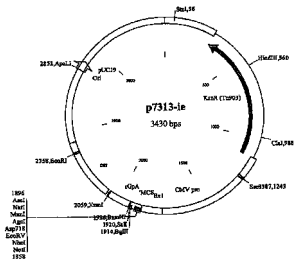
Figure 1



[57] Abstract:

The invention relates to polynucleotides for DNA vaccination which polynucleotides encode an HIV envelope protein or fragment or immunogenic derivative, which is non-glycosylated when expressed in a mammalian target cell, operably linked to a heterologous promoter. Preferably the HIV envelope molecule, such as gp120 or gp140 or gp160, lacks a functional secretion signal. It may be fused to additional HIV proteins such as Nef, Gag, RT or Tat.

[52] US Class: 514044 435005 4352351 435325 435456 530350 53602372 977802

[51] Int'l Class: C07H002102 A61K004800 C07K001416 C12N0015867 C12Q000170 A61K003900

[52] ECLA: C07K001416 C07K001416B C07K001416D C07K001416F K61K003900 K61K003953 M07K020700 M07K031900

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US20070003923A1 MicroPatent Report

MODIFIED FIBER PROTEINS FOR EFFICIENT RECEPTOR BINDING

[71] Applicant: UNIV CALIFORNIA

[75] Inventors: Nemerow, Glen; Wu, Eugene; Stewart, Phoebe

[21] Application No.: NA

[22] Filed: 20061115

[43] Published: 20070104

[30] Priority: US US2003478008P 20030611 ...

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Alignment of the Corresponding Third Repeats of Ad Fiber Shaft Proteins

```
Ad2   GNLTSQNVTTVTQPLKKTKS   SEQ ID NO:42
Ad5   GNLTSQNVTTVSPPLKKTKS   SEQ ID NO:43
Ad37  GSLTVNPK----APLQVNTD   SEQ ID NO:58
Ad8   GKLTVNTE----PPLHLTNN   SEQ ID NO:66
Ad19  GKLTVNAD----PPLQLTNN   SEQ ID NO:67
Ad15  GNLTVNTS----PPLQLTNN   SEQ ID NO:68
```

Figure 1A

[57] Abstract:

Recombinant detargeted and retargeted adenovirus viral particles and vectors are provided. In particular, modified fibers from adenoviruses that bind to coxsackie-adenovirus receptor (CAR) in vivo that contain modifications in the fiber shaft are provided. Adenovirus (Ad) particles that express such fibers exhibit reduced binding to CAR. Hence detargeted Ad particles are provides; also provided are retargeted particles.

[52] US Class: 435005 435456 4352351 530350 977802 435325

[51] Int'l Class: C12N000700 C07K0014075 C12Q000170 C12N001534 C12N0015861

[52] ECLA: C07K0014075 C12N0015861T M07K020700 M07K031901 M12N081060A1

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CELL LINES FOR PRODUCTION OF REPLICATION-DEFECTIVE ADENOVIRUS

[71] Applicant: N/A

[75] Inventors: Howe, John; Wills, Ken; Ralston, Robert; Sherrill, Scott

[21] Application No.: NA

[22] Filed: 20051212

[43] Published: 20061130

[30] Priority: US US2004635561P 20041213 ...

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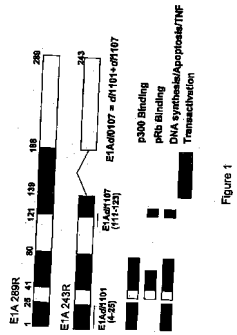

Figure 1

[57] Abstract:

The present invention provides cell lines for the production of E1-deleted adenovirus (rAd) vectors that complement E1A and E1B functions. The present invention also provides cell lines for the production of E1-and E2-deleted adenovirus vectors that complement E1A, E1B and E2B polymerase functions. The invention provides particular cell lines that complement E1A function by insertion of an E1A sequence containing mutations in the 243R and 289R proteins and an E1B sequence comprising the E1B-55K gene. Production yields in the resulting producer cell lines, designated SL0003 and SL0006, were similar to those obtained from 293 cells without generation of detectable recombinant replication competent adenovirus ("RCA").

[52] US Class: 435456 435366

[51] Int'l Class: C12N0015861 C12N000508

[52] ECLA: M12N051000

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ACCELERATED VACCINATION

[71] Applicant: N/A

[75] Inventors: Nabel, Gary; Sullivan, Nancy; Geisbert, Thomas; Jahrling, Peter

[21] Application No.: NA

[22] Filed: 20060117

[43] Published: 20061130

[30] Priority: US US2003491933P 20030801 ...

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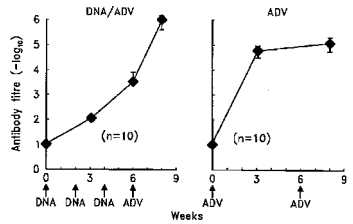

[57] Abstract:

The present invention relates to genetic vaccines for stimulating cellular and humoral immune responses in humans and other hosts, and, in particular, relates to recombinant viruses that express heterologous antigens of pathogenic viruses, in single dose form.

[52] US Class: 4242041 435006

[51] Int'l Class: A61K003912 C12Q000168

[52] ECLA: C12N0015861 A61K003912 K61K0039525C K61K003953 K61K0039545 M12N071019A M12N076003B M12N079904

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NOVEL METHOD FOR THE PROTECTION AND PURIFICATION OF ADENOVIRAL VECTORS

[71] Applicant: INTROGEN THERAPEUTICS INC

[75] Inventors: Pham, Hai; Zhang, Shuyuan; Clarke, Peter

[21] Application No.: NA

[22] Filed: 20050722

[43] Published: 20061207

[30] Priority: US US2004624627P 20041103 ...

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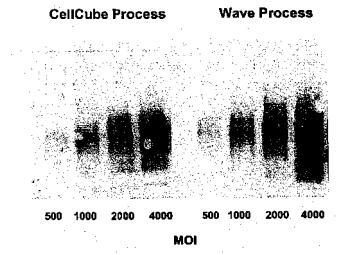

[57] Abstract:

The present invention relates to improved methods for producing adenovirus compositions wherein host cells are grown in a bioreactor and purified by size partitioning purification to provide purified adenovirus compositions.

[52] US Class: 435006 435005

[51] Int'l Class: C12Q000168 C12Q000170

[52] ECLA: C12Q000170

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BROADENING ADENOVIRUS TROPISM

[71] Applicant: N/A

[75] Inventors: Monaci, Paolo; Fontana, Laura

[21] Application No.: NA

[22] Filed: 20051104

[43] Published: 20061214

[30] Priority: US US2003470562P 20030514 ...

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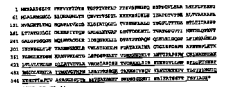

Fig. 1

[57] Abstract:

Recombinant adenoviruses comprising modified fiber proteins which expand the tropism of the adenovirus in comparison to wild-type virus are disclosed. The modified fiber proteins described herein contain a peptide ligand for a cell surface binding site other than CAR comprising a 14 amino acid core sequence containing both fixed and variable amino acid residues. The invention includes isolated nucleic acid molecules encoding the modified adenovirus fiber proteins disclosed, as well as recombinant vectors and host cells containing said nucleic acid molecules. Methods of identifying peptide ligands that bind to cell binding sites other than CAR are included comprising screening a phage-display library of peptide ligands expressed within an adenovirus fiber knob context on CAR-negative cells. Recombinant adenoviruses of the present invention will increase the ability of an adenovirus to transduce important cell and tissue targets as part of a gene therapy/gene vaccination regime that have been shown to be refractory to adenoviral infection.

[52] US Class: 435005 435325 4352351 435456 977802

[51] Int'l Class: C40B005006 C12N0015861 C40B003006

[52] ECLA: C12N0015861 C07K0014075 C12N0015861T M07K0319735 M12N079902A61

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ADENOVIRAL VECTOR-BASED VACCINES

[71] Applicant: N/A

[75] Inventors: Gall, Jason; Wickham, Thomas; Enright, William; Brough, Douglas; . . .

[21] Application No.: NA

[22] Filed: 20060123

[43] Published: 20061221

[30] Priority: US US2003490106P 20030725 ...

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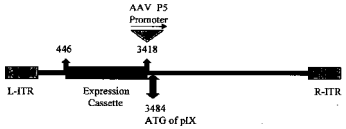

[57] Abstract:

The invention provides a method of inducing an immune response in a mammal. The method comprises administering to the mammal a non-subgroup C adenoviral vector comprising an adenoviral fiber protein having an amino acid sequence comprising about 80% or more identity to an amino acid sequence encoding a subgroup C adenoviral fiber protein. The adenoviral vector further comprises a nucleic acid sequence encoding an antigen which is expressed in the mammal to induce an immune response. The invention further comprises a method of producing an adenoviral vector, and a composition comprising a serotype 41 or a serotype 35 adenoviral vector and a carrier. The invention also provides an adenoviral vector comprising a nucleic acid sequence encoding an adenoviral pIX protein operably linked to a heterologous expression control sequence, as well as a method of enhancing the stability and/or packaging capacity of an adenoviral vector.

[52] US Class: 4241991 4242041 4241301

[51] Int'l Class: A61K0039395 A61K003912

[52] ECLA: C12N0015861T

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RECOMBINANT ADENOVIRAL VECTORS AND APPLICATIONS THEREOF

[71] Applicant: N/A

[75] Inventors: Eloit, Marc; Klonjkowski, Bernard

[21] Application No.: NA

[22] Filed: 20051108

[43] Published: 20061019

[30] Priority: FR FR200212472A 20021008 ...

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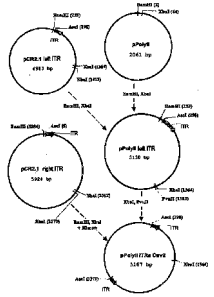

Figure 1

[57] Abstract:

The invention relates to novel recombinant adenoviruses which can be obtained from a replicating adenovirus by deleting all or part of the region of the genome of said replicating adenovirus corresponding to that located in the genome of canine adenovirus type 2 (GenBank J04368) between positions 311 and 499, the aforementioned deletion comprising all or part of the region of the genome of the original replicating adenovirus corresponding to that located between positions 311 and 401 in the genome of canine adenovirus type 2. The invention also relates to the uses of said adenoviruses, particularly for therapeutic purposes.

[52] US Class: 4240932 4242331 4352351 435456

[51] Int'l Class: A61P003500 A61K003923 A61K004800 C12N000700 C12N000701 C12N0015861

[52] ECLA: C12N0015861 K61K003952C K61K004800

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US20060228334A1 MicroPatent Report

MODIFIED ADENOVIRAL FIBER WITH ABLATED TO CELLULAR RECEPTORS

[71] Applicant: N/A

[75] Inventors: Rosa Calatrava, Manuel; Leissner, Philippe; Legrand, Valerie

[21] Application No.: NA

[22] Filed: 20050110

[43] Published: 20061012

[30] Priority: EP EP2002360204A 20020710 ...

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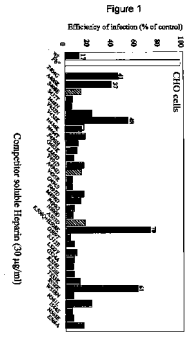

[57] Abstract:

The present invention concerns a modified adenoviral fiber containing at least one mutation affecting one or more amino acid residue(s) of said adenoviral fiber interacting with at least one glycosaminoglycan and/or sialic acid-containing cellular receptor, as well as a trimer of such a modified adenoviral fiber. The present invention also relates to a DNA fragment, an expression vector encoding said modified adenoviral fiber. The present invention also concerns an adenoviral particle lacking a wild-type fiber and comprising the trimer of modified adenoviral fibers as well as a process for producing such an adenoviral particle. Theto present invention also provides a composition comprising such an adenoviral particle and the therapeutic use thereof.

[52] US Class: 4240932 4352351 435456

[51] Int'l Class: C12N0015861 C12N000700 A61K004800

[52] ECLA: C07K0014075 C12N000704A C12N0015861 C12N0015861T K61K004800 M12N071019A M12N081040

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US20060183232A1 MicroPatent Report

PACKAGING CELLS FOR RECOMBINANT ADENOVIRUS

[71] Applicant: N/A

[75] Inventors: Vogels, Ronald; Havenga, Menzo; Zuijdgeest, David Adrianus

[21] Application No.: NA

[22] Filed: 20060320

[43] Published: 20060817

[30] Priority: EP WO2003EP50679A 20031002 ...

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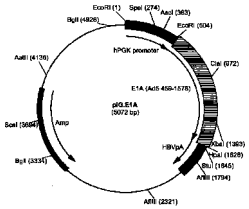

FIG. 1

[57] Abstract:

In the absence of substantial sequence overlap between a recombinant adenoviral vector and the genome of a packaging cell, helper-dependent E1-containing particles (HDEP) can be formed at low frequency. The invention provides means and methods reducing or preventing the generation of HDEP. To this purpose, novel packaging cells and methods of making these are provided.

[52] US Class: 435456 435239 435325

[51] Int'l Class: C12N000702 C12N000510 C12N0015861

[52] ECLA: C07K0014075 C12N000510T C12N0015861 M12N083038

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US20060216272A1 MicroPatent Report

THERAPEUTIC IMMUNIZATION OF HIV-INFECTED INDIVIDUALS

[71] Applicant: N/A

[75] Inventors: Emini, Emilio; Shiver, John; Casimiro, Danilo; Hazuda, Daria; . . .

[21] Application No.: NA

[22] Filed: 20060313

[43] Published: 20060928

[30] Priority: US US2003504522P 20030918 ...

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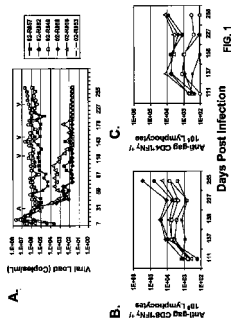

FIG. 1

[57] Abstract:

The present invention provides an improved method for eliciting a therapeutic immune response in an individual infected with human immunodeficiency virus ("HIV"). The method comprises administering an adenoviral vaccine composition expressing an HIV antigen to an individual with controlled viremia. Immunization of infected individuals in this manner elicits a cellular-mediated immune response against the virus that is significant both in the level of the response and the breadth of the response. The therapeutic immune response that ensues is capable of effectively maintaining low titers of virus and, thus, offers the prospect of reducing individual dependency on antiviral therapy.

[52] US Class: 4240932 514044

[51] Int'l Class: A61K004800

[52] ECLA: C07K001416 A61K003921 K61K003953 K61K0039545 K61K003955 M12N071019 M12N079904

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US20060211115A1 MicroPatent Report

METHODS OF GENERATING CHIMERIC ADENOVIRUSES AND USES FOR SUCH CHIMERIC ADEN OVIRUSES

[71] Applicant: TRUSTEES OF THE UNIVERSITY OF

[75] Inventors: Roy, Soumitra; Wilson, James

[21] Application No.: NA

[22] Filed: 20051219

[43] Published: 20060921

[30] Priority: US US2003465302A 20030620 ...

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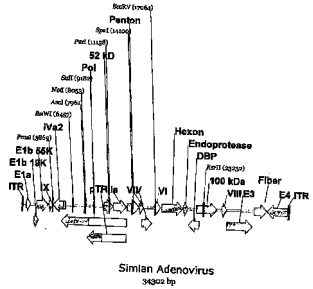
Fig. 1



[57] Abstract:

A method for providing an adenovirus from a serotype which does not grow efficiently in a desired cell line with the ability to grow in that cell line is described. The method involves replacing the left and right termini of the adenovirus with the corresponding termini from an adenovirus which grow efficiently in the desired cell line. At a minimum, the left terminus spans the (5') inverted terminal repeat, the left terminus spans the E4 region and the (3') inverted terminal repeat. The resulting chimeric adenovirus contains the internal regions spanning the genes encoding the penton, hexon and fiber from the serotype which does not grow efficiently in the desired cell. Also provided are vectors constructed from novel simian adenovirus sequences and proteins, host cells containing same, and uses thereof.

[52] US Class: 435456 4352351

[51] Int'l Class: C12N000700 C12N0015861

[52] ECLA: C12N0015861 A61K003912 C07K0014075 C07K001408 K61K0039525C K61K004800

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METHODS FOR INDUCING AN IMMUNE RESPONSE VIA ORAL ADMINISTRATION OF AN ADENOVIRUS

[71] Applicant: N/A

[75] Inventors: Ertl, Hildegund

[21] Application No.: NA

[22] Filed: 20060213

[43] Published: 20060629

[30] Priority: US US2003479425P 20030618 ...

[No drawing]

Go to Fulltext

[57] Abstract:

The present invention provides a method for inducing an immune response to an adenovirus in a subject which has been pre-exposed to an adenovirus or adenoviral vector. The invention further provides a method for inducing a mucosal immune response to an antigen. The methods of the invention are carried out by oral administration of adenoviral vectors.

[52] US Class: 4240932 435456

[51] Int'l Class: C12N001509 C12N001500 A61K004800 C12N001511 C12N0015861

[52] ECLA: C07K0014145 A61K0039205 A61K003921 A61K0039235 C07K001416B C12N0015861 K61K0039525C K61K003953 K61K003954A1 K61K0039545 M12N074003F M12N076002B M12N079902A61

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ADENOVIRAL VECTORS ENCODING AN ANTIBODY FUSED TO A CD4 EXTRACELLULAR DOMAIN

[71] Applicant: TRANSGENE SA

[75] Inventors: Leroy, Pierre; Mehtali, Majid

[21] Application No.: NA

[22] Filed: 20051006

[43] Published: 20060629

[30] Priority: FR FR199410911A 19940913 ...

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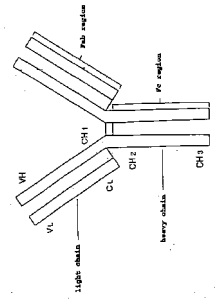

FIGURE 1

[57] Abstract:

Genetically modified cell implant comprising an exogenous nucleotide sequence coding for all or part of an antibody, method for the preparation of such an implant and its therapeutic use for the treatment or prevention of an acquired disease. The invention also concerns an adenoviral vector for the expression of one or more proteins capable of forming a multimer, viral particles and cells containing the adenoviral vector, a pharmaceutical composition and its therapeutic use.

[52] US Class: 42409321 4241331

[51] Int'l Class: C12N000510 A61P003500 A61K000900 C12N001509 A61K004800 C12P002108 A61P003104 A61K003576 C07K001610 C12N0015861 A61P003704 A61K003800 C07K001630 A61K0039395

[52] ECLA: A61K000900M5D A61K004800 C07K001610 C07K001630K C12N0015861 K61K003800 K61K004800 M07K020700 M07K022104 M07K022124 M07K031900 M12N084020 M12N084020A

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METHOD OF INDUCING AN ENHANCED IMMUNE RESPONSE AGAINST HIV

[71] **Applicant:** N/A

[75] **Inventors:** Emini, Emilio; Shiver, John; Casimiro, Danilo; Bett, Andrew; . . .

[21] **Application No.:** NA

[22] **Filed:** 20040909

[43] **Published:** 20060727

[30] **Priority:** US US2002363807P 20020313 ...

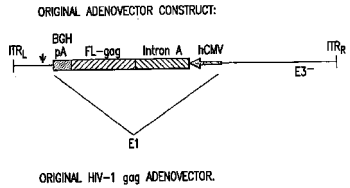

FIG.1

Go to Fulltext

[57] **Abstract:**

An efficient means of inducing an immune response against human immunodeficiency virus (HIV) utilizing specific prime-boost regimes is disclosed. The specific prime-boost regimes employ a heterologous prime-boost protocol employing recombinant adenoviral vectors of alternative and distinct serotypes comprising exogenous genetic material encoding a common HIV antigen. Vaccines administered into living vertebrate tissue in accordance with the disclosed regimes, preferably a mammalian host, such as a human or a non-human mammal of commercial or domestic veterinary importance, express the HIV-1 antigen (e.g., Gag), inducing a cellular immune response which specifically recognizes HIV-1. It is believed that the disclosed prime/boost regime will offer a prophylactic advantage to previously uninfected individuals and/or provide a therapeutic effect by reducing viral load levels within an infected individual, thus prolonging the asymptomatic phase of HIV-1 infection.

[52] **US Class:** 42409321 4242081

[51] **Int'l Class:** A61K003921 A61K004800

[52] **ECLA:** A61K003921 C07K001416B C07K001416F C12N0015861 K61K0039525C K61K0039545 M12N083042

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VIRAL VECTORS AND THE USE OF THE SAME FOR GENE THERAPY

[71] **Applicant:** N/A

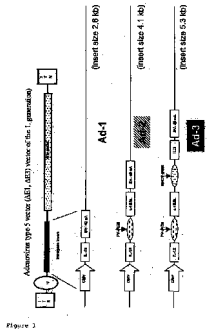
[75] **Inventors:** Walhler, Reinhard; Schnieders, Frank

[21] **Application No.:** NA

[22] **Filed:** 20051122

[43] **Published:** 20060713

[30] **Priority:** DE DE10248141A 20021011 ...



Go to Fulltext

[57] **Abstract:**

The invention relates to viral vectors comprising nucleic acid sequences coding for single chain interleukin-12 (single chain IL-12 or scIL 12) and a costimulator protein, and to the use of said vectors for gene therapy, especially for the treatment of tumours. The invention further relates to adenoviral vectors containing nucleic acid sequences having a sequence homology of at least 90% in relation to the sequence displayed in FIGS. 19 and 20 (IL-12), in FIG. 21 (4-1BB ligand) and in FIG. 22 (IL-2) and optionally also one of the sequences displayed in FIG. 23A (B7-1) or 23B (B7-2).

[52] **US Class:** 4240932 435456

[51] **Int'l Class:** C07K001455 C07K001454 A61K004800 C07K0014705 C12N001586 C12N0015861

[52] **ECLA:** C07K001454M C07K001455 C07K0014705B24 C07K0014705R C12N0015861 M07K022104 M12N084020A M12N084020A2

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US20060142221A1 MicroPatent Report

VACCINE

[71] Applicant: N/A

[75] Inventors: Ertl, Peter

[21] Application No.: NA

[22] Filed: 20051123

[43] Published: 20060629

[30] Priority: GB GB200225786A 20021105 ...

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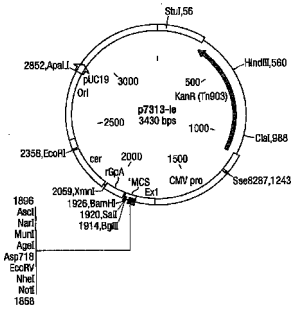
Fig.1.



[57] Abstract:

The invention relates to polynucleotides for DNA vaccination which polynucleotides encode an HIV envelope protein or fragment or immunogenic derivative fused to an additional HIV protein selected from a non-structural protein or capsid protein or fragment or immunogenic derivative thereof. Preferably the HIV envelope molecule is gp120 and preferred fusions include one or more of HIV Nef, Gag, RT or Tat. Preferably the HIV envelope molecule is non-glycosylated in mammalian cells.

[52] US Class: 514044 435005 435006 530350 53602372

[51] Int'l Class: C07H002102 A61K004800 C12Q000170 C07K001416 C12N001548 C12Q000168 A61K003900

[52] ECLA: C07K001416B C07K001416D C07K001416F K61K003900 K61K003953 M07K020700 M07K031900

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US20060120995A1 MicroPatent Report

NEOADJUVANT GENETIC COMPOSITIONS AND METHODS

[71] Applicant: N/A

[75] Inventors: Shah, Maulik

[21] Application No.: NA

[22] Filed: 20041202

[43] Published: 20060608

[30] Priority: US US20042839A 20041202

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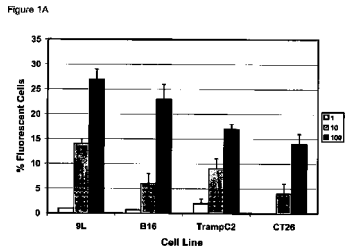
Figure 1A



[57] Abstract:

The present invention relates to a method and composition for the use of a neoadjuvant to be used in with existing therapies to break host immune tolerance to tumor cells or other types of diseased cells. More precisely the present invention is directed to a vaccine which delivers a polypeptide adjuvant such as HSP72, or a cytokine molecule such as GMCSF, which is encoded in a polynucleotide that will be expressed at high levels within tumor cells and may also bind to tumor cell antigens. The vaccine may be administered alone, or in conjunction with a known tumor antigen or vaccine. After a period of time sufficient for expression of the polynucleotide and for the binding of adjuvant to cancer antigens, the cancer will be treated with conventional therapies, allowing the adjuvant/antigen complex to be released to the interstitial fluids where they will be accessible to antigen presenting cells of the host immune system. The presentation of the cancer antigen complexed with adjuvant as well as cytokine stimulation of the host immune system will cause the host to mount a heightened immune response against all remaining cancer cells or tumors which share these antigens.

[52] US Class: 4240851 42409321 514012

[51] Int'l Class: A61K003819 A61K003817 A61K004800

[52] ECLA: A61K003817A2+M A61K003819+M A61K003819B+M A61K003820B+M A61K003820M+M

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REPLICATION-COMPETENT ADENOVIRAL VECTORS

[71] Applicant: ISTITUTO SUPERIORE DE SANITA

[75] Inventors: Peng, Bo; Voltan, Rebecca; Ensoli, Barbara; Robert Guroff, Marjorie

[21] Application No.: NA

[22] Filed: 20051117

[43] Published: 20060601

[30] Priority: US US2004629722P 20041118 ...

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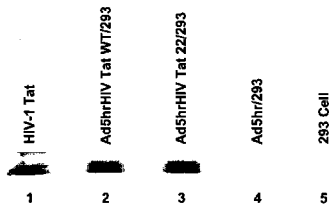

Figure 1

[57] Abstract:

This invention provides improved replication-competent adenoviral vectors. The improved vectors have both a hybrid regulatory unit that provides for high level transgene expression. The vectors can be use, e.g., for therapeutic or prophylactic purposes.

[52] US Class: 4240932 435456

[51] Int'l Class: C12N0015867 C12N0015861 A61K004800

[52] ECLA: C07K001416 C07K001416F C12N0015861 K61K0039525C M07K022104

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NOVEL ADENOVIRUSES, NUCLEIC ACIDS CODING THEREFOR, AND USE THEREOF

[71] Applicant: N/A

[75] Inventors: Holm, Per

[21] Application No.: NA

[22] Filed: 20050414

[43] Published: 20060316

[30] Priority: DE DE10248039A 20021015 ...

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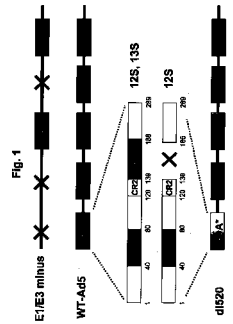

[57] Abstract:

The present invention is related to an adenovirus expressing a first protein which is selected from the group comprising an E1B protein and an E4 protein, priorto a second protein which is selected from the group comprising an E1A protein.

[52] US Class: 4240932 4352351 435456

[51] Int'l Class: C12N000700 A61P003500 A61K004800 C12N000701 C12N0015861

[52] ECLA: A61K003576 C07K0014005

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PRODUCTION OF VACCINES

[71] Applicant: CRUCELL HOLLAND BV

[75] Inventors: Pau, Maria; Uytdehaag, Alphonsus Gerardus; Schouten, Govert

[21] Application No.: NA

[22] Filed: 20051111

[43] Published: 20060309

[30] Priority: US US1999449854A 19991126 ...

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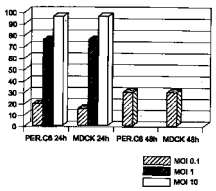

FIG. 1

[57] Abstract:

Means and methods for producing mammalian viruses, the method comprising infecting a culture of immortalized human cells with a virus, incubating the culture infected with virus to propagate the virus under conditions that permit growth of the virus, and to form a virus-containing medium, and removing the virus-containing medium. The viruses can be harvested and be used for the production of vaccines. Advantages include that human cells of the present invention can be cultured under defined serum-free conditions and the cells show improved capability for propagating virus. Methods are provided for producing, in cultured human cells, influenza virus and vaccines derived thereof. This method eliminates the necessity of using whole chicken embryos for the production of Influenza vaccines. The method also provides for the continuous or batch-wise removal of culture media. As such, the present invention allows the large-scale continuous production of viruses to a high titer.

[52] US Class: 435005 4350691 435366 435456 530350 53602372

[51] Int'l Class: C07K0014005 C07H002104 C12Q000170 C12N001586 C12P002106

[52] ECLA: C12N000702 A61K0039145 M12N075002C M12N076005 M12N077013 M12N077017 M12N077017A

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ADENOVIRUS VECTORS FOR IMMUNOTHERAPY

[71] Applicant: N/A

[75] Inventors: Mi, Jie; Lieber, Andre

[21] Application No.: NA

[22] Filed: 20051011

[43] Published: 20060406

[30] Priority: US US2002376498P 20020430 ...

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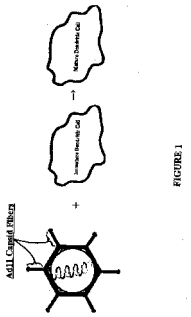

FIGURE 1

[57] Abstract:

The present invention provides compositions, methods and kits comprising viral vectors that may be used for performing immunotherapy. In particular, the present invention provides viral vectors having subgroup B adenoviral capsid fibers that are configured to express a transgene sequence in antigen presenting cells (e.g. dendritic cells) with a high transduction efficiency. Preferably, the transgene sequence is a retrogen cassette and the adenoviral capsid fibers are Ad11 fibers.

[52] US Class: 42409321 435456

[51] Int'l Class: C12N0015861 A61K004800

[52] ECLA: C12N0015861T A61K003900D6 A61K003929B K61K0039525C K61K004800 M12N073001A M12N079902A61

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PRODUCTION OF ADENOVIRUS VECTORS WITH REDUCED LEVELS OF REPLICATION COMPETENT ADENOVIRUS CONTAMINATION

[71] Applicant: N/A

[75] Inventors: Graham, Frank

[21] Application No.: NA

[22] Filed: 20040921

[43] Published: 20060323

[30] Priority: US US2004946484A 20040921

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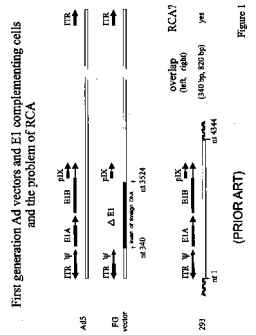

[57] Abstract:

Methods, cells and recombinant adenoviral vectors are disclosed that permit the production of recombinant adenoviral vector stocks with reduced levels of contamination by replication competent adenoviruses (RCA). In certain embodiments are disclosed early region 1 (E1) deficient recombinant adenoviral vectors and complementing E1 positive host cells whose sequences are designed to avoid formation of RCA by homologous recombination between sequences in the vector and E1 sequences in the cells. One aspect of the invention involves the inversion of the packaging signal in a recombinant adenoviral vector relative to an adjacent or nearby inverted terminal repeat (ITR). Methods include use of site-specific intregrase family recombinases such as Cre or FLP and recombinase recognition sites such as lox sites or frt sites.

[52] US Class: 435456 4352351

[51] Int'l Class: C12N000700 C12N0015861

[52] ECLA: C12N0015861 M12N080030 M12N083042 M12N084020

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MINIMAL LENTIVIRAL VECTOR SYSTEM

[71] Applicant: N/A

[75] Inventors: Cannon, Paula;
Ngiam, Celina

[21] Application No.: NA

[22] Filed: 20041203

[43] Published: 20060126

[30] Priority: US US2003526668P 20031204 ...

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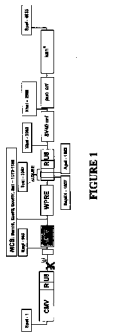

[57] Abstract:

A lentiviral vector system is described. The system comprises a lentiviral transfer vector and a packaging construct. The transfer vector comprises (a) a 5' LTR; (b) a 3' LTR comprising a polyadenylation signal; (c) a minimal packaging signal, (d) (i) at least one heterologous upstream enhancer (UE) sequences, and/or (ii) at least one additional copy of endogenous UE sequences operatively associated with said polyadenylation signal; and (e) a PRE. The packaging construct comprises a nucleic acid encoding and expressing a lentiviral Gag nucleic acid (preferably Gag and Pol). Preferably the lentiviral Gag nucleic acid is a mutated Gag nucleic acid containing one or more substitution mutations, wherein said mutated Gag nucleic acid encodes the same amino acid sequence as the corresponding unmutated Gag nucleic acid, but differs from the nucleic acid sequence of said corresponding unmutated Gag nucleic acid sequence due to the degeneracy of the genetic code. Preferably the packaging construct further comprises a heterologous nucleic acid encoding and expressing an adenovirus VA RNA. The transfer vector and packaging construct can be used together in a producer cell to produce viral particles.

[52] US Class: 435456

[51] Int'l Class: C12N0015867

[52] ECLA: C12N0015867 M12N080010E M12N083048 M12N083050 M12N084020

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US20050196384A1 MicroPatent Report

SETTINGS FOR RECOMBINANT ADENOVIRAL-BASED VACCINES

[71] Applicant: CRUCELL HOLLAND BV

[75] Inventors: Vogels, Ronald; Pau, Maria; Holterman, Lennart; Kostense, Stefan; . . .

[21] Application No.: NA

[22] Filed: 20050414

[43] Published: 20050908

[30] Priority: WO WO2002NL671A 20021023 ...

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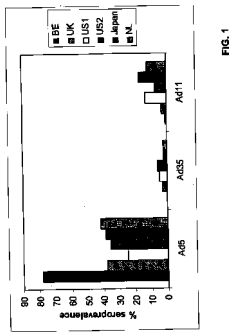

FIG. 1

[57] Abstract:

The present invention provides new uses of recombinant adenoviral vectors in vaccination regimens, such as prime/boost set-ups and subsequent vaccinations and applications for gene therapy. Moreover, the invention provides new assays to determine the best regimen for applying the most suitable recombinant viral vector in a vaccination or gene therapy setting.

[52] US Class: 4240932 435456

[51] Int'l Class: C12N0015861 A61K004800

[52] ECLA:

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US20050175627A1 MicroPatent Report

HIV PHARMACCINES

[71] Applicant: OXXON THERAPEUTICS LTD

[75] Inventors: Schneider, Joerg

[21] Application No.: NA

[22] Filed: 20041209

[43] Published: 20050811

[30] Priority: GB GB200322402A 20030924 ...

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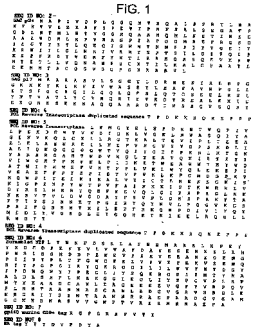
FIG. 1

[57] Abstract:

The invention relates to a recombinant polypeptide comprising amino acid sequence derived from at least one of an HIV gag gene product; an HIV pol gene product; or an HIV nef gene product, said sequence being mutated with respect to the natural sequence of said gene product, and said sequence maintaining each of the naturally occurring CD8+ T cell epitopes of said gene product as defined in p17 and p24 (gag), amino acids 1-440 of RT (pol) and nef shown in Example 8. Furthermore the invention relates to nucleic acids encoding same, and viral vectors encoding same, and to their use in medicine and in immunisation and vaccination.

[52] US Class: 4241881 435005 4350693 435325 435456 514044 530350 53602372

[51] Int'l Class: A61K004800 A61K003921 C07K001416 C12Q000170 A61K003800

[52] ECLA: C07K001416B A61K003921 C07K001416F K61K003800 K61K0039525C K61K003953 K61K0039545 M12N074003F

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US20050176129A1 MicroPatent Report

ADENOVIRUS VECTOR

[71] Applicant: FUMINORI SAKURAI

[75] Inventors: Mizuguchi, Hiroyuki; Hayakawa, Takao; Sakurai, Fuminori

[21] Application No.: NA

[22] Filed: 20041202

[43] Published: 20050811

[30] Priority: JP JP2002164015A 20020605 ...

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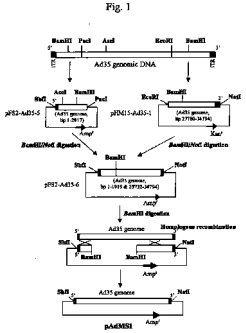
Fig. 1



[57] Abstract:

This invention relates to an adenovirus vector having excellent gene transfection activity on specific cell lines, particularly on hematopoietic cells. This adenovirus vector derives from the adenovirus type 35 genome by at least partial or total deletion of the E1 region therefrom. The adenovirus vector according to this invention has excellent gene transfection activity on specific cell lines, particularly on hematopoietic cells, ES cells, pluripotent stem cells, blood stem cells, and tissue stem cells.

[52] US Class: 4352351 435456

[51] Int'l Class: C12N000701 C12N000510 C12N001509 C12N0015861

[52] ECLA: C12N0015861 M12N051000

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US20050163753A1 MicroPatent Report

STABLE ADENOVIRAL VECTORS AND METHODS FOR PROPAGATION THEREOF

[71] Applicant: N/A

[75] Inventors: Vogels, Ronald; Havenga, Menzo; Zuijdgeest, David Adrianus Theodorus

[21] Application No.: NA

[22] Filed: 20041025

[43] Published: 20050728

[30] Priority: WO WO2002NL281A 20020425 ...

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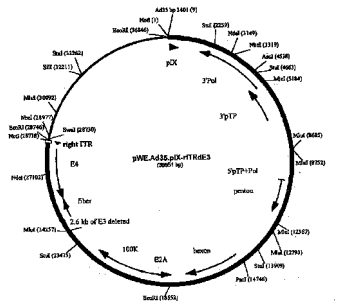
Fig. 1



[57] Abstract:

The present invention provides methods and means to increase the stability and/or the packaging capacity of recombinant adenoviruses, by overexpression of pIX in an adenoviral packaging cell, by retaining at least a part of the E1B 55K region in the recombinant adenoviral vector or by regulating pIX with a heterologous promoter. The invention further relates to methods and means for the production of such adenoviruses on complementing cell lines, wherein the early region 4 open reading frame 6 (E4-orf6) encoding nucleic acid is present in the adenovirus and wherein the E4-orf6 gene product is compatible with one or more products of the E1 gene products in the complementing cell, such that the adenoviral vector can be efficiently produced by the complementing cell.

[52] US Class: 4240932 4352351 435325 435456

[51] Int'l Class: C12N0015861

[52] ECLA: C12N0015861 K61K0039525C M12N084020

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METHODS AND COMPOSITIONS FOR THE PRODUCTION OF ADENOVIRAL VECTORS

[71] Applicant: N/A

[75] Inventors: Zhang, Shuyuan; Pham, Hai

[21] Application No.: NA

[22] Filed: 20050315

[43] Published: 20050721

[30] Priority: US US2003439278A 20030515 ...

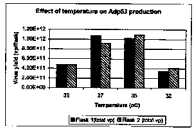

FIG. 1A

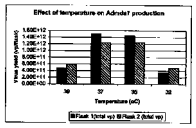

FIG. 1B

Go to Fulltext

[57] Abstract:

The present invention addresses the need to improve the yield of adenovirus when grown in cell culture systems. In particular, it has been demonstrated that for adenovirus, the use of infection temperatures lower than 37° C. in a cell culture system results in improved yields of adenovirus. In addition, it has been demonstrated that when host cells are grow in a bioreactor, initiating adenovirus infection by diluting the host cells with fresh media and adenovirus results in improved yield of adenovirus. Methods of adenoviral production and purification using infection temperatures less than 37° C. are disclosed. Methods of adenoviral production and purification wherein the host cells are grown in a bioreactor and adenovirus infection is initiated by diluting the host cells with fresh media and adenovirus are also disclosed.

[52] US Class: 4240932 4352351 435456

[51] Int'l Class: C12N0015861 C12N000702 C12N000701

[52] ECLA: C12N000702 C12N0015861 M12N071019A

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METHODS OF ADENOVIRUS PURIFICATION

[71] Applicant: N/A

[75] Inventors: Konz Jr., John; Lee, Ann; To, Chin; Goerke, Aaron

[21] Application No.: NA

[22] Filed: 20041025

[43] Published: 20050714

[30] Priority: US US2002380332P 20020514 ...

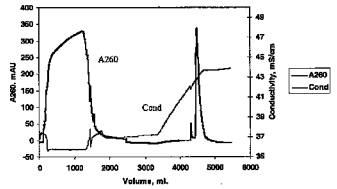

FIGURE 1

Go to Fulltext

[57] Abstract:

A process for purifying virus particles, especially recombinant adenovirus vector particles, is presented. The process relies on various combinations of cell lysis, detergent-based precipitation of host cell contaminants away from the virus, depth filtration or centrifugation, ultrafiltration, nuclease digestion and chromatography to robustly and economically produce highly purified product. This process results in contaminating DNA levels which are consistently below detectable levels.

[52] US Class: 435239

[51] Int'l Class: C12N000702

[52] ECLA: C12N000702 C12N0015861 M12N071019

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US20050129713A1 MicroPatent Report

BAV PACKAGING REGIONS AND E1 TRANSCRIPTIONAL CONTROL REGIONS

[71] Applicant: N/A

[75] Inventors: Tikoo, Suresh; Xing, Li

[21] Application No.: NA

[22] Filed: 20040610

[43] Published: 20050616

[30] Priority: US US2003477540P 20030610 ...

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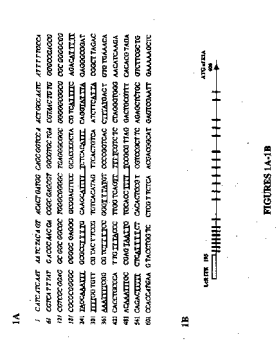

FIGURES 1A-1B

[57] Abstract:

The present invention relates to the identification of bovine adenovirus sequence(s) essential for encapsidation and E1 transcriptional control regions. The present invention provides adenovirus expression systems, host cells and compositions comprising adenovirus vectors which comprise one or more BAV sequence(s) essential for encapsidation, as well as helper virus which express BAV sequences essential for encapsidation. The present invention also provides helper vectors comprising a BAV sequence essential for encapsidation which is used in a helper virus for propagating recombinant adenovirus. The present invention also provides adenovirus expression systems, host cells and compositions comprising adenovirus vectors which comprise modifications in BAV E1 transcriptional control regions. The present invention also provides methods for making adenovirus vectors comprising BAV sequence(s) essential for encapsidation as well as modifications in BAV E1 transcriptional control regions.

[52] US Class: 4242331 4352351 435456

[51] Int'l Class: C12N000700 A61K0039235 A61K003923 C12N0015861 C12Q000170

[52] ECLA:

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US20050123898A1 MicroPatent Report

SYSTEM FOR PRODUCING CLONAL OR COMPLEX POPULATIONS OF RECOMBINANT ADENOVIRUSES, AND THE APPLICATION OF THE SAME

[71] Applicant: N/A

[75] Inventors: Hillgenberg, Moritz

[21] Application No.: NA

[22] Filed: 20041117

[43] Published: 20050609

[30] Priority: EP EP2001117379A 20010718 ...

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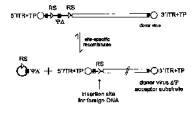

Fig. 1

[57] Abstract:

The invention relates to a novel system for producing recombinant adenoviruses (rAd). The areas of application of said system are medicine, veterinary medicine, biotechnology, genetic engineering, and functional genomic analysis. The inventive system for producing rAds preferably consists of a donor virus, the packaging signal of which is (i) partially deleted and (ii) is surrounded by parallel recognition cites for a site-specific recombinase; a packaging cell line which expresses the site-specific recombinase; and donor plasmids containing (i) at least one recognition site for the site-specific recombinase, (ii) the full viral packaging signal, (iii) optionally two recognition sites for a rarely cutting restriction endonuclease, and (iv) insertion sites for foreign DNA or inserted foreign DNA.

[52] US Class: 435005 4352351 435456

[51] Int'l Class: C12N0015861 C12N000700 A61K004800

[52] ECLA: C12N000700 C12N0015861 K61K0039525C K61K003953 K61K004800 M12N020700 M12N080030 M12N080080 M12N084020A

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DNA VACCINE

[71] **Applicant:** N/A

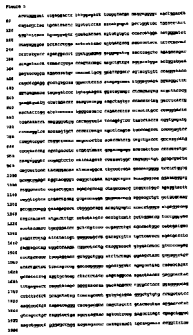
[75] **Inventors:** McCreavy, David; Fraser, William; Gallagher, James

[21] **Application No.:** NA

[22] **Filed:** 20041213

[43] **Published:** 20050609

[30] **Priority:** GB GB200129338A 20011207 ...



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[57] **Abstract:**

We describe vectors for use is DNA vaccination which are adapted such that nucleic acids which encode antigenic polypeptides are presented to the imune system in a folder or partially folded state to facilitate the production of antibodies to the native protein.

[52] **US Class:** 4240932 435005 435456 5303881 53602372

[51] **Int'l Class:** C12N001585 A61P003100 A61K003912 A61K003900 C12N001506 A61P003300 C07K001447 C07K001481

[52] **ECLA:** A61K003900 A61K003912 C07K001447A1 C07K001481 C12N001585 K61K003900 K61K003953 K61K003957 M07K021500 M12N076007 M12N083000A1A M12N083000C M12N083042 M12N083085 M12N084020A

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METHOD OF INDUCING AN ENHANCED IMMUNE RESPONSE AGAINST HIV

[71] **Applicant:** N/A

[75] **Inventors:** Emini, Emilio; Shiver, John; Chastain, Michael; Casimiro, Danilo; . . .

[21] **Application No.:** NA

[22] **Filed:** 20040909

[43] **Published:** 20050519

[30] **Priority:** US US2002363870P 20020313 ...

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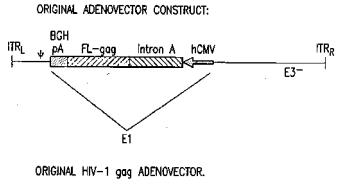

FIG.1

[57] **Abstract:**

An efficient means of inducing an immune response against human immunodeficiency virus ("HIV”) utilizing specific prime-boost regimes is disclosed. The specific prime-boost regimes employ a heterologous prime-boost protocol wherein recombinant adenoviral and poxvirus vectors comprising exogenous genetic material encoding a common HIV antigen are administered in that order. Vaccines administered into living vertebrate tissue in accordance with the disclosed regimes, preferably a mammalian host such as a human or a non-human mammal of commercial or domestic veterinary importance, express the HIV-1 antigen (e.g., Gag), inducing a cellular immune response which specifically recognizes HIV-1. It is believed that the disclosed prime/boost regime will offer a prophylactic advantage to previously uninfected individuals and/or provide a therapeutic effect by reducing viral load levels within an infected individual, thus prolonging the asymptomatic phase of HIV-1 infection.

[52] **US Class:** 4240932 4241991 435456

[51] **Int'l Class:** C12N0015863 C12N0015861 C07K001416

[52] **ECLA:** C07K001416B C12N0015861 C12N0015863V K61K0039545 M12N083042

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US20050100558A1 MicroPatent Report

HETEROLOGOUS BOOSTING IMMUNIZATIONS

[71] Applicant: US GOVERNMENT

[75] Inventors: Chamberlain, Ronald; Irvine, Kari; Rosenberg, Steven; Restifo, . . .

[21] Application No.: NA

[22] Filed: 20041208

[43] Published: 20050512

[30] Priority: US US199615893P 19960422 ...

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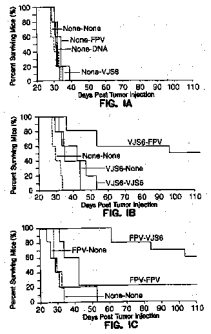

[57] Abstract:

This invention describes methods of vaccination for the effective generation of an antigen-specific immune response. More particularly, this invention describes the use of heterologous vaccination vectors for eliciting an enhanced boosting immunization response. Methods of treatment and prevention of diseases using the vaccination schemes of the invention are also provided.

[52] US Class: 4242321 514044

[51] Int'l Class: A61K003939 A61K003921 A61K003900

[52] ECLA: A61K003900D6 A61K003921 A61K003939 K61K003953

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US20050079158A1 MicroPatent Report

CONSTRUCT OF ANTI-CANCER RECOMBINANT ADENOVIRUS, METHOD FOR PREPARING THE SAME AND USE THEREOF

[71] Applicant: SHENZHEN ALLUCKS BIOTECH CO LT

[75] Inventors: Zhou, Jianfeng; Ma, Ding; Lu, Yunping; Wang, Shixuan; Chen, Gang; Gao, . . .

[21] Application No.: NA

[22] Filed: 20040603

[43] Published: 20050414

[30] Priority: CN CN2003126758A 20030605 ...

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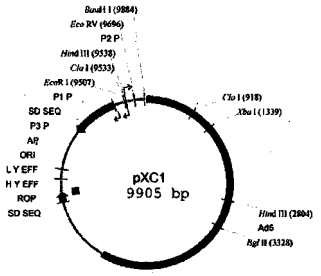
FIG. 1



[57] Abstract:

Disclosed is a recombinant human adenovirus type 5 adenovirus construct, in which a fragment in the E1A region of the ADV5 genome and a fragment in the E3 region are deleted while a foreign cDNA fragment is reversely inserted into the deleted E3 region. A method for preparing the recombinant ADV5 construct is also provided. The construct provided herein presents a tumor-specific replication, tumor-specific expression of the inserted anti-gene and tumor-specific bystander effects, and is suitable for use in tumor therapy.

[52] US Class: 4240932 4352351 435456

[51] Int'l Class: A61K003845 A61K003576 C12N0015861 A61K004800

[52] ECLA: A61K003576 A61K003845 C12N0015861 K61K004800 M07K021300 M12N071019A M12N080010E

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US20050032039A1 MicroPatent Report

HIV-SPECIFIC T-CELL INDUCTION

[71] Applicant: N/A

[75] Inventors: Sastry, K., Jagannadha; Arlinghaus, Ralph, B.; Nehete, Pramod, . . .

[21] Application No.: NA

[22] Filed: 20030929

[43] Published: 20050210

[30] Priority: US US1998108563P 19981116 ...

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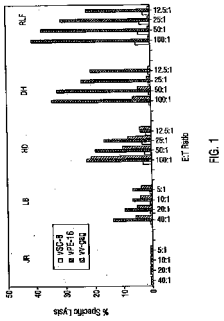

FIG. 1

[57] Abstract:

This invention discloses diagnostic, preventative, and treatment therapies of AIDS involving determining whether a subject exhibits an HLA-Cw7-restricted CTL response. Some methods are directed to the use of HLA-Cw7 as a genetic marker for long-term non-progression and amenability to treatment therapies. Diagnostic methods include a method for predicting long term non-progression in an HIV-infected subject. Preventative and treatment methods encompass determining whether a subject exhibits or can exhibit an HLA-Cw7-restricted CTL response. They also encompass ways of eliciting such a response, if necessary. Furthermore, some of the methods involve administering one or more HIV polypeptides or peptides, or polynucleotides encoding them, as a treatment therapy to prevent the development of AIDS.

[52] US Class: 435005 435006

[51] Int'l Class: G01N003350 C07K001416 G01N0033569 A61K003900

[52] ECLA: C07K001416D G01N003350D4 G01N0033569H4 G01N0033569K2 K61K003900 S01N033316 S01N033316D

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US20050019752A1 MicroPatent Report

NOVEL CHIMERIC REV, TAT, AND NEF ANTIGENS

[71] Applicant: N/A

[75] Inventors: Franchini, Genoveffa; Hel, Zdenek; Tartaglia, James

[21] Application No.: NA

[22] Filed: 20040513

[43] Published: 20050127

[30] Priority: US US2001332433P 20011116 ...

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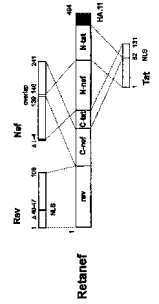

[57] Abstract:

This invention provides novel HIV antigens comprising chimeric rev, tat, and nef for use in inducing an immune response. The novel antigens can be used as vaccines to prevent and/or attenuate HIV infection.

[52] US Class: 435005 4350693 4352351 435325 435456 530350 53602372

[51] Int'l Class: C12N001586 C07K0014005 C07H002104 C12Q000170

[52] ECLA:

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ADENOVIRUS PACKAGING CELL LINES

[71] **Applicant:** N/A

[75] **Inventors:** Li, Yuanhao; Farson, Deborah; Tao, Luqun; Yu, DeChao

[21] **Application No.:** NA

[22] **Filed:** 20030703

[43] **Published:** 20050106

[30] **Priority:** US US2003613106A 20030703

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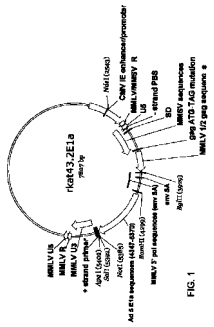

FIG. 1

[57] Abstract:

Adenovirus packaging cell lines for growth of an E1A/E1B deficient adenovirus that is substantially free of replication competent adenovirus (RCA) are provided. Methods for producing adenovirus substantially free of RCA are also provided, wherein the adenovirus is grown in a cell line containing coding sequences for adenovirus E1A and E1B, which are operably linked to promoters that lack polynucleotide sequences sharing substantial sequence identity with the native adenovirus E1A and E1B promoters.

[52] **US Class:** 435456 435325 435366

[51] **Int'l Class:** C12N001533 C12N000510 C12N000508 C12N001534

[52] **ECLA:** C12N000510T

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METHODS OF INDUCING A CYTOTOXIC IMMUNE RESPONSE AND RECORMBINANT SIMIAN ADENOVIRUS COMPOSITIONS USEFUL THEREIN

[71] **Applicant:** N/A

[75] **Inventors:** Ertl, Hildeghund, C. J.; Wilson, James, M.

[21] **Application No.:** NA

[22] **Filed:** 20031219

[43] **Published:** 20041202

[30] **Priority:** US US2001300131P 20010622 ...

Go to Fulltext



Figure 1

[57] Abstract:

A method of inducing a CD8+ T-cell response against a selected molecule by delivering the molecule via a recombinant simian adenovirus is provided. Also provided are methods of inducing interferon-α and interferon-β by delivering a recombinant simian adenovirus to a subject. The methods of the invention are particularly well suited for prophylaxis and treatment of infections with human immunodeficiency virus and human papilloma virus, among others, and cancer therapy.

[52] **US Class:** 4241861 435005

[51] **Int'l Class:** C12Q000170 A61K003912

[52] **ECLA:**

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US20040248827A1 MicroPatent Report

HYBRID ADENOVIRAL VECTOR

[71] Applicant: N/A

[75] Inventors: Zheng, Changyu; Baum, Bruce, J.

[21] Application No.: NA

[22] Filed: 20030729

[43] Published: 20041209

[30] Priority: US US2001265198P 20010130 ...

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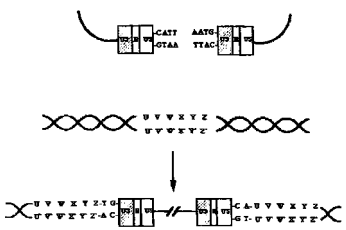
FIG. 1



[57] Abstract:

An adenoviral vector is disclosed that includes two adenoviral ITRs, wherein the two adenoviral ITRs flank a pack-aging signal and a single retroviral LTR operably linked to a nucleic acid sequence of interest, wherein the adenoviral vector does not include a nucleic acid sequence encoding the retroviral structural proteins and wherein the adenoviral vector does not include a second retroviral LTR. In one embodiment, a method for transforming a cell is disclosed. In another embodiment, a method is disclosed for introducing a transgene into a cell with a single viral vector. In a further embodiment, a method is provided for preventing or treating disorder in a subject. A pharmaceutical composition is also provided.

[52] US Class: 514044 4240932 435456

[51] Int'l Class: C12N0015861 A61K004800

[52] ECLA: C12N0015861 M12N081060D1

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US20040253210A1 MicroPatent Report

ADENOVIRUS TYPE7 VECTORS

[71] Applicant: N/A

[75] Inventors: Robert Guroff, Marjorie; Nan, Xinli; Peng, Bo; Hahn, Tae Wook

[21] Application No.: NA

[22] Filed: 20040805

[43] Published: 20041216

[30] Priority: US US2001316361P 20010830 ...

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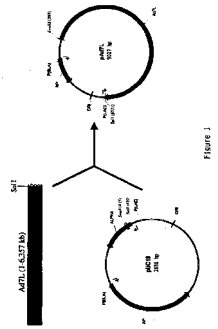

[57] Abstract:

The current invention provides novel adenovirus type 7 cosmid vectors for the production of adenovirus type 7 for use in gene transfer. In particular, the invention provides a replication-defective adenovirus type 7 that expresses one or more HIV polypeptides for use in stimulating an immune response to HIV-1.

[52] US Class: 4240932 4352351 435456

[51] Int'l Class: C12N000700 C07H002104 A61K004800 C12N0015861

[52] ECLA: A61K003921 A61K003900 C12N0015861 K61K0039525C

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PAV REGIONS FOR ENCAPSIDATION AND E1 TRANSCRIPTIONAL CONTROL

[71] Applicant: N/A

[75] Inventors: Tikoo, Suresh, K.

[21] Application No.: NA

[22] Filed: 20030718

[43] Published: 20041028

[30] Priority: US US2002397251P 20020719 ...

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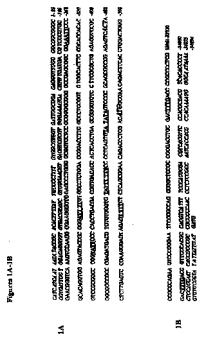

[57] Abstract:

The present invention provides porcine adenovirus sequence essential for encapsidation and provides adenovirus vectors comprising such sequences. The present invention provides host cells and composition comprising adenovirus vectors comprising porcine adenovirus sequence essential for encapsidation as well as methods for making and using such adenovirus vectors. The present invention discloses porcine adenovirus sequence for E1 transcriptional control and provides porcine adenovirus vectors comprising a modification(s) in the E1 transcriptional control region.

[52] US Class: 435005 53602372

[51] Int'l Class: C12N0015861 A61K004800

[52] ECLA: C12N0015861 K61K0039525C K61K004800 M12N083030 M12N083032

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NOVEL RECOMBINANT AND MUTANT ADENOVIRUSES

[71] Applicant: N/A

[75] Inventors: Chiang, Christina, H.; Cochran, Mark, D.

[21] Application No.: NA

[22] Filed: 20040623

[43] Published: 20041125

[30] Priority: US US1999128766P 19990409 ...

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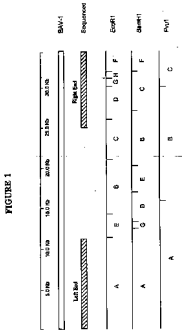

[57] Abstract:

The present invention provides novel viral vectors. In one embodiment, the present invention provides mutant and recombinant bovine adenoviruses having a deletion and/or insertion of DNA in the early gene region 4 (E4). In another embodiment, the present invention provides mutant and recombinant bovine adenovirus 1 viruses having a deletion and/or insertion of DNA in the early gene region 3 (E3). The present invention also contemplates the use of the viral vectors for vaccination, gene therapy or other applications as suitable.

[52] US Class: 4241991 4352351

[51] Int'l Class: C12N0015861

[52] ECLA: C12N0015861

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METHODS AND COMPOSITIONS FOR THE PRODUCTION OF ADENOVIRAL VECTORS

[71] Applicant: INTROGEN THERAPEUTICS INC

[75] Inventors: Zhang, Shuyuan; Pham, Hai

[21] Application No.: NA

[22] Filed: 20030515

[43] Published: 20041118

[30] Priority: US US2003439278A 20030515

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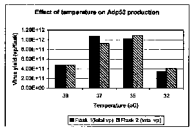

FIG. 1A

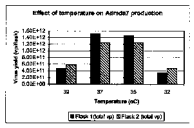

FIG. 1B

[57] Abstract:

The present invention addresses the need to improve the yield of adenovirus when grown in cell culture systems. In particular, it has been demonstrated that for adenovirus, the use of infection temperatures lower than 37° C. in a cell culture system results in improved yields of adenovirus. In addition, it has been demonstrated that when host cells are grow in a bioreactor, initiating adenovirus infection by diluting the host cells with fresh media and adenovirus results in improved yield of adenovirus. Methods of adenoviral production and purification using infection temperatures less than 37° C. are disclosed. Methods of adenoviral production and purification wherein the host cells are grown in a bioreactor and adenovirus infection is initiated by diluting the host cells with fresh media and adenovirus are also disclosed.

[52] US Class: 4352351 435456

[51] Int'l Class: C12N0015861 C12N000702 C12N000701

[52] ECLA: C12N000702 C12N0015861 M12N071019A

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VIRAL VECTORS CONTAINING RECOMBINATION SITES

[71] Applicant: INVITROGEN CORP

[75] Inventors: Bennett, Robert, P. ; Welch, Peter, J.; Harwood, Steven; Madden, Knut; . . .

[21] Application No.: NA

[22] Filed: 20030718

[43] Published: 20041104

[30] Priority: US US2002396335P 20020718 ...

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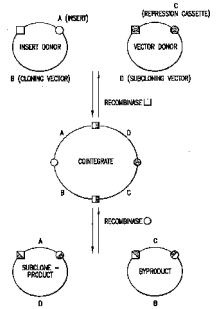

FIG.1

[57] Abstract:

The present invention provides compositions and methods for the construction of nucleic acids comprising all or portion of a viral genome. Nucleic acid molecules of the invention may be constructed to contain multiple recombination and/or topoisomerase recognition sites. The compositions include vectors having multiple recombination sites with unique specificity that contain all or a portion of a viral genome. The methods permit the insertion of a sequence of interest into a viral genome using recombinational and/or topoisomerase-mediated cloning. The present invention also provides methods of constructing recombinant virus, methods of expressing polypeptides, and methods of expressing fusion polypeptides.

[52] US Class: 435005 4350693 4353201 435325 435456 530350 53602372

[51] Int'l Class: C12N0015867 C12N001586

[52] ECLA: C12N001586 C12N0015867 M12N080010E M12N080030 M12N080070 M12N083000 M12N083000A1A M12N083015 M12N083042 M12N083060 M12N083085 M12N084020

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MODIFIED ADENOVIRAL E1A CONSTRUCTS AND METHODS OF USE THEREOF

[71] Applicant: N/A

[75] Inventors: Routes, John, M.

[21] Application No.: NA

[22] Filed: 20030327

[43] Published: 20040930

[30] Priority: US US2003402339A 20030327

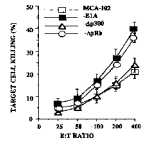

FIG. 1A

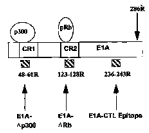

FIG. 1B

Go to Fulltext

[57] Abstract:

Recombinant nucleic acid molecules encoding a mutated Group C adenoviral E1A protein and an antigen are disclosed, as well as mutated E1A-antigen fusion proteins produced by such constructs, and compositions comprising such fusion proteins and individual proteins produced by the recombinant constructs. Also included are modified adenoviral vectors and therapeutic uses for the nucleic acids, proteins, compositions, and viral vectors of the invention.

[52] US Class: 435005 4350693 4352351 435325 435456 530350 53602372

[51] Int'l Class: C12N0015861 C07K0014075 A61K003900

[52] ECLA: C07K0014075 C12N0015861 K61K003900 K61K003953 M07K031900

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ADENOVIRUS SEROTYPE 24 VECTORS, NUCLEIC ACIDS AND VIRUS PRODUCED THEREBY

[71] Applicant: N/A

[75] Inventors: Emini, Emilio, A.; Shiver, John, W.; Bett, Andrew, J.; Casimiro, . . .

[21] Application No.: NA

[22] Filed: 20030821

[43] Published: 20040923

[30] Priority: US US2003455312P 20030317 ...

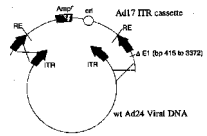

FIG. 1

Go to Fulltext

[57] Abstract:

Adenoviral serotypes differ in their natural tropism. The various serotypes of adenovirus have been found to differ in at least their capsid proteins (e.g., penton-base and hexon proteins), proteins responsible for cell binding (e.g, fiber proteins), and proteins involved in adenovirus replication. This difference in tropism and capsid proteins among serotypes has led to the many research efforts aimed at redirecting the adenovirus tropism by modification of the capsid proteins. The present invention bypasses such requirement for capsid protein modification as it presents a recombinant, replication-defective adenovirus of serotype 24, a rare adenoviral serotype, and methods for generating the alternative, recombinant adenovirus. Additionally, means of employing the recombinant adenovirus for the delivery and expression of exogenous genes are provided.

[52] US Class: 4353201 4240932 4240936 4352351 53602372

[51] Int'l Class: C12N0015861 C12N000701 C07K001416

[52] ECLA: C07K001416 C12N0015861 K61K0039525C M07K022104

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US20040170647A1 MicroPatent Report

RECOMBINANT ADENOVIRUS VACCINES

[71] Applicant: WYETH CORP

[75] Inventors: Davis, Alan, R.; Lubeck, Michael, D. ; Natuk, Robert, J. ; Chanda, Pranab, . . .

[21] Application No.: NA

[22] Filed: 20040305

[43] Published: 20040902

[30] Priority: US US1992926491A 19920807 ...

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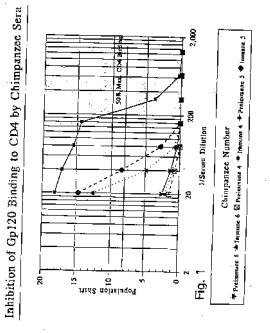

[57] Abstract:

This invention provides a method of protecting a primate from an infectious organism by stimulating the production of antibodies or cell mediated immunity to the infectious organism which comprises administering to said primate intranasally, intramuscularly, or subcutaneously, live recombinant adenoviruses in which the virion structural protein is unchanged from that in the native adenovirus from which the recombinant adenovirus is produced, and which contain the gene coding for the antigen corresponding to said antibodies or inducing said cell mediated immunity. Preferably, the infectious organism is HIV and the primate is a human.

[52] US Class: 4241991 4240932

[51] Int'l Class: C12N001507 C07K001416 C12N001548 C12N0015861 A61K003900

[52] ECLA: C07K001416 C07K001416B C07K001416D C12N0015861 K61K003900 M07K020700

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US20040136963A1 MicroPatent Report

SIMIAN ADENOVIRUS VECTORS AND METHODS OF USE

[71] Applicant: TRUSTEES OF THE UNIVERSITY OF

[75] Inventors: Wilson, James, M.; Gao, Guangping; Roy, Soumitra

[21] Application No.: NA

[22] Filed: 20031219

[43] Published: 20040715

[30] Priority: US US2001300131P 20010622 ...

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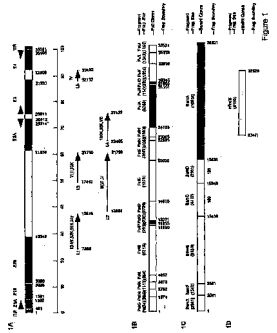

[57] Abstract:

A recombinant vector comprises a simian adenovirus capsid and a heterologous gene under the control of regulatory sequences. A cell line which expresses simian adenovirus gene(s) is also disclosed. Methods of using the vectors and cell lines are provided.

[52] US Class: 4240932 435456

[51] Int'l Class: C12N000704 C07K0014025 C07K001416 C07K0014075 C12N0015861 C07K001408 C07K0014145 A61K004800 A61K003900

[52] ECLA: C07K0014025 C07K0014075 C07K001408 C07K0014145 C07K001416B C12N000704A C12N0015861 K61K003900 K61K0039525C K61K004800 M12N022104 M12N083000A M12N083055

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NOVEL ADENOVIRAL VECTOR AND METHODS FOR MAKING AND USING THE SAME

[71] Applicant: N/A

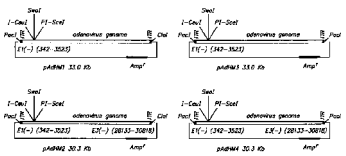
[75] Inventors: Kay, Mark, A.; Mizuguchi, Hiroyuki

[21] Application No.: NA

[22] Filed: 20010815

[43] Published: 20040603

[30] Priority: US US1998109057P 19981119 ...



Go to Fulltext

[57] Abstract:

In vitro methods for making a recombinant adenoviral genome, as well as kits for practicing the same and the recombinant adenovirus vectors produced thereby, are provided. In the subject methods, the subject genomes are prepared from first and second vectors. The first vector includes an adenoviral genome having an E region deletion and three different, non-adenoviral restriction endonuclease sites located in the E region. The second vector is a shuttle vector and includes an insertion nucleic acid flanked by two of the three different non-adenoviral vectors present in the first vector. Cleavage products are prepared from the first and second vectors using the appropriate restriction endonucleases. The resultant cleavage products are then ligated to produce the subject recombinant adenovirus genome. The subject adenoviral genomes find use in a variety of application, including as vectors for use in a variety of applications, including gene therapy.

[52] US Class: 4353201 4241991 4242331 4350691

[51] Int'l Class: C12N0015861 C07K001481 A61K004800

[52] ECLA: C07K001481B1B1 C12N0015861 K61K004800 M07K020700 M07K022104 M12N080080

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ENHANCED FIRST GENERATION ADENOVIRUS VACCINES EXPRESSING CODON OPTIMIZED HIV1-GAG, POL.NEF AND MODIFICATIONS

[71] Applicant: N/A

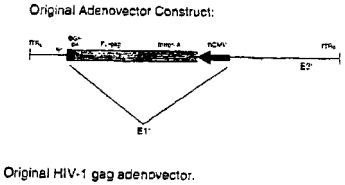
[75] Inventors: Emini, Emilio, A.; Youil, Rima; Bett, Andrew, J.; Chen, Ling; Kaslow, . . .

[21] Application No.: NA

[22] Filed: 20030314

[43] Published: 20040527

[30] Priority: US WO2001US28861A 20010914 ...



Original HIV-1 gag adenovector.

Go to Fulltext

[57] Abstract:

First generation adenoviral vectors and associated recombinant adenovirus-based HIV vaccines which show enhanced stability and growth properties and greater cellular-mediated immunity are described within this specification. These adenoviral vectors are utilized to generate and produce through cell culture various adenoviral-based HIV-1 vaccines which contain HIV-1 gag, HIV-1 pol and/or HIV-1 nef polynucleotide pharmaceutical products, and biologically relevant modifications thereof. These adenovirus vaccines, when directly introduced into living vertebrate tissue, preferably a mammalian host such as a human or a non-human mammal of commercial or domestic veterinary importance, express the HIV-1 Gag, Pol and/or Nef protein or biologically modification thereof, inducing a cellular immune response which specifically recognizes HIV-1. The exemplified polynucleotides of the present invention are synthetic DNA molecules encoding HIV-1 Gag, encoding codon optimized HIV-1 Pol, derivatives of optimized HIV-1 Pol (including constructs wherein protease, reverse transcriptase, RNAse H and integrase activity of HIV-1 Pol is inactivated), HIV-1 Nef and derivatives of optimized HIV-1 Nef, including nef mutants which effect wild type characteristics of Nef, such as myristylation and down regulation of host CD4. The adenoviral vaccines of the present invention, when administered alone or in a combined modality regime, will offer a prophylactic advantage to previously uninfected individuals and/or provide a therapeutic effect by reducing viral load levels within an infected individual, thus prolonging the asymptomatic phase of HIV-1 infection.

[52] US Class: 4353201 435006 4350691

[51] Int'l Class: C12N0015861 C12N001563 C07K001416

[52] ECLA: C07K001416B C07K001416F C12N001563 C12N0015861 K61K0039525C M07K022104 M12N083042

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US20040106184A1 MicroPatent Report

CHROMATOGRAPHIC METHODS FOR ADENOVIRUS PURIFICATION

[71] Applicant: INTROGEN THERAPEUTICS INC

[75] Inventors: Senesac, Joseph

[21] Application No.: NA

[22] Filed: 20030827

[43] Published: 20040603

[30] Priority: US US2002406591P 20020828 ...

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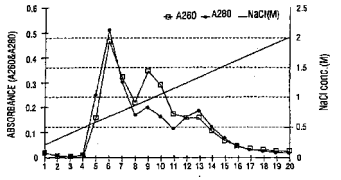

FIGURE 1

[57] Abstract:

This invention provides methods for passing adenovirus particle preparations through chromatographic media to provide purified adenovirus particles.

[52] US Class: 435239

[51] Int'l Class: C12N000702

[52] ECLA: C12N000702 M12N071019A

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US20040106194A1 MicroPatent Report

METHODS FOR PROPAGATING ADENOVIRUS AND VIRUS PRODUCED THEREBY

[71] Applicant: N/A

[75] Inventors: Bett, Andrew, J.; Chastain, Michael; Sandig, Volker; Emini, Emilio, A.; . . .

[21] Application No.: NA

[22] Filed: 20030821

[43] Published: 20040603

[30] Priority: US US2002405182P 20020822 ...

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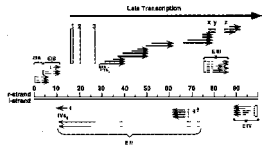

FIG. 1

[57] Abstract:

Various methods for propagating and rescuing multiple serotypes of replication-defective adenovirus in a single adenoviral E1-complementing cell line are disclosed. Typically, replication-defective adenovirus vectors propagate only in cell lines which express E1 proteins of the same serotype or subgroup as the vector. The disclosed methods offer the ability to propagate vectors derived from multiple adenoviral serotypes in a single production cell line which expresses E1 proteins from a single serotype. Propagation in this manner is accomplished by providing all or a portion of an E4 region in cis within the genome of the replication-defective adenovirus. The added E4 region or portion thereof is cloned from a virus of the same or highly similar serotype as that of the E1 gene product(s) of the complementing cell line. Interaction between the expressed E1 of the cell line and the heterologous E4 of the replication-defective adenoviral vectors enables their propagation and rescue. The invention bypasses a need in the art to customize specific cell lines to the serotype or subgroup of the adenoviral vector being propagated and enables one to easily and rapidly develop alternative adenoviral serotypes as gene delivery vectors for use as vaccines or as a critical component in gene therapy.

[52] US Class: 4353201 435006 4352351

[51] Int'l Class: C12Q000168 C12N001500 C12N000701 C12N000700 C12N001574 C12N001509 C12N001563 C12N001570

[52] ECLA: C12N0015861 A61K003921 M12N071019 M12N074003F

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MODIFIED ADENOVIRAL FIBER AND USES

[71] Applicant: TRANSGENE SA

[75] Inventors: Van Raaij, Mark, Johan; Cusack, Stephen; Legrand, Valerie; Leissner, . . .

[21] Application No.: NA

[22] Filed: 20030926

[43] Published: 20040226

[30] Priority: FR FR199910859A 19990827 ...

Go to Fulltext

[No drawing]

[57] Abstract:

The present invention relates to a modified fiber of an adenovirus, comprising at least one mutation at one or more residues within the region of said fiber stretching from pleated sheet A to pleated sheet B, and including loop AB.

[52] US Class: 435005 4352351 530350

[51] Int'l Class: C12N0015861

[52] ECLA: C12N0015861T M12N081010 M12N081040 M12N081085A M12N081085C M12N081085G

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VECTORS AND VIRAL VECTORS, AND PACKAGING CELL LINES FOR PROPAGATING SAME

[71] Applicant: N/A

[75] Inventors: Liu, Dakai; Rabbani, Elazar

[21] Application No.: NA

[22] Filed: 20030604

[43] Published: 20040226

[30] Priority: US US1997822963A 19970321 ...

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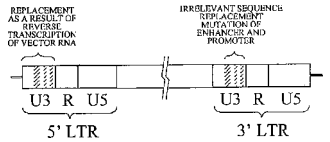

Figure 1

[57] Abstract:

Provided are novel vectors and viral vectors capable of expressing exogenous gene or exogenous nucleic acid sequences in a target cell of interest, such as T cells, bone marrow cells, epithelial cells, liver cells and the like. The nucleic acid components of the vectors may include one or more native promoter/enhancer regions having modified sequence segments, one or more non-native promoter/enhancer or non-native promoter's gene or gene segment, and a native viral vector terminator or processing signal or segment thereof. The viral vectors comprise a virus or viral portion having on the surfaces or envelopes adsorption components, one for a packaging cell line and the other for delivery to a target cell. Other viral vectors provided by this invention have two components on their surfaces or envelopes, one of which is native to the virus and the other being non-native and capable of adsorbing to the target cell while being incapable of adsorbing to a native cell for the viral vector. Packaging cell lines for propagating the vectors and viral vectors are also provided, as are novel processes for propagating any of the disclosed vectors or viral vectors.

[52] US Class: 435456 4352351

[51] Int'l Class: C12N0015867 C12N001586 C12N000700

[52] ECLA: C12N0015867 C12N000700 M12N072006C M12N074003 M12N079902A67

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FIBER SHAFT MODIFICATIONS FOR EFFICIENT TARGETING

[71] Applicant: NOVARTIS AG; SCRIPPS RESEARCH INST

[75] Inventors: Kaleko, Michael; Nemerow, Glen, R.; Smith, Theodore; Stevenson, Susan, . . .

[21] Application No.: NA

[22] Filed: 20030124

[43] Published: 20040101

[30] Priority: US US2002350388P 20020124 ...

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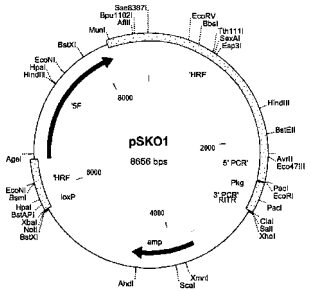

FIG. 1

[57] Abstract:

Provided are adenoviral vectors and the production of such vectors. In particular, fiber shaft modifications for efficient targeting of adenoviral vectors are provided. The fiber shaft modifications can be combined with other modifications, such as fiber knob and/or penton modifications, to produce fully ablated (detargeted) adenoviral vectors. A scale-up method for the propagation of detargeted adenoviral vectors is also provided.

[52] US Class: 435005 4350693 4352351 4353201 435325 435456 530350 53602372

[51] Int'l Class: C12N000702 C12N000508 C07K0014075 C12N0015861

[52] ECLA: C07K0014075 C12N000702 C12N0015861 C12N0015861T M07K020700 M12N071019A M12N081060A1 M12N080030 M12N081040A

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ADENOVIRAL VECTORS HAVING NUCLEIC ACIDS ENCODING IMMUNOMODULATORY MOLECULES

[71] Applicant: N/A

[75] Inventors: Scaria, Abraham; Wadsworth, Samuel

[21] Application No.: NA

[22] Filed: 20021112

[43] Published: 20040205

[30] Priority: US US1999130415P 19990421 ...

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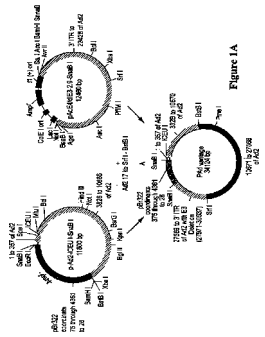

Figure 1A

[57] Abstract:

The invention relates to recombinant adenoviral vectors for use in delivering a nucleic acid(s) encoding an immunomodulatory molecule(s) to the cells of an individual that allows the vector to reduce or evade the host immune response from the cells of said individual. These vectors could be used to induce tolerance to an adenovirus antigen or transgenic products by transduction of antigen-presenting cells of an individual and/or increase the half-life of antigen-presenting cells in order to enhance immune response against tumor antigens.
The invention further relates to recombinant adenoviral vectors for use in delivering desired therapeutic transgenes to cells in patients, said vectors containing at least one nucleic acid encoding an immunomodulatory molecule that allow the vectors containing said nucleic acid(s) to reduce or evade the host antiviral immune response to the adenovirus and one or more transgenes. These vectors are capable of increased persistence in the individual to whom they are administered, thereby facilitating longer term administration of transgenes and reduced immunologic response upon administration. The invention also relates to methods for the use of such vectors in delivering transgenes to patients for therapeutic uses.

[52] US Class: 435456 4240932 4352351 4353201

[51] Int'l Class: C07K0014705 C07K001401 A61K004800 C12N0015861

[52] ECLA: A61K004800 C07K001401 C07K0014705Q C12N0015861 K61K004800 M07K022104 M12N022104 M12N081060A

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SELF-REARRANGING DNA VECTORS

[71] **Applicant:** N/A

[75] **Inventors:** Seed, Brian; Freeman, Mason, Wright; Kovtun, Alexander; . . .

[21] **Application No.:** NA

[22] **Filed:** 20030307

[43] **Published:** 20040212

[30] **Priority:** US US2000231053P 20000908 ...

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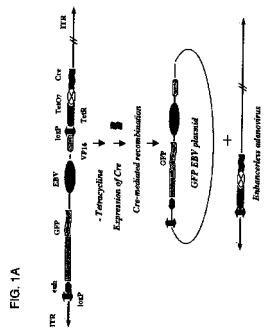

FIG. 1A

[57] **Abstract:**

Disclosed are replicatable viral DNA vectors encoding a site-specific DNA-altering enzyme and a DNA target recognized by the enzyme, the enzyme selectively converting, in a cell expressing the enzyme, the DNA vector to a rearranged form. The invention further relates to methods for assembling recombinant adenoviral DNAs. These methods include the steps of: (a) providing a first linearized DNA vector including a restriction site and a cos site and a second linearized DNA vector including the restriction site, an adenoviral nucleic acid molecule, and a cos site; and (b) ligating the first and second linearized DNA vectors, the ligation assembling a recombinant adenoviral DNA.

[52] **US Class:** 4240932 4352351 435456

[51] **Int'l Class:** C12N0015861 A61K004800

[52] **ECLA:** C12N0015861 K61K004800 M12N080010E M12N080030 M12N083000A2A M12N083000C M12N083015 M12N083020A M12N083038 M12N083044 M12N083085 M12N084020A

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FIBER SHAFT MODIFICATIONS FOR EFFICIENT TARGETING

[71] **Applicant:** SCRIPPS RESEARCH INST; NOVARTIS AG

[75] **Inventors:** Kaleko, Michael; Nemerow, Glen, R.; Smith, Theodore; Stevenson, Susan, . . .

[21] **Application No.:** NA

[22] **Filed:** 20030327

[43] **Published:** 20031120

[30] **Priority:** US US2002350388P 20020124 ...

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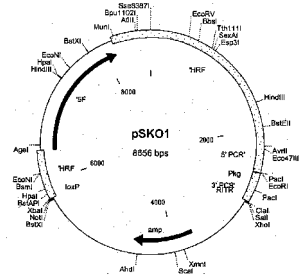

FIG. 1

[57] **Abstract:**

Provided are adenoviral vectors and the production of such vectors. In particular, fiber shaft modifications for efficient targeting of adenoviral vectors are provided. The fiber shaft modifications can be combined with other modifications, such as fiber knob and/or penton modifications, to produce fully ablated (detargeted) adenoviral vectors. A scale-up method for the propagation of detargeted adenoviral vectors is also provided.

[52] **US Class:** 435456 4352351 4353201 435370

[51] **Int'l Class:** C12N000702 C12N000508 C07K0014075 C12N0015861

[52] **ECLA:** C07K0014075 C12N000702 C12N0015861 C12N0015861T M07K020700 M12N071019A M12N081060A1 M12N080030 M12N081040A

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DNA-BASED PLASMID FORMULATIONS AND VACCINES AND PROPHYLACTICS CONTAINING THE SAME

[71] Applicant: N/A

[75] Inventors: Lasher, Alfred, W.; Kittle, Joseph, D. ; Widen, Steven, G.

[21] Application No.: NA

[22] Filed: 20021104

[43] Published: 20031211

[30] Priority: US US2001337860P 20011105 ...

Go to Fulltext

Figure 1. Coding nucleotide sequence for the parental antigen for pol HTLV-IIIb fragment (wild type clade B).

GTG CTG GAG GAG ATG TCC CTG CCC GGG CGC TGG AAG CCC AAG
ATG ATC GGC GGC ATC GGC GGC TTC ATC AAG GTC CGC CAG TAC
GAC CAG ATC CTG ATC GAG ATC TGC GGC CAC AAG GCC ATC GGC
ACC GTG CTG GTG GGA CCC ACC CCC GTG AAC ATC ATC GGC CGC
AAC CTG CTG ACC CAG ATC GGC TGC ACC CTG AAC TTC CCC ATC
TCC CCC ATC GAG ACC GTG CCC GTG AAG CTG AAG CCC GGC ATG
GAC GGC CCC AAG GTG AAG CAG TGG CCC CTG ACC GAG GAG AAG
ATC AAG GCC CTG GTC GAA ATC TGC ACC GAG ATG GAG AAG GAG
GGC AAA ATC TCC AAG ATC GGC CCC GAG AAC CCC TAC AAC ACC
CCC GTG TTC GCC ATC AAG AAG AAG GAC TCC ACC AAG TGG CGC
AAG CTG GTG GAC TTC CGC GAG CTG AAC AAG CGC ACC CAG GAC
TTC TGG GAG GTC CAG CTG GGC ATC CCC CAC CCC GCC GGC CT

Go to Fulltext

[57] Abstract:

The invention is a general method for improving the performance of the DNA-based vaccines. The method utilizes a complex DNA-generated profile of antigens to extend the effects of DNA-based vaccines and to broaden the immune response. This broadened immune response in turn improves the protection of the recipient from divergent (but related) strains of a pathogen. In addition, it effectively improves the efficacy of DNA-based vaccines used for treatment of viral diseases, including acquired immunity disorder (AIDS). One embodiment, where the target viral pathogen is HIV (the causative agent for aids), the method identifies an orderly set of plasmids of related sequences that may be used to prime a broad and strong immune response to HLA-restricted viral antigens. This mixture of plasmids is thus capable of priming an appropriate immune response to reduce the viral burden in HIV infected patients or to protect uninfected patients from HIV infection.

[52] US Class: 4241881 42409321 4242081

[51] Int'l Class: A61K004800 A61K003921

[52] ECLA: A61K003921 A61K004800B2 K61K003953 M07K022104

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ADENOVIRUS CARRYING GAG GENE HIV VACCINE

[71] Applicant: MERCK CO INC

[75] Inventors: Chen, Ling; Shiver, John, W.; Bett, Andrew, J.; Casimiro, Danilo, R.; . . .

[21] Application No.: NA

[22] Filed: 20030613

[43] Published: 20031211

[30] Priority: US US1999142631P 19990706 ...

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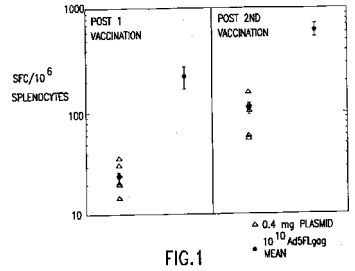

FIG.1

[57] Abstract:

An adenoviral vector is described which carries a codon-optimized gag gene, along with a heterologous promoter and transcription terminator. This viral vaccine can effectively prevent HIV infection when administered to humans either alone or as part of a prime and boost regime also with a vaccine plasmid.

[52] US Class: 4241991 4352351 435456

[51] Int'l Class: C12Q000170 C12N0015861 C07K001416

[52] ECLA: C07K001416B C12N0015861 C12Q000170B2B K61K0039525C K61K003953 M07K022104

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US20030219460A1 MicroPatent Report

COTTON RAT LUNG CELLS FOR VIRUS CULTURE

[71] Applicant: N/A

[75] Inventors: David, Frederic, R. ; Reddy, Sudhir, K. ; Tanner, Michael, E.

[21] Application No.: NA

[22] Filed: 20030318

[43] Published: 20031127

[30] Priority: US US2002366014P 20020320 ...

[No drawing]

Go to Fulltext

[57] Abstract:

A cotton rat cell line, uses of cotton rat cells for growing, propagating, or culturing organisms, pathogens or viruses, such as PRRSV, and uses of the resultant organisms, pathogens or viruses, are disclosed.

[52] US Class: 4242041 4352351 435353 435456

[51] Int'l Class: A61K003921 C12N000500 C12N000506 C12N000700 C12N000702 A61K003942

[52] ECLA: A61K003921 C12N000506B12L C12N000702 M12N077014

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US20030219410A1 MicroPatent Report

ADENOVIRAL VECTORS FOR MODULATING THE CELLULAR ACTIVITIES ASSOCIATED TO PODS

[71] Applicant: TRANSGENE SA

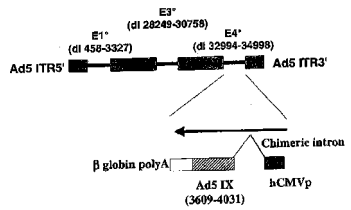
[75] Inventors: Calatrava, Manuel, Rosa

[21] Application No.: NA

[22] Filed: 20030131

[43] Published: 20031127

[30] Priority: EP EP2002360050A 20020201 ...



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[57] Abstract:

The present invention concerns a method of modulating one or more cellular activities dependent on a POD nuclear structure in a host cell through the action of a molecule of adenoviral origin, wherein said molecule of adenoviral origin is capable of interacting with the cellular function of said POD nuclear structure. In a first aspect, the present invention provides a method, a replication-defective adenoviral vector and a composition intended to reduce or inhibit one or more POD-dependent cellular activities by introducing said adenoviral molecule in the host cell. The invention also relates to the use of such replication-defective adenoviral vector or molecule to provide a reduction or an inhibition of the antiviral or apoptosis cellular activities as well as to provide a reduction of the toxicity induced by a replication-defective adenovirus vector or to enhance transgene expression driven from said replication-defective adenovirus vector. In a second aspect, the present invention provides a replication-competent adenoviral vector having native pIX or E4orf3 gene non-functional or deleted, as well as a viral particle, a host cell and a composition comprising such a replication-competent adenoviral vector and a method of treatment using such a replication-competent adenoviral vector. The present invention also concerns a method of enhancing apoptosis in a host cell using such a replication-competent adenoviral vector.

[52] US Class: 4240932 435456

[51] Int'l Class: C12N0015861 A61K003816 A61K004800

[52] ECLA: A61K003816A C12N0015861 K61K004800 M12N083042

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COMPLEMENTING CELL LINES

[71] **Applicant:** N/A

[75] **Inventors:** Vogels, Ronald; Havenga, Menzo, Jans Emco; Mehtali, Majid

[21] **Application No.:** NA

[22] **Filed:** 20011115

[43] **Published:** 20031002

[30] **Priority:** US US2000713678A 20001115 ...

Go to Fulltext



[57] **Abstract:**

A packaging cell line capable of complementing recombinant adenoviruses based on serotypes from subgroup B, preferably adenovirus type 35. The cell line is preferably derived from primary, diploid human cells (e.g., primary human retinoblasts, primary human embryonic kidney cells and primary human amniocytes) which are transformed by adenovirus E1 sequences either operatively linked on one DNA molecule or located on two separate DNA molecules, the sequences being operatively linked to regulatory sequences enabling transcription and translation of encoded proteins. Also disclosed is a cell line derived from PER.C6 (ECACC deposit number 96022940), which cell expresses functional Ad35 E1B sequences. The Ad35-E1B sequences are driven by the E1B promoter or a heterologous promoter and terminated by a heterologous poly-adenylation signal. The new cell lines are useful for producing recombinant adenoviruses designed for gene therapy and vaccination. The cell lines can also be used for producing human recombinant therapeutic proteins such as human growth factors and human antibodies. In addition, the cell lines are useful for producing human viruses other than adenovirus such as influenza virus, herpes simplex virus, rotavirus, measles virus.

[52] **US Class:** 4240932 4352351 435325 435456

[51] **Int'l Class:** C12N000510 C12N000502 C12N001509 C12N000700 C12N000701 C12N0015861

[52] **ECLA:** C12N000510T C12N0015861 M12N084020

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MINIMAL ADENOVIRAL VECTOR

[71] **Applicant:** GENSTAR THERAPEUTICS CORP

[75] **Inventors:** Zhang, Wei Wei; Alemany, Ramon; Dai, Yifan; Josephs, Steven; Balague, . . .

[21] **Application No.:** NA

[22] **Filed:** 20020528

[43] **Published:** 20031009

[30] **Priority:** US WO1997US10218A 19970530 ...

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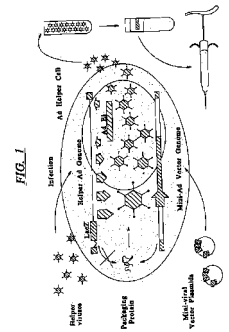

[57] **Abstract:**

This invention is related to adenoviral (Ad) vectors and their applications in the field of genetic medicine, including gene transfer, gene therapy, and gene vaccination. More specifically, this invention is related to the Ad vectors that carry the minimal cis-element of the Ad genome (mini-Ad vector) and are capable of delivering transgenes and/or heterologous DNA up to 36 kb. The generation and propagation of the mini-Ad vectors require trans-complementation of a packaging-attenuated and replication-defective helper Ad (helper) in an Ad helper cell line. This invention further comprises a methodology for generating a mini-adenoviral (mini-Ad) vector for use in gene therapy of hemophilia and animal test systems for in vivo evaluation of the Ad vectors. More specifically, this invention describes factor VIII (FVIII) Ad vectors that only contain minimal cis-elements of the Ad genome (so called mini-Ad) and comprise a human FVIII cDNA with other supporting DNA elements up to 36 kb. The FVIII mini-Ad can be generated and preferentially amplified through the assistance of a packaging-attenuated helper Ad and a helper cell line. This invention also reports designs and methods for producing transgenic mouse models that can be used for in vivo testing the mini-Ad.

[52] **US Class:** 800008 4240932 4352351 4353201 435456 5360232 800021

[51] **Int'l Class:** A01K0067027 C12N0015861 C07K0014755 C12N001534 C12N001585 A61K004800 A61K003800

[52] **ECLA:** C12N0015861 A01K0067027M A01K0067027M2 A01K0067027M4 C07K0014755 C12N001585A3B C12N001585A3D K01K021700 K01K021702 K01K021706 K01K022710M K01K026703D K61K003800 K61K004800 M07K020700 M07K022104 M12N080010E M12N080030 M12N083000A1A M12N083000C M12N083015 M12N083038 M12N083042 M12N083085 M12N084020A M12N084020A2 K01K026703R

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VIRAL VECTORS HAVING TISSUE TROPISM FOR T-LYMPHOCYTES, B-AND MAST CELLS

[71] Applicant: N/A

[75] Inventors: van Es, Helmuth, Hendrikus Gerardus; van Zutphen, Marlijn; Ma, Libin; . . .

[21] Application No.: NA

[22] Filed: 20010925

[43] Published: 20030925

[30] Priority: NL WO2000NL325A 20000516 ...

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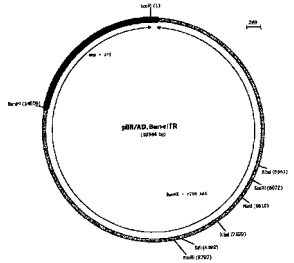
Figure 1



[57] Abstract:

The present invention relates to a method of introducing an expressible non-viral nucleic acid sequence into a cell having a common non-universal binding receptor and selected from T lymphocytes, B-, and mast cells, comprising contacting said cell with a viral vector comprising a recombinant nucleic acid sequence containing sequence for said expressible non-viral nucleic acid and comprising a modified viral coat consisting of native viral coat proteins and modified coat protein containing adenoviral amino acid sequence from an adenoviral serotype 35 or 51 fibre protein, wherein said adenoviral sequence of said modified protein is a ligand for said binding receptor. Alternatively said vector comprises a sequence coding for a viral capsid consisting of native adenoviral capsid proteins and modified capsid protein containing amino acid sequence from an adenoviral serotype other than the serotype of said native capsid proteins, wherein said modified protein is a ligand for said binding receptor. The present invention also relates to a method for transducing a cell, said cell selected from the group consisting of T lymphocytes, B cells, and mast cells comprising contacting said cells with an adenovirus particle comprising a non-adenovirus nucleic acid sequence and a chimeric capsid protein comprising amino acid sequence derived from at least two adenovirus serotypes, wherein said particle has a greater tropism for said cells relative to at least one of the adenovirus serotypes comprising said chimeric capsid protein. The present invention further relates to transduced cells, arrays of subpopulations of cells, a method for ex vivo transduction of a population of

[52] US Class: 4240932 435456

[51] Int'l Class: C12N0015861 A61K004800

[52] ECLA: C12N0015861T K61K004800 M12N081060 M12N081060A1 M12N081060D1

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ADENOVIRUS VECTORS, PACKAGING CELL LINES, COMPOSITIONS, AND METHODS FOR PREPARATION AND USE

[71] Applicant: N/A

[75] Inventors: Von Seggern, Daniel, J.; Nemerow, Glen, R.; Hallenbeck, Paul; . . .

[21] Application No.: NA

[22] Filed: 20000114

[43] Published: 20030821

[30] Priority: US US1996719806A 19960925 ...

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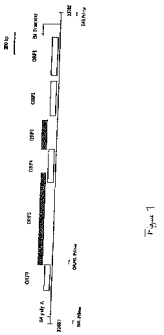

[57] Abstract:

The present invention relates to methods for gene therapy, especially to adenovirus-based gene therapy, and related cell lines and compositions. In particular, novel nucleic acid constructs and packaging cell lines are disclosed, for use in facilitating the development of high-capacity and targeted vectors. The invention also discloses a variety of high-capacity adenovirus vectors and related compositions and kits including the disclosed cell lines and vectors. Finally, the invention discloses methods of preparing and using the disclosed vectors, cell lines and kits.

[52] US Class: 4352351 4240932 435325 435456 5360232

[51] Int'l Class: C12N0015861 C07K0014075 A61K004800

[52] ECLA: C07K0014075 C12N0015861 C12N0015861C C12N0015861T K61K004800 M07K020700 M12N080010E M12N081060A1 M12N083048

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MODIFIED ADENOVIRAL FIBER AND TARGET ADENOVIRUSES

[71] Applicant: TRANSGENE SA

[75] Inventors: Legrand, Valerie; Mehtali, Majid; Boulanger, Pierre

[21] Application No.: NA

[22] Filed: 20030401

[43] Published: 20030918

[30] Priority: FR FR19973987A 19970402 ...

Go to Fulltext

[No drawing]

[57] Abstract:

The invention relates to an adenovirus fiber modified by the mutation of one or more residues. The residues are directed towards the natural cell receptor in the three-dimensional structure of said adenovirus. The invention further relates to a DNA fragment, and expression vector, and a cell line expressing said fiber, and also concerns an adenovirus, the process for producing this type of adenovirus, and a infectable host cell, as well as their therapeutic application and a corresponding pharmaceutical composition.

[52] US Class: 4240932 4352351 435325 435456 530350

[51] Int'l Class: C12N0015861 C07K0014075 A61K003800

[52] ECLA: C07K0014075 C12N0015861 K61K003800 M07K020500 M07K020700 M07K021300 M07K022104 M07K031900 M12N083000 M12N083042 M12N083060

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CELL-SPECIFIC ADENOVIRUS VECTORS COMPRISING AN INTERNAL RIBOSOME ENTRY SITE

[71] Applicant: N/A

[75] Inventors: Yu, De Chao; Li, Yuanhao; Little, Andrew, S.; Henderson, Daniel, R.

[21] Application No.: NA

[22] Filed: 20010321

[43] Published: 20030807

[30] Priority: US US2000192156P 20000324 ...

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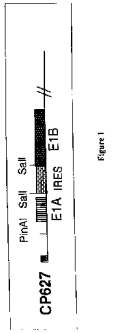

[57] Abstract:

Disclosed herein are replication-competent adenovirus vectors comprising co-transcribed first and second genes under transcriptional control of a heterologous, target cell-specific transcriptional regulatory element (TRE), wherein the second gene is under translational control of an internal ribosome entry site. Methods for the preparation and use of such vectors are also provided. The vectors provide target cell-specific virus replication in applications such as cancer therapy and gene therapy.

[52] US Class: 435456 4240932 4352351 4353201

[51] Int'l Class: C12N0015861 C07K0014075 A61K004800

[52] ECLA: C07K0014075 C12N0015861 K61K004800 M12N083000 M12N083000A M12N083000C M12N083085 M12N084020A2

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RECEPTOR-TARGETED ADENOVIRAL VECTORS

[71] Applicant: N/A

[75] Inventors: Davidson, Beverly, L.; Xia, Haibin; Law, Lane, K.

[21] Application No.: NA

[22] Filed: 20021107

[43] Published: 20030717

[30] Priority: US US2001339282P 20011211 ...

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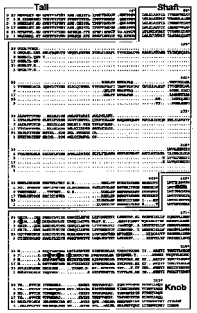

[57] Abstract:

The invention provides adenoviral vectors possessing fibers that do not bind CAR, a receptor-targeting ligand sequence, the non-receptor targeting sequence derived from HIV-TAT, a sequence encoding the HI loop of the non-CAR binding adenovirus fiber, which permits specific receptor-targeted transduction with the recombinant adenovirus vectors. The invention also provides related chimeric proteins, adenovirus particles and mammalian cells.

[52] US Class: 4240932 4352351 4353201 435366 435456

[51] Int'l Class: C07K0014075 C12N000508 C12N0015864 A61K004800 A61K003800

[52] ECLA: C07K0014075 C12N0015864 K61K003800 K61K004800 M07K020700 M07K022104 M07K031900

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PORCINE ADENOVIRUS TYPE 3 GENOME

[71] Applicant: N/A

[75] Inventors: Reddy, Police, Seshidhar; Tikoo, Suresh, Kumar; Babiuk, Lorne, A.

[21] Application No.: NA

[22] Filed: 20020916

[43] Published: 20030710

[30] Priority: US US199881882P 19980415 ...

Go to Fulltext



FIG..1-1

[57] Abstract:

The complete nucleotide sequence of the genome of porcine adenovirus type 3 (PAV-3) is provided. Methods for construction of infectious PAV genomes by homologous recombination in procaryotic cells are provided. Recombinant PAV viruses are obtained by transfection of mammalian cells with recombinant PAV genomes. The PAV-3 genome can be used as a vector for the expression of heterologous nucleotide sequences, for example, for the preparation and administration of subunit vaccines to swine or other mammals. In addition, PAV-3 vectors can be used for gene therapy and expression of heterologous polypeptides. PAV-3 genome sequences can also be used for diagnostic purposes, to detect the presence of PAV-3 DNA in a subject or biological sample.

[52] US Class: 514012 435005 435006 4352351 4353201 435456 530350

[51] Int'l Class: C12N000704 C07K0014075 C12N0015861 A61K004800

[52] ECLA: C07K0014075 C12N000704A C12N0015861 K61K003953 K61K004800 M07K020700 M07K021500

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US20030118555A1 MicroPatent Report

TARGET CELL-SPECIFIC ADENOVIRAL VECTORS CONTAINING E3 AND METHODS OF USE THEREOF

[71] Applicant: N/A

[75] Inventors: Henderson, Daniel, R.; Yu, De, Chao

[21] Application No.: NA

[22] Filed: 20020821

[43] Published: 20030626

[30] Priority: US US1998114262P 19981230 ...

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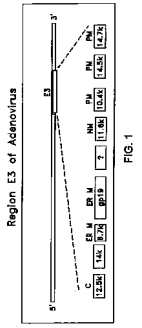

[57] Abstract:

The invention provides adenoviral vectors (preferably replication competent) comprising both an E3 sequence and at least one adenoviral gene under transcriptional control of a target cell-specific transcriptional response element. These vectors display significantly improved cytotoxicity, which is especially useful in the cancer context, in which selective destruction of target cells is desirable. The invention further provides host cells comprising the vectors. The invention further provides methods of using the adenoviral vectors.

[52] US Class: 4240932 4352351 4353201 435456

[51] Int'l Class: C12N0015861

[52] ECLA: C12N0015861T

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US20030152914A1 MicroPatent Report

METHOD FOR GENERATING REPLICATION DEFECTIVE VIRAL VECTORS THAT ARE HELPER FREE

[71] Applicant: N/A

[75] Inventors: Kaplitt, Michael, G.; Moussatov, Sergei

[21] Application No.: NA

[22] Filed: 20020531

[43] Published: 20030814

[30] Priority: US US2001294797P 20010531 ...

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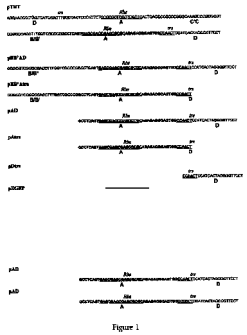
Figure 1

[57] Abstract:

Sequences are provided that are capable of directing circular adeno-associated virus replication, useful in vectors for providing therapeutic agents to a subject in need thereof. The vectors of the invention are particularly useful in the treatment of acute medical conditions requiring rapid gene expression. Further provided are methods for producing packaged defective viral vectors.

[52] US Class: 435005 435006 4352351 4353201 435456

[51] Int'l Class: C12N0015864 C12N000704

[52] ECLA: C12N000704A C12N0015864A

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PORCINE ADENOVIRUS E1 REGION

[71] **Applicant:** N/A

[75] **Inventors:** Tikoo, Suresh, K.

[21] **Application No.:** NA

[22] **Filed:** 20010924

[43] **Published:** 20030731

[30] **Priority:** US US2001963038A 20010924

Go to Fulltext



[57] **Abstract:**

The present invention relates to the characterization of the porcine adenovirus E1 region. The complete nucleotide sequence of the genome of porcine adenovirus type 3 (PAV-3), providing the characterization of the PAV3 E1 region, is described herein. Methods for construction of infectious PAV genomes by homologous recombination in procaryotic cells are provided. Recombinant PAV viruses are obtained by transfection of mammalian cells with recombinant PAV genomes. The PAV-3 genome can be used as a vector for the expression of heterologous nucleotide sequences, for example, for the preparation and administration of subunit vaccines to swine or other mammals.

[52] **US Class:** 4240932 4352351 4353201 435456 514044

[51] **Int'l Class:** C12N001586 C12N000700 A61K004800 C12N0015869

[52] **ECLA:**

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METHOD OF VACCINATION THROUGH SEROTYPE ROTATION

[71] **Applicant:** N/A

[75] **Inventors:** Wang, Danher

[21] **Application No.:** NA

[22] **Filed:** 20030317

[43] **Published:** 20030724

[30] **Priority:** US US2000585599A 20000602 ...

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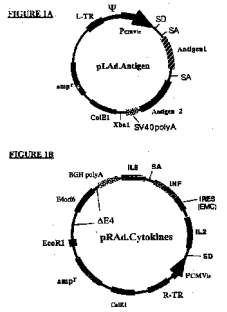

[57] **Abstract:**

Recombinant adenovirus and methods of administration to a host are provided for eliciting immune response of the host to various pathogens. In one aspect of the invention, a vaccination method is provided for enhancing immunity of the host to the pathogen through rotation of the serotypes of the recombinant adenoviruses administered to the host. The method comprises administering to the host a first recombinant adenovirus comprising a first antigen sequence heterologous to native adenovirus and encoding a first viral antigen from the first pathogenic virus, expression of the first viral antigen by the first recombinant adenovirus eliciting an immune response directed against the first viral antigen in a host upon infection of the host by the first recombinant adenovirus; and administering to the host a second recombinant adenovirus comprising a second antigen sequence heterologous to native adenovirus and encoding a second viral antigen from the second pathogenic virus, expression of the second viral antigen by the second recombinant adenovirus eliciting an immune response directed against the second viral antigen in a host upon infection of the host by the first recombinant adenovirus. The serotype of the second recombinant adenovirus is different from that of the first recombinant adenovirus, or certain region(s) in the backbone of the second recombinant adenovirus (e.g., the fiber region) is of different serotype from the corresponding region(s) in the backbone of the first recombinant adenovirus.

[52] **US Class:** 4242331 4241881 4241991 4242081 4242271 4242281 4242311 4353201

[51] **Int'l Class:** A61K003929 A61K003921 A61K003912 C07K001402 C07K001408 C07K001416

[52] **ECLA:** A61K003912 A61K003921 A61K003929B C07K001402 C07K001408

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RECOMBINANT PROTEIN PRODUCTION IN A HUMAN CELL

[71] Applicant: N/A

[75] Inventors: Bout, Abraham; Hateboer, Guus; Verhulst, Karina, Cornelia; . . .

[21] Application No.: NA

[22] Filed: 20020903

[43] Published: 20030515

[30] Priority: US US1999129452P 19990415 ...

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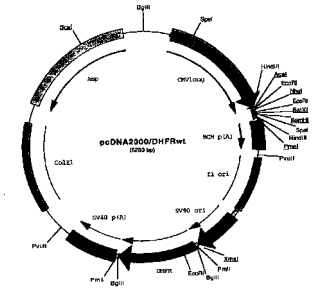

FIG. 1

[57] Abstract:

Methods and compositions for the production of recombinant proteins in a human cell line. The methods and compositions are particularly useful for generating stable expression of human recombinant proteins of interest that are modified post-translationally, for example, by glycosylation. Such proteins may have advantageous properties in comparison with their counterparts produced in non-human systems such as Chinese hamster ovary cells.

[52] US Class: 4352351 435325 435456

[51] Int'l Class: C07K001416 C07K001411 C07K0014075 C12N0015861

[52] ECLA: C07K0014075 C07K001411 C07K001416D C12N0015861 M07K020700 M12N080010E M12N083000 M12N083015 M12N083060

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NOVEL ONCOLYTIC ADENOVIRAL VECTORS

[71] Applicant: N/A

[75] Inventors: Cheng, Cheng; Clarke, Lori; Connelly, Sheila; Ennist, David, . . .

[21] Application No.: NA

[22] Filed: 20020222

[43] Published: 20030605

[30] Priority: US US2001270922P 20010223 ...

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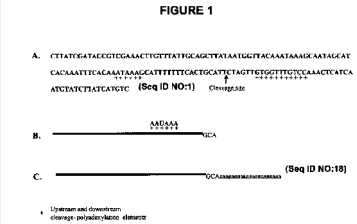

[57] Abstract:

The present invention relates to oncolytic adenoviral vectors and their use in methods of gene therapy. Provided is a recombinant viral vector comprising an adenoviral nucleic acid backbone, wherein said nucleic acid backbone comprises in sequential order: A left ITR, a termination signal sequence, an E2F responsive promoter which is operably linked to a gene essential for replication of the recombinant viral vector, an adenoviral packaging signal, and a right ITR.

[52] US Class: 435456 435199 4352351 4353201

[51] Int'l Class: C12N0015861

[52] ECLA: C12N0015861 M12N080030 M12N083000B M12N083000C M12N083085 M12N084020A

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DEFECTIVE ADENOVIRUS VECTORS AND USE THEREOF IN GENE THERAPY

[71] Applicant: N/A

[75] Inventors: Perricaudet, Michel; Vigne, Emmanuelle; Yeh, Patrice

[21] Application No.: NA

[22] Filed: 20021121

[43] Published: 20030522

[30] Priority: FR FR19938596A 19930713 ...

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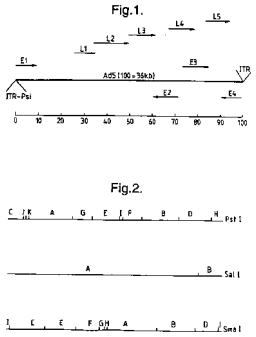

[57] Abstract:

Novel adenovirus-derived viral vectors, the preparation thereof, and the use thereof in gene therapy, are disclosed.

[52] US Class: 514044 4240932

[51] Int'l Class: C12N0015861 C12N000704 C07K0014075

[52] ECLA: C07K0014075 C12N000704A C12N0015861 M07K020700 M12N083000A1

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ADENOVIRUS PROTEIN IX, ITS DOMAINS INVOLVED IN CAPSID ASSEMBLY, TRANSCRIPTIONAL ACTIVITY AND NUCLEAR REORGANIZATION

[71] Applicant: N/A

[75] Inventors: Calatrava, Manuel, Rosa

[21] Application No.: NA

[22] Filed: 20020530

[43] Published: 20030612

[30] Priority: US US2001293974P 20010530 ...

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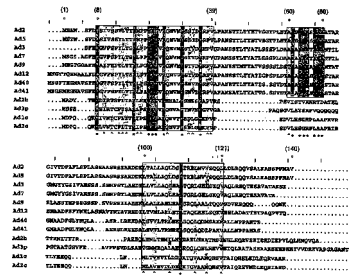

[57] Abstract:

Described are adenovirus pIX proteins which are modified by mutating one or more amino acids and/or by the inclusion of a binding moiety. Preferably, said modification is carried out in the N-terminal part or in the C-terminal leucine-repeat of the pIX protein. It is described that viruses or virus-like particles containing such a modified pIX protein show an improved gene delivery efficiency. Furthermore, described are corresponding adenoviral vectors, viruses or virus-like particles, host cells, complementation cell lines and methods for producing such viruses or virus-like particles. In addition, described are pharmaceutical compositions comprising an adenoviral vector, virus or virus-like particle, host cell or complementation cell line as mentioned above and therapeutical applications thereof.

[52] US Class: 4240932 4241861 4350693 4352351 4353201 435325 435456 530350 53602372

[51] Int'l Class: C12N000510 C07K0014075 C12N0015861 A61K004800

[52] ECLA: C07K0014075 C12N000510T C12N0015861 K61K004800

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CANINE ADENOVIRUS VECTORS FOR THE TRANSFER OF GENES IN TARGETED CELLS

[71] Applicant: N/A

[75] Inventors: Kremer, Eric; Chillon Rodriguez, Miguel; Soudais, Claire; Boutin, . . .

[21] Application No.: NA

[22] Filed: 20020607

[43] Published: 20030529

[30] Priority: EP EP1999403061A 19991207 ...

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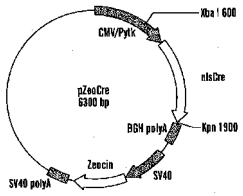

FIG. 1

[57] Abstract:

Recombinant Canine Adenovirus (CAV) vectors based on CAV-2 strain Toronto in which the CAV-2 E1 region has been deleted are described herein. Methods for the preparation of recombinant vectors include the use of transcomplementation cell lines which are specifically employed to reduce the likelihood of generating replication competent CAV-2 during propagation of the vectors. The resultant replication-defective, E1-deficient CAV preparations are highly desirable for the transfer of nucleic acid sequences in vitro and in vivo.

[52] US Class: 435456 4240932 4352351 4353201 435325 53602372

[51] Int'l Class: C12N0015861 A61K004800

[52] ECLA: C12N0015861 K61K004800 M12N080030 M12N083038 M12N083042

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METHOD AND COMPOSITION FOR TARGETING AN ADENOVIRAL VECTOR

[71] Applicant: GENVEC INC

[75] Inventors: Wickham, Thomas, J. ; Kovesdi, Imre; Roelvink, Petrus, W.; Einfeld, David; . . .

[21] Application No.: NA

[22] Filed: 20021125

[43] Published: 20030529

[30] Priority: US US2000208451P 20000531 ...

Go to Fulltext

[No drawing]

[57] Abstract:

The invention provides adenoviral coat proteins comprising various non-native ligands. Further, the present invention provides an adenoviral vector that elicits less reticulo-endothelial system (RES) clearance in a host animal than a corresponding wild-type adenovirus. Also provided by the invention is a system comprising a cell having a non-native cell-surface receptor and a virus having a non-native ligand, wherein the non-native ligand of the virus binds the non-native cell-surface receptor of the cell. Using this system, a virus can be propagated. Further provided by the invention is a method of controlled gene expression utilizing selectively replication competence, a method of assaying for gene function, a method of isolating a nucleic acid, and a method of identifying functionally related coding sequences. Additionally, the invention provides a cell-surface receptor, which facilitates internalization.

[52] US Class: 4240932 435005 4352351 435325 435456 530350

[51] Int'l Class: C12N000700 A61K004800 A61K003576 C12N001509 C12N000510 A61P003500 C12N0015861 C12N000702 C07K0014075 C12Q000102 C07K0014705

[52] ECLA: C12N0015861T K61K004800 M12N081040 M12N081040A M12N081060 M12N081080 M12N083000C

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PORCINE ADENOVIRUS E1 AND E4 REGIONS

[71] Applicant: N/A

[75] Inventors: Tikoo, Suresh, K.

[21] Application No.: NA

[22] Filed: 20020719

[43] Published: 20030529

[30] Priority: US US2001963038A 20010924 ...

Go to Fulltext



[57] Abstract:

The present invention relates to the characterization of the porcine adenovirus E1 and E4 regions. The complete nucleotide sequence of the genome of porcine adenovirus type 3 (PAV-3), providing the characterization of the PAV3 E1 region, is described herein. Methods for construction of infectious PAV genomes by homologous recombination in procaryotic cells are provided. Recombinant PAV viruses are obtained by transfection of mammalian cells with recombinant PAV genomes. The PAV-3 genome can be used as a vector for the expression of heterologous nucleotide sequences, for example, for the preparation and administration of subunit vaccines to swine or other mammals.

[52] US Class: 4240932 4352351 435456 514044

[51] Int'l Class: C12N001586 C12N000700 A61K004800 C12N0015869

[52] ECLA:

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INFECTION WITH CHIMAERIC ADENOVIRUSES OF CELLS NEGATIVE FOR THE ADENOVIRUS SEROTYPE 5 COXSACKI ADENOVIRUS RECEPTOR (CAR)

[71] Applicant: N/A

[75] Inventors: Havenga, Menzo; Vogels, Ronald

[21] Application No.: NA

[22] Filed: 20020107

[43] Published: 20030522

[30] Priority: US US1999142557P 19990707 ...

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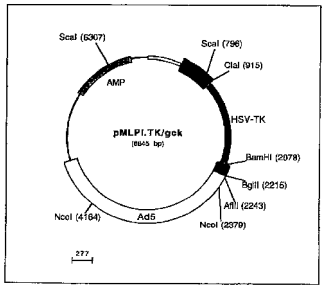
Figure 1



[57] Abstract:

A method for delivering a nucleic acid of interest to a host cell ("gene therapy") using a gene delivery vehicle based on adenoviral material. The gene delivery vehicle delivers the nucleic of acid of interest to the host cell by associating with a binding site and/or a receptor present on adenovirus serotype 5 Coxsacki adenovirus receptor ("CAR")-negative cells. The binding site and/or receptor is a binding site for adenovirus subgroup D and/or adenovirus subgroup F. Associated methods and pharmaceutical compositions are also disclosed.

[52] US Class: 435456 4240932 4352351 4353201

[51] Int'l Class: C07K0014705 C07K0014075 C12N000510 C12N0015861 A61K004800

[52] ECLA: C07K0014075 C07K0014705 C12N000510T C12N0015861C C12N0015861T K61K004800 M07K020700 M12N071019 M12N071019B M12N081060A1

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COMPOSITIONS AND METHODS FOR PRODUCTION OF RECOMBINANT VIRUSES, AND USES THEREFOR

[71] Applicant: TRUSTEES OF THE UNIVERSITY OF

[75] Inventors: Gao, Guangping; Wilson, James, M.; Alvira, Mauricio, R.

[21] Application No.: NA

[22] Filed: 20020919

[43] Published: 20030515

[30] Priority: US US2001323352P 20010919 ...

[No drawing]

Go to Fulltext

[57] Abstract:

An efficient method of producing recombinant virus is described. The method involves transfecting an uncut, circular plasmid containing a recombinant viral genome, a first I-SceI recognition site located 5' to the viral genome, and a second I-SceI recognition site located 3' to the adenovirus genome into a host cell. The host cell is then cultured under conditions in which it expresses I-SceI endonuclease. The endonuclease cleaves the I-SceI recognition sites, thereby rescuing the recombinant virus from the plasmid, making it available for packaging into an infectious virus.

[52] US Class: 4352351 435239 435456

[51] Int'l Class: C12N0015861 C12N000700 C12N000510

[52] ECLA: C12N000510T C12N000700 C12N0015861 M12N071019 M12N080080

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SITE SPECIFIC RECOMBINASE BASED METHOD FOR PRODUCING ADENOVIRAL VECTORS

[71] Applicant: N/A

[75] Inventors: Farmer, Andrew, Alan; Quinn, Thomas, Patrick

[21] Application No.: NA

[22] Filed: 20020917

[43] Published: 20030320

[30] Priority: US US2001323536P 20010918 ...

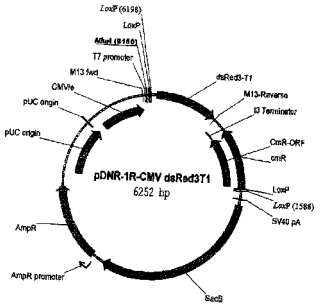

Figure 1

Go to Fulltext

[57] Abstract:

Site-specific recombinase based methods for making a recombinant adenoviral genome, as well as kits for practicing the same and the recombinant adenovirus vectors produced thereby, are provided. In the subject methods, the subject genomes are prepared from donor and acceptor vectors that each include at least one site recombinase recognition site, where in certain preferred embodiments, one of the donor and acceptor vectors includes a single recombinase recognition site while the other includes two recombinase recognition sites. The acceptor vector includes an adenoviral genome having an E region deletion. The donor vector includes an insertion nucleic acid. In the subject methods, the donor and acceptor vectors are combined in the presence of a recombinase to produce an adenoviral genome that includes the insertion nucleic acid. The subject adenoviral genomes find use in a variety of applications, including as vectors for use in a variety of applications.

[52] US Class: 435456 4352351

[51] Int'l Class: C12N0015861

[52] ECLA: C12N0015861 M12N080030

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CHIMERIC ADENOVIRUSES

[71] Applicant: N/A

[75] Inventors: Havenga, Menzo; Vogels, Ronald; Bout, Abraham

[21] Application No.: NA

[22] Filed: 20010914

[43] Published: 20030417

[30] Priority: EP EP1998202297A 19980708 ...

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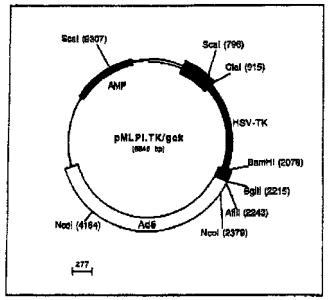
Figure 1



[57] Abstract:

Methods and vector systems for generating chimeric recombinant adenoviruses. These hybrid adenoviruses contain a genome that is derived from different adenovirus serotypes. In particular, novel hybrid adenoviruses are disclosed that have improved properties for gene therapy purposes. These properties include, but are not limited to, a decreased sensitivity towards neutralizing antibodies, a modified host range, a change in the titer to which adenovirus can be grown, the ability to escape trapping in the liver upon in vivo systemic delivery, and absence or decreased infection of antigen presenting cells of the immune system, such as macrophages or dendritic cells. These chimeric adenoviruses thus represent improved tools for gene therapy and vaccination, since they overcome the limitations observed with the currently used serotype subgroup C adenoviruses.

[52] US Class: 435005 4350071 4352351 435456

[51] Int'l Class: C12N0015861 C07K0014075

[52] ECLA: C07K0014075 C12N0015861C

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ENHANCED FIRST GENERATION ADENOVIRUS VACCINES EXPRESSING CODON OPTIMIZED HIV1-GAG, POL, NEF AND MODIFICATIONS

[71] Applicant: N/A

[75] Inventors: Emini, Emilio, A.; Youil, Rima; Bett, Andrew, J.; Chen, Ling; Kaslow, . . .

[21] Application No.: NA

[22] Filed: 20010914

[43] Published: 20030306

[30] Priority: US US2000233180P 20000915 ...

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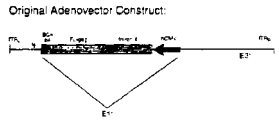

Figure 1: Original HIV-1 gag adenovector.

[57] Abstract:

First generation adenoviral vectors and associated recombinant adenovirus-based HIV vaccines which show enhanced stability and growth properties and greater cellular-mediated immunity are described within this specification. These adenoviral vectors are utilized to generate and produce through cell culture various adenoviral-based HIV-1 vaccines which contain HIV-1 gag, HIV-1 pol and/or HIV-1 nef polynucleotide pharmaceutical products, and biologically relevant modifications thereof. These adenovirus vaccines, when directly introduced into living vertebrate tissue, preferably a mammalian host such as a human or a non-human mammal of commercial or domestic veterinary importance, express the HIV1-Gag, Pol and/or Nef protein or biologically modification thereof, inducing a cellular immune response which specifically recognizes HIV-1. The exemplified polynucleotides of the present invention are synthetic DNA molecules encoding HIV-1 Gag, encoding codon optimized HIV-1 Pol, derivatives of optimized HIV-1 Pol (including constructs wherein protease, reverse transcriptase, RNAse H and integrase activity of HIV-1 Pol is inactivated), HIV-1 Nef and derivatives of optimized HIV-1 Nef, including nef mutants which effect wild type characteristics of Nef, such as myristylation and down regulation of host CD4. The adenoviral vaccines of the present invention, when administered alone or in a combined modality regime, will offer a prophylactic advantage to previously uninfected individuals and/or provide a therapeutic effect by reducing viral load levels within an infected individual, thus prolonging the asymptomatic phase of HIV-1 infection.

[52] US Class: 4241871 4352351 4353201 435456 514044

[51] Int'l Class: C12N000702 C12N000701 C07K001416 C12N0015861

[52] ECLA: C07K001416B C07K001416F C12N000702 C12N0015861 K61K0039525C K61K003953 K61K0039545 K61K003957 M12N071019A

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US20030017138A1 MicroPatent Report

CHIMERIC ADENOVIRUSES

[71] Applicant: N/A

[75] Inventors: HAVENGA, MENZO; VOGELS, RONALD; BOUT, ABRAHAM

[21] Application No.: NA

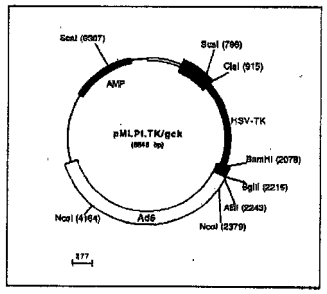
[22] Filed: 19990707

[43] Published: 20030123

[30] Priority: EP EP1998202297A 19980708 ...

Go to Fulltext

Figure 1



[57] Abstract:

The present invention provides methods and vector systems for the generation of chimeric recombinant adenoviruses. These hybrid adenoviruses contain a genome that is derived from different adenovirus serotypes. In particular, novel hybrid adenoviruses are disclosed with improved properties for gene therapy purposes. These properties include: a decreased sensitivity towards neutralizing antibodies, a modified host range, a change in the titer to which adenovirus can be grown, the ability to escape trapping in the liver upon in vivo systemic delivery, and absence or decreased infection of antigen presenting cells (APC) of the immune system, such as macrophages or dendritic cells. These chimeric adenoviruses thus represent improved tools for gene therapy and vaccination since they overcome the limitations observed with the currently used serotype subgroup C adenoviruses.

[52] US Class: 4240932 42409321 4350691 4353201 435325 514044 53038822 5360231

[51] Int'l Class: C12N000700 C07K0014075 A61P003702 C12N001509 C12N000500 C12N000115 C12N0015861 C12N000119 C12N000121

[52] ECLA: C07K0014075 C12N0015861C

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US20030017597A1 MicroPatent Report

HYBRID VECTORS FOR GENE THERAPY

[71] Applicant: N/A

[75] Inventors: Kasahara, Noriyuki; Higo, Collin; Soifer, Harris; Mitani, Kohnosuke

[21] Application No.: NA

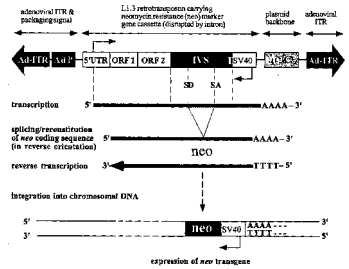
[22] Filed: 20020319

[43] Published: 20030123

[30] Priority: US US1999116150P 19990115 ...

Go to Fulltext

Figure 1



[57] Abstract:

The invention discloses hybrid vectors for delivering genes or other nucleic acids into mammalian cells. The hybrid vectors of the invention contain both a helper dependent adenoviral portion and a second portion derived from a transposon. Such vectors provide efficient transduction of quiescent cells and provide for stable integration of the gene to be delivered.

[52] US Class: 435456 4353201 435457

[51] Int'l Class: C12N0015861 A61K004800

[52] ECLA: C12N0015861 C12N0015861C K61K004800 M12N080030 M12N080090 M12N083044 M12N084020

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AN IMPROVED METHOD FOR THE PRODUCTION AND PURIFICATION OF ADENOVIRAL VECTORS

[71] Applicant: INTROGEN THERAPEUTICS INC

[75] Inventors: Zhang, Shuyuan; Thwin, Capucine; Wu, Zheng; Cho, Toohyon; Gallagher, . . .

[21] Application No.: NA

[22] Filed: 20010612

[43] Published: 20021205

[30] Priority: US US1998203078A 19981201 ...

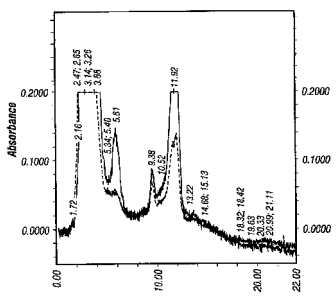

FIG. 1A

Go to Fulltext

[57] Abstract:

The present invention addresses the need to improve the yields of viral vectors when grown in cell culture systems. In particular, it has been demonstrated that for adenovirus, the use of low-medium perfusion rates in an attached cell culture system provides for improved yields. In other embodiments, the inventors have shown that there is improved Ad-p53 production witrh cells grown in serum-free conditions, and in particular in serum-free suspension culture. Also important to the increase of yields is the use of detergent lysis. Combination of these aspects of the invention permits purification of virus by a single chromatography step that results in purified virus of the same quality as preparations from double CsCl banding using an ultracentrifuge.

[52] US Class: 4353201 4242331 4352351 435239 53602372 5360241

[51] Int'l Class: C07K001447 A61K003576 C12N0015861 C12N000510 C12N000701 C12N000702 A61K004800

[52] ECLA: A61K003576 C07K001447A32 C12N000510T C12N000702 C12N0015861 K61K004800 M07K022104 M12N071019A

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NOVEL REPLICATION DEFICIENT ADENOVIRUS VECTORS AND METHODS FOR MAKING AND USING THEM

[71] Applicant: UNIV MICHIGAN

[75] Inventors: Imperiale, Michael, J.

[21] Application No.: NA

[22] Filed: 20020429

[43] Published: 20021212

[30] Priority: US US2000488867A 20000121 ...

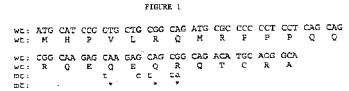

FIGURE 1

Go to Fulltext

[57] Abstract:

The invention provides novel replication deficient adenovirus vectors and methods for making and using these viruses. The invention also provides vector systems and kits using a serotype specific strategy for making adenoviral vector preparations substantially free of replication competent "helper" virus. The helper virus-free preparations provide novel pharmaceutical compositions substantially free of helper virus for use in gene transfer and gene therapy.

[52] US Class: 4240932 4352351 4353201 435456

[51] Int'l Class: C12N000701 C12N000510 C12N0015861 A61K004800

[52] ECLA: C12N000510T C12N0015861 K61K004800

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US20020168342A1 MicroPatent Report

NOVEL ADENOVIRAL VECTORS, PACKAGING CELL LINES, RECOMBINANT ADENOVIRUSES AND METHODS

[71] Applicant: CELL GENESYS INC

[75] Inventors: Wang, Qing; Finer, Mitchell, H.; Jia, Xiao Chi

[21] Application No.: NA

[22] Filed: 20011113

[43] Published: 20021114

[30] Priority: US US1994333680A 19941103 ...

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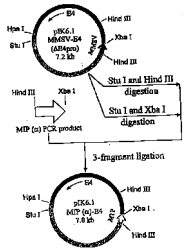

Figure 1

[57] Abstract:

The present invention is directed to novel replication-deficient adenoviral vectors characterized in that they harbor at least two lethal early region gene deletions (E1 and E4) that normally transcribe adenoviral early proteins. These novel recombinant vectors find particular use in human gene therapy treatment whereby the vectors additionally carry a transgene or therapeutic gene that replaces the E1 or E4 regions. The present invention is further directed to novel packaging cell lines that are transformed at a minimum with the adenoviral E1 and E4 gene regions and function to propagate the above novel replication-deficient adenoviral vectors.

[52] US Class: 4240932 4241991 435456

[51] Int'l Class: C12N0015861 C07K0014075 C07K0014015 C12N0015864

[52] ECLA: C07K0014015 C07K0014075 C12N0015861 C12N0015864A M07K020700 M12N083000A1 M12N083085

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US20020164353A1 MicroPatent Report

REPLICATION-DEFECTIVE ADENOVIRUS HUMAN TYPE 5 RECOMBINANT AS A VACCINE CARRIER

[71] Applicant: TRUSTEES OF THE UNIVERSITY OF

[75] Inventors: Ertl, Hildegund, C. J.; Wilson, James, M.

[21] Application No.: NA

[22] Filed: 20010702

[43] Published: 20021107

[30] Priority: US US1995461837A 19950605 ...

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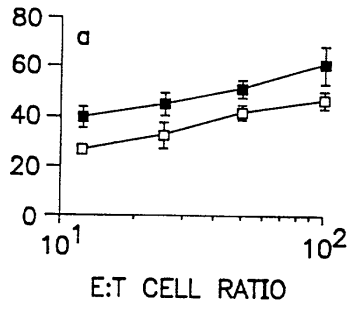

[57] Abstract:

A replication defective recombinant adenovirus is provided which contains a complete deletion of its E1 gene and at least a partial deletion of its E3 gene, said virus containing in the site of the E1 deletion a sequence comprising a non-adenovirus promoter directing the replication and expression of DNA encoding a heterologous protein from a disease-causing agent, which, when administered to a mammal in said recombinant virus, elicits a substantially complete protective immune response against the agent. Pharmaceutical and veterinary products containing the recombinant adenovirus are provided.

[52] US Class: 4241991 4242041 4242331 4352351 4353201 53602372

[51] Int'l Class: C12N001509 A61K0039235 A61K003923 A61K003912 C12N001500 C07H002104 C12N001570 C12N001563 C12N000700 C12N001574 C12N000701

[52] ECLA:

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US20020188103A1 MicroPatent Report

CHIMERIC DNA-BINDING/DNA METHYLTRANSFERASE NUCLEIC ACID AND POLYPEPTIDE AND USES THEREOF

[71] Applicant: N/A

[75] Inventors: BESTOR, TIMOTHY H.

[21] Application No.: NA

[22] Filed: 19981009

[43] Published: 20021212

[30] Priority: US US199851013A 19981009

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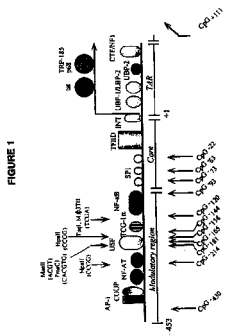

FIGURE 1

[57] Abstract:

The present invention provides a chimeric protein which comprises a mutated DNA methyltransferase portion and a DNA binding protein portion that binds sufficiently close to a promoter sequence of a target gene which promoter sequence contains a methylation site, to specifically methylate the site and inhibit activity of the promoter and thus inhibit expression of the target gene. This invention also provides for a method for inhibiting the expression of a target gene which includes contacting a promoter of the target gene with the chimeric protein, so as to specifically methylate the promoter sequence of the target gene thus inhibiting expression of the target gene.

[52] US Class: 530350 4240932 4353201 435325 435455 435456 435458 435459 435461 5360231 5360232 5360235 800013

[51] Int'l Class: C07K000708 C07K000706 C07K0014705 C07K001900 C12N000910 A61K003800

[52] ECLA: C07K000706A C07K000708A C07K0014705Z C07K001900 C12N000910A1 K01K021700 K61K003800 M07K031900

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US20020123057A1 MicroPatent Report

IN VITRO METHODS OF PRODUCING AND IDENTIFYING IMMUNOGLOBULIN MOLECULES IN EUKARYOTIC CELLS

[71] Applicant: UNIV ROCHESTER

[75] Inventors: Zauderer, Maurice; Smith, Ernest, S.

[21] Application No.: NA

[22] Filed: 20011114

[43] Published: 20020905

[30] Priority: US US2000249268P 20001117 ...

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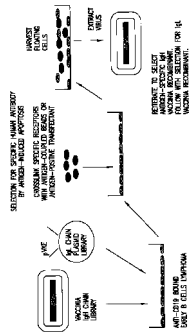

FIG.1

[57] Abstract:

The present invention relates to a high efficiency method of expressing immunoglobulin molecules in eukaryotic cells. The invention is further drawn to a method of producing immunoglobulin heavy and light chain libraries, particularly using the trimolecular recombination method, for expression in eukaryotic cells. The invention further provides methods of selecting and screening for antigen-specific immunoglobulin molecules, and antigen-specific fragments thereof. The invention also provides kits for producing, screening and selecting antigen-specific immunoglobulin molecules. Finally, the invention provides immunoglobulin molecules, and antigen-specific fragments thereof, produced by the methods provided herein.

[52] US Class: 435006 4350071 4350691 4353201 435326 53602353

[51] Int'l Class: C07K001600

[52] ECLA: C07K001600 M07K020700 M07K022120 M07K0316210 M07K0316220 M07K0316550 M07K0316561

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HUMAN GLANDULAR KALLIKREIN ENHANCER, VECTORS COMPRISING THE ENHANCER AND METHODS OF USE THEREOF

[71] Applicant: N/A

[75] Inventors: Yu, De Chao; Henderson, Daniel, R.; Schuur, Eric, R.

[21] Application No.: NA

[22] Filed: 20010605

[43] Published: 20020926

[30] Priority: US US199754523P 19970804 ...

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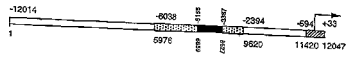

FIGURE 1

[57] Abstract:

Enhancers which preferentially increase the transcription of cis-linked coding sequences in prostate cells are provided. Methods of using DNA constructs comprising the enhancers to control transcription of heterologous polynucleotides are also provided. Delivery vehicles comprising the enhancers and methods of using the vehicles are also provided. Adenovirus vectors in which one or more genes are under transcriptional control of the enhancers of the invention are also provided. Further provided are methods of using the adenovirus vectors of the invention to confer selective cytotoxicity in mammalian cells.

[52] US Class: 42409321 514044 5360232

[51] Int'l Class: C12N001557 C07K0014075 C12N0015861 A61K004800

[52] ECLA: C07K0014075 C12N0015861 K61K004800 M12N083000C M12N083000A1

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MICROPARTICLES AND METHODS FOR DELIVERY OF RECOMBINANT VIRAL VACCINES

[71] Applicant: N/A

[75] Inventors: Hural, John; Johnson, Mark, E.; Spies, A. , Gregory

[21] Application No.: NA

[22] Filed: 20020107

[43] Published: 20021010

[30] Priority: US US2001260164P 20010105 ...

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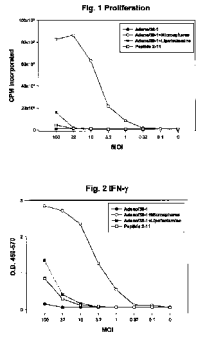

[57] Abstract:

Disclosed is a viral vector conjugated to a microparticle, wherein the viral vector comprises a polynucleotide encoding a heterologous polypeptide. Conjugation of the viral vector to the microparticle results in a dramatic increase in the efficacy of the elicited immune response. Also disclosed is a method for delivering a polynucleotide to a cell comprising contacting the cell with a viral vector of the invention. In a preferred embodiment, the cell is an antigen-presenting cell, such as a dendritic cell. The invention further provides a vaccine comprising a viral vector of the invention. The invention thus provides a method for delivering a polynucleotide to a subject, a method of stimulating an immune response in a subject, a method of treating cancer in a subject, a method of inhibiting tumor growth in a subject, and a method of treating an infection in a subject.

[52] US Class: 435456 4352351 4353201

[51] Int'l Class: C12N0015861 A61K003900

[52] ECLA: C12N0015861 K61K003900 K61K0039525C M12N080070

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US20020119942A1 MicroPatent Report

PACKAGING SYSTEMS FOR HUMAN RECOMBINANT ADENOVIRUS TO BE USED IN GENE THERAPY

[71] Applicant: N/A

[75] Inventors: Vogels, Ronald; Bout, Abraham

[21] Application No.: NA

[22] Filed: 20010706

[43] Published: 20020829

[30] Priority: US US199865752A 19980424 ...

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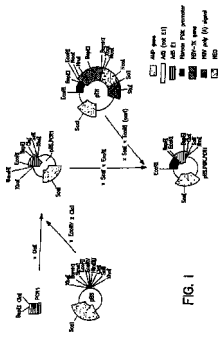

FIG. 1

[57] Abstract:

Improved methods and products based on adenoviral materials which can advantageously be used in, for instance, gene therapy. In one aspect, an adenoviral vector is provided which has no overlap with a suitable packaging cell line, the packaging cell line comprising another aspect of the invention. This combination excludes the possibility of homologous recombination, thereby excluding the possibility of the formation of replication competent adenovirus. In another aspect, an adenovirus based helper construct which by its size is incapable of being encapsulated is disclosed. This helper virus can be transferred into any suitable host cell making it a packaging cell. Additionally, a number of useful mutations to adenoviral based materials and combinations of such mutations are disclosed. Furthermore, a method of intracellular amplification is provided.

[52] US Class: 514044 42409321 4353201 435456 5360231

[51] Int'l Class: C07K0014075 C12N001509 C12N000510 C12N000700 C12N0015861 A61K004800 C12R000101

[52] ECLA: C07K0014075 C12N000510T C12N0015861 K61K004800 M07K020700 M07K022104 M12N083000 M12N083015 M12N083038 M12N083060

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US20020155127A1 MicroPatent Report

GENETIC VACCINE AGAINST HUMAN IMMUNODEFICIENCY VIRUS

[71] Applicant: N/A

[75] Inventors: Wang, Danher

[21] Application No.: NA

[22] Filed: 20011101

[43] Published: 20021024

[30] Priority: US US2000585599A 20000602 ...

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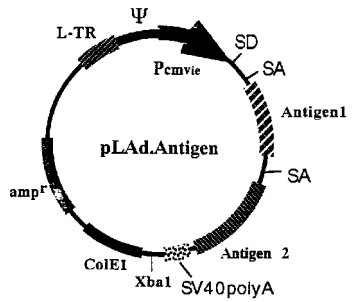

[57] Abstract:

Recombinant adenovirus and methods of administration to a host are provided for eliciting immune response of the host to human immunodeficiency virus (HIV). The recombinant adenovirus is capable of expressing multiple wild type or mutant HIV antigens such as HIV envelope proteins without the cleavage site or the cytosolic domain, structural proteins such as Gag and its proteolytical fragments in a natural, secreted or membrane-bound form, and regulatory proteins such as Tat, Rev and Nef. Immuno-stimulators such as cytokines can also be expressed by the recombinant adenovirus to further enhance the immunogenicity of the HIV antigens.

[52] US Class: 4241991 4242021 4242081 4242331 4352351 4353201

[51] Int'l Class: C07K001408 A61K003929 A61K003902 A61K003900 C12N001509 C12N000700 A61K0039245 A61K003912 A61P003112 C07K001416 C12N001583 C12N001533 A61P003104 A61K003921 A61P003300 A61K0039235

[52] ECLA: A61K003912 A61K003921 A61K003929B C07K001408 C07K001416 K61K0039525C K61K003953 K61K0039555B2 K61K003957 M07K020700 M07K022104 M12N076003

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US20020137678A1 MicroPatent Report

TREATMENT OF OCULAR NEOVASCULARIZATION AND RELATED DISEASES

[71] Applicant: N/A

[75] Inventors: Gendron, Robert, L. ; Paradis, Helene

[21] Application No.: NA

[22] Filed: 20010417

[43] Published: 20020926

[30] Priority: US US2000197977P 20000417 ...

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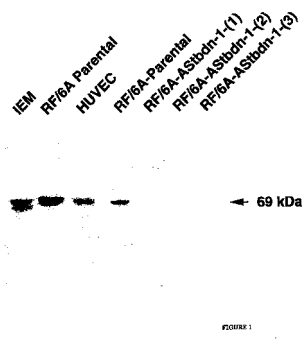

[57] Abstract:

Tubedown-1 (tbdn-1), a protein associated with acetyltransferase activity has been characterized and its cDNA isolated. Tbdn-1 regulates endothelial differentiation through protein acetylation, DNA-binding or by interacting with and/or acetylating other protein targets important for endothelial differentiation. In normal adult eyes, tbdn-1 is expressed highly in the corneal endothelium proper and in the vascular endothelium of the limbus and retina. Tbdn-1 is absent or downregulated in the vascular endothelia of diseased and injured eyes, including eyes from patients with proliferative retinopathies involving neovascularization. Inhibition of tbdn-1 expression in endothelial cells in vitro indicates tbdn-1 acts as an inhibitor of angiogenesis. Thus, high levels of tbdn-1 expression present in normal ocular endothelial cells is associated with suppression of abnormal neovascularization in the eye demonstrating the therapeutic usefulness of tbdn-1 as a regulator of retinal angiogenesis.

[52] US Class: 514012 4350691 435193 4353201 435325 5360232

[51] Int'l Class: C12N000910 A61K003800

[52] ECLA: C12N000910 K61K003800 M12N020700 M12N021300 M12N022100

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US20020127690A1 MicroPatent Report

METHODS AND COMPOSITIONS FOR STABILIZING MICROTUBULES AND INTERMEDIATE FILAMENTS IN STRIATED MUSCLE CELLS

[71] Applicant: N/A

[75] Inventors: Olson, Eric, N.; Spencer, Jeffrey, A.

[21] Application No.: NA

[22] Filed: 20010718

[43] Published: 20020912

[30] Priority: US US2000219020P 20000718 ...

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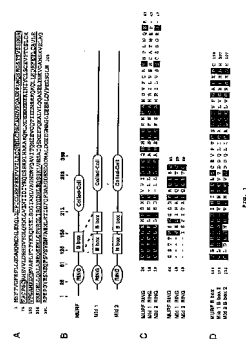

[57] Abstract:

The present invention discloses new muscle ring finger (MURF) proteins designate MURF-1, MURF-2 and MURF-3. The genes encoding these MURFs also are provided. MURFs interact with microtubules and thus play a role in cytoskeletal function, mitosis and cell growth. Thus, the uses of MURFs in diagnosis, treatment and drug screening, in particular relation to cardiomyopathies, are described.

[52] US Class: 435226 4350691 4353201 435325 435456 5360232

[51] Int'l Class: C12N001512 C07K001447 A61K003800

[52] ECLA: C07K001447 C07K001447A7 K61K003800 M07K020300 M07K020302 M07K020500 M07K020700

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HYBRID ADENOVIRUS/ADENO-ASSOCIATED VIRUS VECTORS AND METHODS OF USE THEREOF

[71] Applicant: UNIV NEW YORK

[75] Inventors: Hearing, Patrick; Bahou, Wadie, F.; Sandalon, Ziv; Gnatenko, Dmitri, V.

[21] Application No.: NA

[22] Filed: 20010212

[43] Published: 20020801

[30] Priority: US US2000237747P 20001002 ...

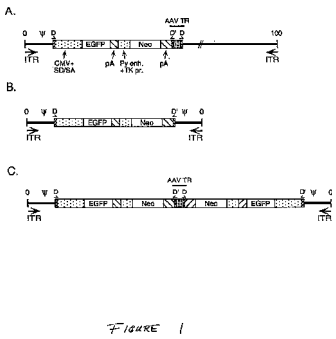

FIGURE 1

Go to Fulltext

[57] Abstract:

The invention provides recombinant vectors including adenovirus/adeno-associated virus (Ad/AAV) vectors and mini-adenovirus (mAd) vectors. Further, the invention provides cells containing these vectors, and methods for making and using the vectors and cells. The compositions and methods of the invention are useful in transferring nucleotide sequences of interest into a cell, including, but not limited to, in gene therapy applications.

[52] US Class: 435456 4353201

[51] Int'l Class: C12N0015864 C12N0015861 A61K004800

[52] ECLA: C12N0015861C C12N0015864A K61K004800

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ANTI-INFLAMMATORY VECTORS

[71] Applicant: N/A

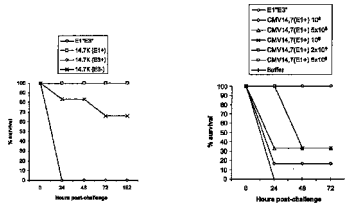
[75] Inventors: Rooke, Ronald

[21] Application No.: NA

[22] Filed: 20011004

[43] Published: 20020808

[30] Priority: EP EP2000440267A 20001006 ...



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[57] Abstract:

The present invention concerns a recombinant adenoviral vector derived from an adenovirus genome in which at least a part of the E3 region is deleted or is non functional, wherein said adenoviral vector retains E3 sequences encoding a functional 14.7K protein, a functional 14.5K protein, and/or a functional 10.4K protein. The present invention further relates to the use of a polynucleotide comprising at least one or more gene(s) of an E3 region of an adenovirus, taken individually or in combination, to protect from an inflammatory reaction in a host cell, tissue or organism. The present invention additionally concerns a viral particle, a host cell and a composition comprising said recombinant adenoviral vector or said polynucleotide, as well as their use for therapeutic or prophylactic purpose.

[52] US Class: 43509133 42409321 4241991 4242041 4242331 43509141 4352351 4353201 435456 5303887 53602372

[51] Int'l Class: C07K0014075 C12N0015861 A61K004800 A61K003900

[52] ECLA: C07K0014075 C12N0015861 K61K003900 K61K0039525C K61K003953 K61K004800 M07K020700 M12N083042 M12N083044 M12N084020A

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US20020098165A1 MicroPatent Report

RECOMBINANT ADENOVIRUSES CONTAINING AN INDUCIBLE PROMOTER CONTROLLING A GENE OF VIRAL ORIGIN

[71] Applicant: RHONE POULENC SA

[75] Inventors: PERRICAUDET, MICHEL; LATTA, MARTINE; PROST, EDOUARD; YEH, . . .

[21] Application No.: NA

[22] Filed: 19971219

[43] Published: 20020725

[30] Priority: FR FR19957570A 19950623 ...

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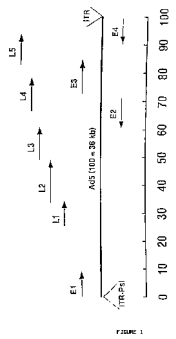

[57] Abstract:

A recombinant adenovirus in which the expression of a nucleic acid sequence coding for at least one homologous or heterologous gene of viral origin is placed under the control of an inducible promoter, is disclosed. The use of such recombinant adenoviruses for preparing AAVs, and a complementary cell line and preparation method therefor, are also disclosed. Furthermore, pharmaceutical compositions containing such an adenovirus are disclosed.

[52] US Class: 4240931 4240932 4240936 4353201 435455 435456 5360232 5360241

[51] Int'l Class: C12N0015861 A61K004800 A61K003576 C12N001509 C12N001563 C12N000510 C12N0015864 C12N000700 C12N000701

[52] ECLA: C12N001563 C12N0015861 C12N0015864A M12N083000A1A

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US20020090717A1 MicroPatent Report

CELL LINES AND CONSTRUCTS USEFUL IN PRODUCTION OF E1-DELETED ADENOVIRUSES IN ABSENCE OF REPLICATION COMPETENT ADENOVIRUS

[71] Applicant: TRUSTEES OF THE UNIVERSITY OF

[75] Inventors: Gao, Guangping; Wilson, James, M.

[21] Application No.: NA

[22] Filed: 20020116

[43] Published: 20020711

[30] Priority: US US1999156644P 19990929 ...

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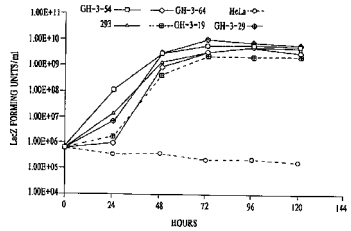

[57] Abstract:

Novel cell lines useful for trans-complementing E1-deleted adenoviral vectors are described. The cell lines are capable of providing high yields of E1-deleted adenoviral vectors in the absence of replication-competent adenovirus over multiple passages.

[52] US Class: 435239 4350703 4352351 435367 435455 435456 435464 435465 435476

[51] Int'l Class: C12N000510 C07K0014075 C12N0015861 C12P002104 A61K004800

[52] ECLA: C07K0014075 C12N000510T C12N0015861 K61K004800 M07K020700 M12N022104

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US20020086837A1 MicroPatent Report

ACNE VACCINE

[71] Applicant: N/A

[75] Inventors: Gauldie, Jack; Braciak, Todd

[21] Application No.: NA

[22] Filed: 20001221

[43] Published: 20020704

[30] Priority: US US2000742892A 20001221

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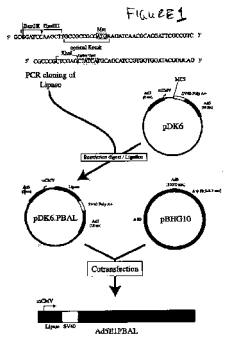

[57] Abstract:

Disclosed herein are vectors and methods for use in the prevention and treatment of acne. Specifically exemplified are adenovirus vectors or plasmid DNA that encode a variety of target antigens from proprionibacterium acnes with or without cytokines, chemokines or co-stimulatory receptors. These vectors in both viral and DNA vector form are prolific molecular adjuvants and can be used in combination with vectors and DNA encoding the lipase, hyaluronidase, phosphatase and other genes on the same operon, to elicit protective immune responses against colonization of the bacterium in the skin follicles.

[52] US Class: 514044 424401

[51] Int'l Class: C12N0015861 A61P003104 A61K003905

[52] ECLA: A61K003905 C12N0015861 K61K003953 K61K0039555B2L2 K61K0039555B2L12 M07K022104

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US20020085999A1 MicroPatent Report

MAREK'S DISEASE VIRUS GENES AND THEIR USE IN VACCINES FOR PROTECTION AGAINST MAREK'S DISEASE

[71] Applicant: USA SECRETARY OF AGRICULTURE A

[75] Inventors: Lee, Lucy, F.; Nazerian, Keyvan; Witter, Richard, L. ; Wu, Ping; . . .

[21] Application No.: NA

[22] Filed: 20010803

[43] Published: 20020704

[30] Priority: US US1995499474A 19950707 ...

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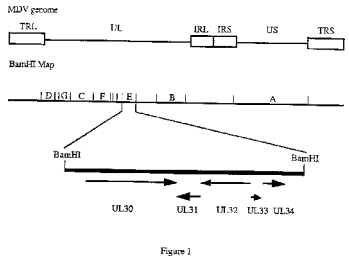

Figure 1

[57] Abstract:

A nucleotide sequence encoding the gp82 polypeptide of Marek's disease virus is disclosed. Also disclosed are recombinant viruses which are useful as vaccines for protecting against Marek's Disease, preferably containing two more genes encoding Marek's Disease Virus antigens such as glyprotein B and glycoprotein gp82, under the control of a poxvirus promoter within a region of the DNA of fowlpox virus which is not essential for virus growth. Also provided is a vaccine exhibiting a synergistic immunoprotective effect, comprising a recombinant fowlpox virus expressing Marek's Disease Virus gB protein in combination with turkey herpesvirus. A method of immunizing poultry, comprising administering any of the disclosed vaccines, is also provided.

[52] US Class: 42409321 4352351 4353201 5360232

[51] Int'l Class: C07K0014055 A61K003900

[52] ECLA: C07K0014055 K61K003900 M07K020700 M07K031900

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US20020037280A1 MicroPatent Report

RECOMBINANT, MODIFIED ADENOVIRAL VECTORS FOR TUMOR SPECIFIC GENE EXPRESSION AND USES THEREOF

[71] Applicant: N/A

[75] Inventors: Lieber, Andre; Steinwaerder, Dirk, S.; Carlson, Cheryl, A.; Mi, . . .

[21] Application No.: NA

[22] Filed: 20010503

[43] Published: 20020328

[30] Priority: US US2000202367P 20000503 ...

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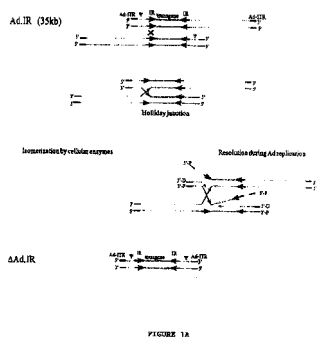

[57] Abstract:

This invention provides modified recombinant Ad vectors (e.g., AdE1-vectors) undergoing defined homologous recombination in order to create predictably rearranged genomic derivatives in a host cell. Genomic rearrangements can be achieved, for example, by incorporating two IR sequences within one vector genome and enabling genomic rearrangement by coinfection with two parental vectors of one type (also referred to herein as a one vector system) or by homologous recombination of overlapping regions in two distinct types of parental vectors (with or without IR sequences) and enabling genomic rearrangement only upon coinfection of the host cell with the two distinct parental vectors (also referred to herein as two vector system).

[52] US Class: 42409321 4352351 4353201 435456

[51] Int'l Class: C12N0015861 A61K004800

[52] ECLA: C12N0015861 K61K004800 M12N083000 M12N083015 M12N083040 M12N083042 M12N083085 M12N084020

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US20020058045A1 MicroPatent Report

ADENOVIRUS VECTOR

[71] Applicant: NAT INST OF HEALTH SCIENCES

[75] Inventors: Mizuguchi, Hiroyuki; Hayakawa, Takao

[21] Application No.: NA

[22] Filed: 20010501

[43] Published: 20020516

[30] Priority: JP JP2000161577A 20000531 ...

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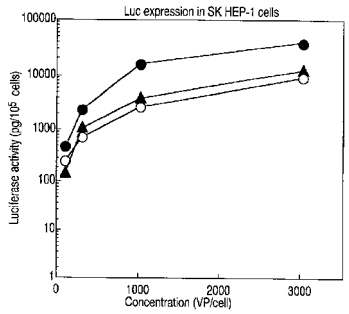

[57] Abstract:

The present invention provides a method for constructing a fiber-mutant adenovirus vector in which a foreign peptide is introduced by a simple system into the fiber HI loop-coding gene of adenovirus; and provides a fiber-mutant adenovirus vector which is constructed by this method.

[52] US Class: 4242331 42409321 4241991 4352351 4353201 435456

[51] Int'l Class: A61K003576 C12N001509 C12N0015861 A61K004800

[52] ECLA: C12N0015861 C12N0015861C K61K004800 M12N081040A

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HELPER VIRUSES FOR THE PREPARATION OF RECOMBINANT VIRAL VECTORS

[71] Applicant: N/A

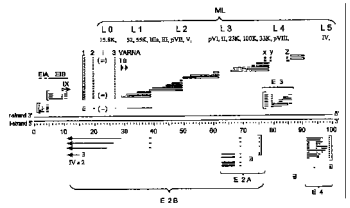
[75] Inventors: Lusky, Monika; Mehtali, Majid

[21] Application No.: NA

[22] Filed: 20010803

[43] Published: 20020613

[30] Priority: FR FR19959289A 19950731 ...



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[57] Abstract:

Novel helper vectors are provided for complementing defective recombinant viral vectors, characterized in that they are provided with recombination sequences recognized by a recombinase. A complementation cell expressing the recombinase, and a method for preparing recombinant viral vectors as infectious viral particles for transferring and expressing genes of interest in a host organism or cell, are also provided. The invention is particularly suitable for use in gene therapy, especially in humans.

[52] US Class: 435457 4350691 4352351 435325

[51] Int'l Class: C12N0015861

[52] ECLA: C12N0015861 M12N022104 M12N080030

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ADENOVIRUS VECTORS COMPRISING INTRONS

[71] Applicant: N/A

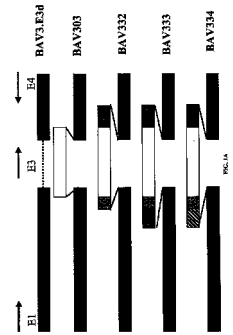
[75] Inventors: Tikoo, Suresh, K.

[21] Application No.: NA

[22] Filed: 20010713

[43] Published: 20020530

[30] Priority: US US2000218283P 20000714 ...



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[57] Abstract:

The invention disclosed herein provides adenovirus vectors comprising introns 5' to transgenes. Such adenovirus vectors are useful for expression of proteins. Methods of making and using these adenovirus vectors are provided herein. In particular, methods of obtaining increased expression of viral proteins from the adenovirus vectors comprising introns 5' to transgenes is provided.

[52] US Class: 4352351 4241991 4353201

[51] Int'l Class: C12N0015861

[52] ECLA: C12N0015861 K61K0039525C

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US20020061517A1 MicroPatent Report

ADENOVIRUS CARRYING GAG GENE HIV VACCINE

[71] Applicant: N/A

[75] Inventors: Chen, Ling; Shiver, John, W.; Bett, Andrew, J.; Casimiro, Danilo, R.; . . .

[21] Application No.: NA

[22] Filed: 20010327

[43] Published: 20020523

[30] Priority: US US1999142631P 19990706 ...

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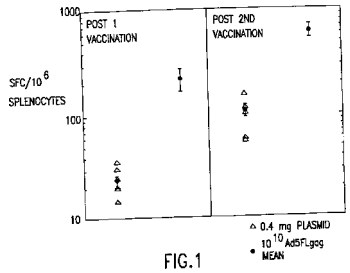

FIG.1

[57] Abstract:

An adenoviral vector is described which carries a codon-optimized gag gene, along with a heterologous promoter and transcription terminator. This viral vaccine can effectively prevent HIV infection when administered to humans either alone or as part of a prime and boost regime also with a vaccine plasmid.

[52] US Class: 435005 4241881 4242081 4242331 4352351 4353201 435325

[51] Int'l Class: C12Q000170 C12N0015861 C07K001416

[52] ECLA: C07K001416B C12N0015861 C12Q000170B2B K61K0039525C K61K003953 M07K022104

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US20020051966A1 MicroPatent Report

EFFICIENT GENERATION OF ADENOVIRUS-BASED LIBRARIES BY POSITIVE SELECTION OF ADENOVIRAL RECOMBINANTS THROUGH ECTOPIC EXPRESSION OF THE

[71] Applicant: N/A

[75] Inventors: Massie, Bernard; Elahi, Seyyed, Mehdy; Qualikene, Wahiba

[21] Application No.: NA

[22] Filed: 20010430

[43] Published: 20020502

[30] Priority: US US1999258209A 19990225 ...

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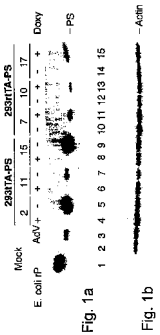

Fig. 1a Fig. 1b

[57] Abstract:

Disclosed is a new system for generating recombinant adenovirus vectors and adenovirus-based expression libraries, by positive selection of recombinants deleted for the endogenous protease gene, which gene is expressibly cloned into another region of the adenoviral genome. In a preferred embodiment, the invention allows positive selection of E1-deleted, protease-deleted recombinant adenovirus vectors comprising an exogenous gene or an expressible piece of exogenous DNA, by providing an expression cassette comprising the protease gene and the exogenous DNA inserted in place of E1 region in a shuttle vector. In vivo recombination of the shuttle vector with a protease-deleted adenoviral genome in suitable non-complementing cells generates viable recombinants only when rescuing the protease cloned in E1 region. Non-recombinant viral genomes are not able to grow due to the deletion of the protease gene, ensuring that only recombinant viral plaques are generated. This positive selection can be used for the generation of a large number of high purity recombinant adenovirus vectors and allows generation of adenovirus-based libraries with diversity exceeding 10^6clones.

[52] US Class: 435005 4350071 4352351 435236 4353201 435456 5360231

[51] Int'l Class: C12N0015861 C12N000701 C12N000510

[52] ECLA: C12N000510T M12N079902A61 M12N081050 M12N083000A1A M12N084020A

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US20020034519A1 MicroPatent Report

MODIFIED BOVINE ADENOVIRUS HAVING ALTERED TROPISM

[71] Applicant: N/A

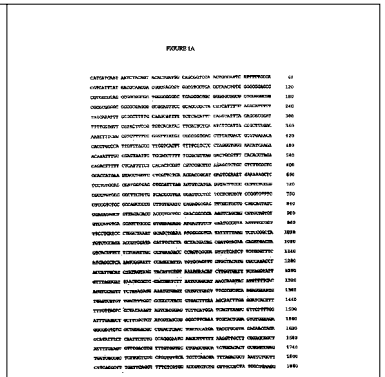
[75] Inventors: Tikoo, Suresh, K.; Babiuk, Lorne, A.; Zhang, Linong; Wu, Qiaohua

[21] Application No.: NA

[22] Filed: 20010531

[43] Published: 20020321

[30] Priority: US US2000208678P 20000531 ...



Go to Fulltext

[57] Abstract:

The present invention provides modified bovine adenoviruses comprising a modification in a capsid protein wherein said protein is associated with adenovirus tropism and wherein said modification is associated with altered tropism. The present invention provides adenovirus vectors and host cells comprising such vectors. The present invention also provides methods of making and using such adenoviruses.

[52] US Class: 4242331 4353201 5360235 53602372

[51] Int'l Class: C12N0015861 C12N000704 A61K004800

[52] ECLA: C12N000704A C12N0015861T K61K0039525C K61K004800 M12N081060A1

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US20020006395A1 MicroPatent Report

DEFECTIVE ADENOVIRUSES INCLUDING A THERAPEUTIC GENE AND AN IMMUNOPROTECTIVE GENE

[71] Applicant: N/A

[75] Inventors: PERRICAUDET, MICHEL; LEE, MARTIN

[21] Application No.: NA

[22] Filed: 19970415

[43] Published: 20020117

[30] Priority: FR FR199412346A 19941017 ...

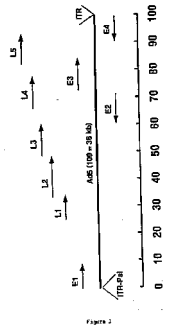

Figure 2

Go to Fulltext

[57] Abstract:

Novel adenovirus-derived viral vectors, the preparation thereof, and the use of such vectors in gene therapy, are disclosed. In particular, defective adenoviruses having a genome that includes a first recombinant DNA containing a therapeutic gene and a second recombinant DNA containing an immunoprotective gene, are disclosed.

[52] US Class: 42409321 4352351

[51] Int'l Class: C07K0014075 A61K004800 C12N001509 C12N000700 C12N000701 C12N0015861

[52] ECLA: C07K0014075 C12N0015861 K61K004800 M07K020700 M07K022104

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DEFECTIVE ADENOVIRUSES AND CORRESPONDING COMPLEMENTATION LINES

[71] Applicant: N/A

[75] Inventors: Imler, Jean Luc; Mehtali, Majid; Pavirani, Andrea

[21] Application No.: NA

[22] Filed: 20001130

[43] Published: 20011206

[30] Priority: FR FR19936482A 19930528 ...

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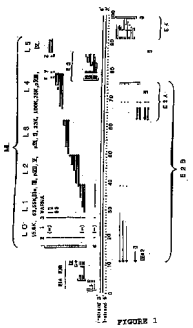

[57] Abstract:

Novel eective adenoviruses for the transfer and expression of an exogenous nucleotide sequence in a host cell or organism. The invention also relates to novel complementation lines and to the process for the preparation of these novel defective adenoviruses and their use in therapy and to a pharmaceutical composition containing same.

[52] US Class: 4353201 4352351 435325

[51] Int'l Class: C12N000701 C07K001457 C07K0014075 C12N0015861 C12N000704 C07K0014395 C07K001447 A61K004800 A61K003800 A61K003512

[52] ECLA: C07K0014075 C07K0014395 C07K001447A4 C07K001457 C12N000704A C12N0015861 K61K003512 K61K003800 K61K004800 M07K020700 M12N083000A1 M12N084020

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METHOD FOR PRODUCING RECOMBINANT ADENOVIRUS

[71] Applicant: N/A

[75] Inventors: BLANCHE, FRANCIS; GUILLAUME, JEAN MARC

[21] Application No.: NA

[22] Filed: 19981216

[43] Published: 20020307

[30] Priority: FR FR19968164A 19960701 ...

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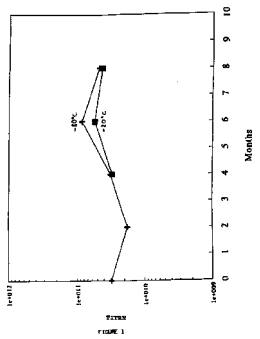

[57] Abstract:

The invention concerns a method for producing recombinant adenovirus by which viral DNA is introduced in a packaging cell culture and the viruses produced are harvested after liberation in the supernatant. The invention also concerns the viruses produced and their use.

[52] US Class: 4352351

[51] Int'l Class: B01J004120 B01D006114 B01D001508 C12N000701 C12N000702 C12N0015861 G01N003002

[52] ECLA: B01D001508 B01D006114 B01J004120 C12N000702 C12N0015861 M12N071019A S01N003002+L01D15/36B4

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CHIMERIC ADENOVIRAL VECTORS

[71] Applicant: N/A

[75] Inventors: Lusky, Monika; Winter, Arend, Jan

[21] Application No.: NA

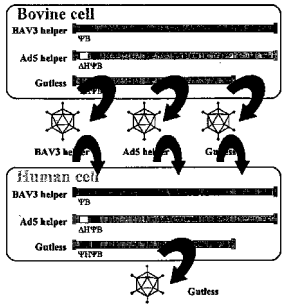
[22] Filed: 20010531

[43] Published: 20020214

[30] Priority: FR FR19986654A 19980527 ...

Go to Fulltext

Figure 1



[57] Abstract:

The invention concerns adenoviral vectors having the characteristic of containing a region essential for heterologous packaging with respect to the adenoviral genome from which they are derived. The invention also concerns a method for making a viral preparation containing said adenoviral vectors, a cell, a pharmaceutical composition or material comprising them and their therapeutic or prophylactic use. Finally, the invention concerns an adenoviral genome of animal origin having attenuated packaging properties with respect to the native genome from which it is derived.

[52] US Class: 435457 4352351

[51] Int'l Class: C12N0015861

[52] ECLA: C12N0015861 M12N083038 M12N083042

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ADENOVIRUS E1-COMPLEMENTING CELL LINES

[71] Applicant: N/A

[75] Inventors: Ayares, David; Alemany, Ramon; Zhang, Wei Wei

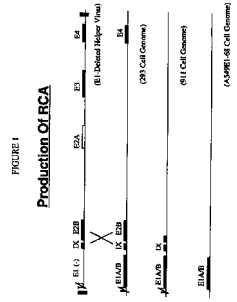
[21] Application No.: NA

[22] Filed: 20010208

[43] Published: 20011129

[30] Priority: US US1996658961A 19960531 ...

Go to Fulltext



[57] Abstract:

A new series of helper cell lines for the complementation, amplification, and controlled attenuation of E1-deleted adenovirus are disclosed in the present invention. These cell lines are advantageous because they can complement adenovirus E1 gene deletions without production of replication competent adenovirus (RCA), thus making them safer for the large-scale production of adenovirus stock for use in human gene therapy trials. A preferred embodiment is an A549E1 cell line that contains only the Ad5 E1 DNA sequences sufficient for complementation of E1-deleted adenoviral vectors without sequences that overlap with the adenovirus vector. In another aspect, the present invention embodies methods for the production of second generation A549-E1 complementing cell lines that, in addition to producing E1, also produce proteins required for further manipulation of adenoviral vectors. A preferred embodiment is an A549E1 cell line with DNA sequences that encode a polypeptide sufficient for packaging attenuation of E1-deleted helper virus, in order to enrich for packaging of mini-adenovirus.

[52] US Class: 514044 4352351 435325 435456

[51] Int'l Class: C07K0014755 C12N0015864 C12N000510 C12N001585 C12N0015861 A61K004800 A61K003800

[52] ECLA: C12N0015864A C07K0014755 C12N000510T C12N001585A1 C12N0015861 C12N0015861T K01K021700 K01K021720 K01K026701 K01K026703D K61K003800 K61K004800 M07K020700 M07K022104 M12N080030 M12N081085G M12N083000C M12N080010E M12N083000A1A

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USE OF TRANS-ACTIVATION AND CIS-ACTIVATION TO MODULATE THE PERSISTENCE OF EXPRESSION OF A TRANSGENE IN AN AT LEAST E4-DEFICIENT ADENOVIRUS

[71] Applicant: GENVEC INC

[75] Inventors: Brough, Douglas, E. ; Kovesdi, Imre

[21] Application No.: NA

[22] Filed: 20010129

[43] Published: 20010802

[30] Priority: US US1998205014A 19981204 ...

[No drawing]

Go to Fulltext

[57] Abstract:

The present invention provides a method of modulating the persistence of expression of a transgene in an at least E4Δ adenoviral vector in a cell. In one embodiment, the method comprises contacting the cell with an at least E4Δ adenoviral vector comprising (i) a transgene and (ii) a gene encoding a trans-acting factor, which is not from the E4 region of an adenovirus and which modulates the persistence of expression of the transgene. In another embodiment, the method comprises contacting the cell simultaneously or sequentially with (i) an at least E4Δ adenoviral vector comprising a transgene and (ii) a viral vector comprising a gene encoding a trans-acting factor, which is not from the E4 region of an adenovirus and which modulates the persistence of expression of the transgene. In addition, the present invention provides a recombinant at least E4Δ adenoviral vector for use in the method and a composition comprising the vector and a carrier therefor. Also provided by the present invention is a system for modulation of a recombinant at least E4Δ adenoviral vector for use in the method and a composition comprising the system and a carrier therefor.

[52] US Class: 4353201 42409321 4352351

[51] Int'l Class: C07K0014075 A61K003800 A61K003576 C12N001509 C07K0014035 A61K004800 C12N001563 C12N001535 A61P003100 C12N0015861 A61P003500

[52] ECLA: C07K0014035 C07K0014075 C12N001563 C12N0015861 M07K020700

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ADENOVIRUS MUTANTS WITH DELETED PROTEASE GENE, COMPLEMENTING CELL LINES, AND CORRESPONDING VECTORS FOR GENE TRANSFER AND POSITIVE SELECTION

[71] Applicant: N/A

[75] Inventors: Massie, Bernard; Qualikene, Wahiba

[21] Application No.: NA

[22] Filed: 20010330

[43] Published: 20011004

[30] Priority: US US1999258209A 19990225 ...

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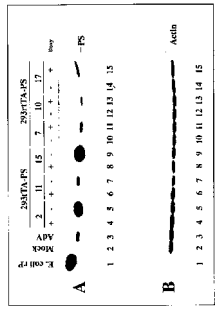
Fig. 1



[57] Abstract:

An adenovirus vector/packaging cell line system is disclosed, in which the vector replication is blocked by deletion of a single gene, which deletion does not interfere with any other viral functions. The deleted gene is the gene of the adenovirus protease. The protease is expressed in a complementing (packaging) cell line through a regulatable expression cassette which induces no toxic effects in the cells, thus making the generation and propagation of the vector easier and more efficient. As the deleted gene is highly specific of adenovirus, no complementation of the gene in transduced cells is expected, which increases the safety of the new vectors for gene transfer purposes. Also disclosed is a new system of generating recombinant adenovirus vectors by positive selection of recombinants deleted for the endogenous protease gene, which gene is cloned in another region of the adenoviral genome.

[52] US Class: 435369 4352351 4353201 435325 435456 436172 436526 5360231 53602372

[51] Int'l Class: C12N0015861 C12N000701 C12N000510

[52] ECLA: C12N000510T M12N079902A61 M12N081050 M12N083000A1A M12N084020A

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COMBINATION THERAPY FOR LYMPHOPROLIFERATIVE DISEASES

[71] Applicant: N/A

[75] Inventors: BYRD, JOHN C.; GREVER, MICHAEL R.; FLINN, IAN W.; WASELENKO, JAMIE K.

[21] Application No.: NA

[22] Filed: 19990224

[43] Published: 20010705

[30] Priority: US US1999256666A 19990224

Go to Fulltext

[No drawing]

[57] Abstract:

Disclosed are methods and kits for treating lymphoproliferative diseases in a host including (co)administering to the host pentostatin, at least one alkylating agent and at least one methylated xanthine.

[52] US Class: 514330

[51] Int'l Class: A61K0031675 A61K0031565 A61K003155 A61K003324 A61K004506 A61P003502

[52] ECLA: A61K003155+M A61K0031565+M A61K0031675+M A61K003324+M A61K004506+M

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RECOMBINANT ADENOVIRUSES PREPARATION AND ADENOVIRUS BANKS

[71] Applicant: AVENTIS PHARMA SA

[72] Inventors: Robert, Jean-Jacques

[21] Application No.: NA

[22] Filed: 20001005

[43] Published: 20070228

[30] Priority: FR FR199912521A 19991007 ...

Go to Fulltext

[No drawing]

[57] Abstract:

The invention concerns compositions and methods for preparing recombinant adenoviruses. The resulting adenoviruses can be used for transferring and/or expressing genes in cells, in vitro, ex vivo or in vivo, or also in functional genomics. More particularly, the invention concerns in particular efficient methods for producing adenovirus banks and the use of said banks in functional genomics. The invention also concerns plasmids used for constructing said adenoviruses.

[52] US Class:

[51] Int'l Class: C12N001510 A61K003576 G01N003353 C12N0015861 C12N001509 A61K004800 C12Q000170 C12Q000168 C12N000510 G01N0033566 C12N000700

[52] ECLA: C12N001510C C12N0015861 M12N080030 M12N084020

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EP1785488A1 MicroPatent Report

ADENOVIRAL VECTORS WITH TWO SEPARATE EXPRESSION CASSETTES

[71] Applicant: CRUCELL HOLLAND BV

[72] Inventors: Vogels, Ronald;
Zuijdgeest, David A.T.M.

[21] Application No.: NA

[22] Filed: 20051109

[43] Published: 20070516

[30] Priority: EP EP2005110516A 20051109

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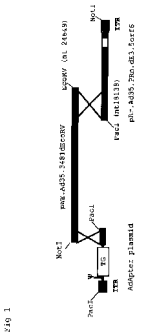

[57] Abstract:

The invention relates to recombinant replication-defective adenoviral vectors comprising two separate expression cassettes, each cassette enabling the high expression of a protein encoded by a nucleic acid of interest. Each cassette comprises a promoter and a polyadenylation signal. An important aspect of the recombinant adenoviruses according to the invention is that they remain stable upon numerous passages in cell culture. Assays to monitor the stability of such adenoviruses over multiple passages are provided.

[52] US Class:

[51] Int'l Class: A61K004800 C12N0015861

[52] ECLA: C12N0015861 M12N071019 M12N084020

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EP1201761A1 MicroPatent Report

METHOD OF CONSTRUCTING RECOMBINANT ADENOVIRUS VECTOR

[71] Applicant: JAPAN SCIENCE
TECH CORP

[72] Inventors: MIYAZAKI, Junichi;
TASHIRO, Fumi

[21] Application No.: NA

[22] Filed: 20000718

[43] Published: 20020502

[30] Priority: JP JP1999205355A 19990719 ...

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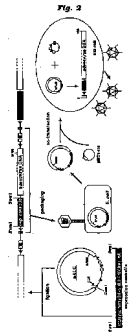

[57] Abstract:

A recombinant adenovirus vector comprising an adenovirus genome DNA and an expression cassette is produced by inserting and ligating a cosmid sequence having recombinase recognition sequences at both ends and the expression cassette into either deletion sites of the adenovirus genome DNA with the deletion of the E1 region or E1 and E3 regions to thereby construct a recombinant cosmid/adenovirus vector; cotransfecting this recombinant cosmid/adenovirus vector and a recombinase-expression vector into a cell line producing adenovirus E1 protein; and deleting the cosmid vector sequence from the recombinant cosmid/adenovirus vector in the cells. This method makes it possible to conveniently and efficiently construct a recombinant adenovirus vector.

[52] US Class:

[51] Int'l Class: C12N0015861 C07K001454 A61K004800

[52] ECLA: C07K001454C C12N0015861 K61K004800 M07K020700 M12N080030 M12N083000 M12N083015 M12N083060 M12N083090 M12N084020A

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METHOD OF CONSTRUCTING RECOMBINANT ADENOVIRUS VECTOR

[71] Applicant: JAPAN SCIENCE TECH CORP

[72] Inventors: MIYAZAKI JUNICHI; TASHIRO FUMI

[21] Application No.: NA

[22] Filed: 20000718

[43] Published: 20040519

[30] Priority: JP JP1999205355A 19990719 ...

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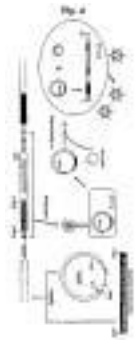

[57] Abstract:

[52] US Class:

[51] Int'l Class: C12N0015861 C07K001454 A61K004800

[52] ECLA: C07K001454C C12N0015861 K61K004800 M07K020700 M12N080030 M12N083000 M12N083015 M12N083060 M12N083090 M12N084020A

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ADENOVIRUS DERIVED GENE DELIVERY VEHICLES COMPRISING AT LEAST ONE ELEMENT OF ADENOVIRUS TYPE 35

[71] Applicant: INTROGENE BV

[72] Inventors: Bout, Abraham; Vogels, Ronald; Havenga, Menzo Jans Emco

[21] Application No.: NA

[22] Filed: 20000516

[43] Published: 20001122

[30] Priority: EP EP1999201545A 19990517 ...

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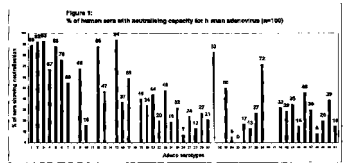

[57] Abstract:

The serotypes differ in their natural tropism. The adenovirus serotypes 2, 4, 5 and 7 all have a natural affiliation towards lung epithelia and other respiratory tissues. In contrast, serotypes 40 and 41 have a natural affiliation towards the gastrointestinal tract. The serotypes described above, differ in at least capsid proteins (penton-base, hexon), proteins responsible for cell binding (fiber protein), and proteins involved in adenovirus replication. This difference in tropism and capsid protein among serotypes has led to the many research efforts aimed at redirecting the adenovirus tropism by modification of the capsid proteins

[52] US Class:

[51] Int'l Class: C12N0015861 C12N001534 C07K0014075

[52] ECLA: C07K0014075 C12N0015861 M07K031900 M07K031974 M12N081060A1

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EP1000628A1 MicroPatent Report

USE OF ANTIGENIC COMPLEXES OF HIV ENVELOPE AND HLA CLASS I ANTIGENS AS HIV VACCINE

[71] Applicant: FOND MONDIALE RECH PREV SIDA

[72] Inventors: The designation of the inventor has not yet been filed

[21] Application No.: NA

[22] Filed: 19980928

[43] Published: 20000517

[30] Priority: EP EP1998402381A 19980928

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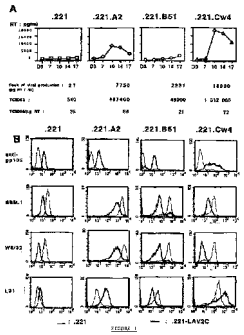

[57] Abstract:

Immunogenic compositions able to induce a protection against human immunodeficiency virus type 1 and type 2 (HIV-1 and HIV-2) and its applications.
Said compositions comprise:
a composition essentially containing a multimolecular complex consisting essentially in at least an immunogenic fragment of the Env glycoprotein of an HIV and an HLA class I heavy chain (HC) or a fragment thereof, said elements being preferably non-covalently associated;
a composition essentially containing particles containing, preferably at their surface, a multimolecular complex comprising essentially at least an immunogenic fragment of the Env glycoprotein of HIV and an HLA class I heavy chain or a fragment thereof or
a composition containing a mixture of at least a fragment of HIV envelope glycoprotein and virion associated HLA class I heavy chains or a fragment thereof.

[52] US Class:

[51] Int'l Class: A61P003118 A61K003939 A61K003921 A61P003704 C07K001416

[52] ECLA: A61K003921 A61K003939 C07K001416D K61K0039525B K61K0039555B5

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WO2008025015A2 MicroPatent Report

EPITOPE-TRANSPLANT SCAFFOLDS AND THEIR USE

[71] Applicant: GOVERNMENT OF THE USA AS REPRE; UNIV WASHINGTON; KWONG PETER; . . .

[72] Inventors: KWONG, Peter; OFEK, Gilad; GUENAGA, Javier; WYATT, Richard, T.; YANG, . . .

[21] Application No.: NA

[22] Filed: 20070824

[43] Published: 20080228

[30] Priority: US US2006840119P 20060825 ...

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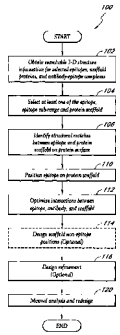

[57] Abstract:

Computational protocols for the design of epitope-protein scaffolds which elicit selected neutralizing antibodies are disclosed, and related compositions and uses.

[52] US Class:

[51] Int'l Class: G06F001900

[52] ECLA: G06F001900C2

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WO2008025015A3 MicroPatent Report

EPITOPE-PROTEIN SCAFFOLDS AND THEIR USE

[71] Applicant: GOVERNMENT OF THE USA AS REPRE; UNIV WASHINGTON; KWONG PETER; . . .

[72] Inventors: KWONG, Peter; OFEK, Gilad; GUENAGA, Javier; WYATT, Richard, T.; YANG, . . .

[21] Application No.: NA

[22] Filed: 20070824

[43] Published: 20080912

[30] Priority: US US2006840119P 20060825 ...

Go to Fulltext



[57] Abstract:

Computational protocols for the design of epitope-protein scaffolds which elicit selected neutralizing antibodies are disclosed, and related compositions and uses.

[52] US Class:

[51] Int'l Class: G06F001900

[52] ECLA: G06F001900C2

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WO2006120034A1 MicroPatent Report

VACCINE COMPOSITION

[71] Applicant: GLAXO GROUP LTD; ERTL PETER FRANZ; TITE JOHN PHILIP; VAN WELY CATHERINE . . .

[72] Inventors: ERTL, Peter, Franz; TITE, John, Philip; VAN WELY, Catherine Ann

[21] Application No.: NA

[22] Filed: 20060510

[43] Published: 20061116

[30] Priority: US US2005680389P 20050512 ...

Go to Fulltext

[No drawing]

[57] Abstract:

The present invention relates to virus vectors comprising oligonucleotides encoding HIV polypeptides, more particularly wherein the virus vector is an adenovirus. In particular, such adenoviruses are non-human primate adenoviruses such as simian adenoviruses, more particularly chimpanzee adenoviruses. In particular the invention relates to adenovirus vectors which comprise HIV polynucleotide sequences which encode multiple different HIV antigens, for example two or three or more HIV antigens. The invention further relates to methods of preparing the virus vectors, to the virus vectors produced by the methods and to the use of the vectors in medicine especially prophylactic or therapeutic vaccination.

[52] US Class:

[51] Int'l Class: A61K003921 A61K003576 C12N0015861 C07K001416

[52] ECLA: A61K003921 K61K0039525D M12N079902A61

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WO2006120034A8 MicroPatent Report

VACCINE COMPOSITION

[71] Applicant: GLAXO GROUP LTD; ERTL PETER FRANZ; TITE JOHN PHILIP; VAN WELY CATHERINE . . .

[72] Inventors: ERTL, Peter, Franz; TITE, John, Philip; VAN WELY, Catherine Ann

[21] Application No.: NA

[22] Filed: 20060510

[43] Published: 20071115

[30] Priority: US US2005680389P 20050512 ...

Go to Fulltext

[No drawing]

[57] Abstract:

The present invention relates to virus vectors comprising oligonucleotides encoding HIV polypeptides, more particularly wherein the virus vector is an adenovirus. In particular, such adenoviruses are non-human primate adenoviruses such as simian adenoviruses, more particularly chimpanzee adenoviruses. In particular the invention relates to adenovirus vectors which comprise HIV polynucleotide sequences which encode multiple different HIV antigens, for example two or three or more HIV antigens. The invention further relates to methods of preparing the virus vectors, to the virus vectors produced by the methods and to the use of the vectors in medicine especially prophylactic or therapeutic vaccination.

[52] US Class:

[51] Int'l Class: A61K003921 A61K003576 C12N0015861 C07K001416

[52] ECLA: A61K003921 K61K0039525D M12N079902A61

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WO2007136763A2 MicroPatent Report

IMMUNOLOGICAL COMPOSITION

[71] Applicant: SANOFI PASTEUR INC; TARTAGLIA JAMES; PANTALEO GUISEPPE; HARARI ALEXANDRI

[72] Inventors: TARTAGLIA, James; PANTALEO, Guiseppe; HARARI, Alexandri

[21] Application No.: NA

[22] Filed: 20070518

[43] Published: 20071129

[30] Priority: US US2006801853P 20060519 ...

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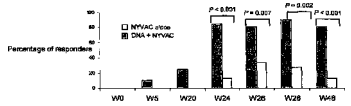

[57] Abstract:

The disclosure relates to immunological compositions for vaccinating human beings against infection by the Human Immunodeficiency Virus (HIV).

[52] US Class:

[51] Int'l Class: A61K

[52] ECLA: A61K003921 C07K001416B C07K001416D K61K003900 K61K003953 M07K031900 M12N074003F M12N079902A63

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METHOD OF ELICITING IMMUNE RESPONSE

[71] **Applicant:** GLAXO GROUP LTD; BARBER KAREN A; BAXTER GILLIAN MARGARET; BRETT ...

[72] **Inventors:** BARBER, Karen, A; BAXTER, Gillian, Margaret; BRETT, Sara, Jane; HAMBLIN, ...

[21] **Application No.:** NA

[22] **Filed:** 20061220

[43] **Published:** 20070628

[30] **Priority:** US US2005752342P 20051221 ...

Go to Fulltext



[57] **Abstract:**

The present invention relates to methods of eliciting an immune response by use of a prime-boost schedule for delivering a polynucleotide encoding a heterologous non-self antigen. In particular, the invention relates to a prime-boost schedule wherein the priming polynucleotide composition is delivered by an adenoviral vector, and the boosting polynucleotide composition is coated on or incorporated in a particle and is administered by a particle acceleration device.

[52] **US Class:**

[51] **Int'l Class:** IntClass::

[52] **ECLA:** A61K003921 K61K0039525C K61K003953 K61K0039545 K61K0039555B K61K0039555B2 M12N079902A61

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METHOD OF ELICITING IMMUNE RESPONSE

[71] **Applicant:** GLAXO GROUP LTD; BARBER KAREN A; BAXTER GILLIAN MARGARET; BRETT ...

[72] **Inventors:** BARBER, Karen, A; BAXTER, Gillian, Margaret; BRETT, Sara, Jane; HAMBLIN, ...

[21] **Application No.:** NA

[22] **Filed:** 20061220

[43] **Published:** 20070907

[30] **Priority:** US US2005752342P 20051221 ...

Go to Fulltext



[57] **Abstract:**

The present invention relates to methods of eliciting an immune response by use of a prime-boost schedule for delivering a polynucleotide encoding a heterologous non-self antigen. In particular, the invention relates to a prime-boost schedule wherein the priming polynucleotide composition is delivered by an adenoviral vector, and the boosting polynucleotide composition is coated on or incorporated in a particle and is administered by a particle acceleration device.

[52] **US Class:**

[51] **Int'l Class:** A61P003118 A61K003900

[52] **ECLA:** A61K003921 K61K0039525C K61K003953 K61K0039545 K61K0039555B K61K0039555B2 M12N079902A61

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RECOMBINANT ADENOVIRUSES BASED ON SEROTYPE 26 AND 48, AND USE THEREOF

[71] Applicant: CRUCELL HOLLAND BV; BETH ISRAEL HOSPITAL; BAROUCH DAN H; HAVENGA . . .

[72] Inventors: BAROUCH, Dan H.; HAVENGA, Menzo Jans Emko

[21] Application No.: NA

[22] Filed: 20070315

[43] Published: 20070920

[30] Priority: US US2006782918P 20060316 ...

Go to Fulltext

[No drawing]

[57] Abstract:

ABSTRACT The present application relates to recombinant adenoviruses, more in particular those that encounter low levels of pre-existing neutralizing activity in hosts that are in need of treatment or vaccination. Particularly, the invention relates to recombinant vectors derived from two subgroup D adenoviruses: Ad26 and Ad48.

[52] US Class:

[51] Int'l Class: C12N0015861 A61K004800 C07K001400

[52] ECLA: C12N0015861T C12N0015861 M12N071019A M12N079904 K61K004800

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RECOMBINANT ADENOVIRUSES BASED ON SEROTYPE 26 AND 48, AND USE THEREOF

[71] Applicant: CRUCELL HOLLAND BV; BETH ISRAEL HOSPITAL; BAROUCH DAN H; HAVENGA . . .

[72] Inventors: BAROUCH, Dan H.; HAVENGA, Menzo Jans Emko

[21] Application No.: NA

[22] Filed: 20070315

[43] Published: 20080306

[30] Priority: US US2006782918P 20060316 ...

Go to Fulltext

[No drawing]

[57] Abstract:

The present application relates to recombinant adenoviruses, more in particular those that encounter low levels of pre-existing neutralizing activity in hosts that are in need of treatment or vaccination. Particularly, the invention relates to recombinant vectors derived from two subgroup D adenoviruses: Ad26 and Ad48.

[52] US Class:

[51] Int'l Class: A61K004800 C12N0015861

[52] ECLA: C12N0015861T C12N0015861 M12N071019A M12N079904 K61K004800

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WO2007094653A1 MicroPatent Report

ADENOVIRUS PARTICLES HAVING A CHIMERIC ADENOVIRUS SPIKE PROTEIN, USE THEREOF AND METHODS FOR PRODUCING SUCH PARTICLES.

[71] Applicant: VERENIGING VOOR CHRISTELIJK HO; VAN BEUSECHEM VICTOR WILLEM; . . .

[72] Inventors: VAN BEUSECHEM, Victor, Willem; SCHAGEN, Frederik, Hubertus, Emanuel

[21] Application No.: NA

[22] Filed: 20060213

[43] Published: 20070823

[30] Priority: NL WO2006NL72A 20060213

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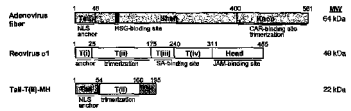

[57] Abstract:

The present invention is concerned with means and methods for producing adenovirus particles comprising a chimeric adenovirus spike protein that essentially lacks a functional knob domain. One aspect of the invention is concerned with a method for producing adenovirus particles comprising providing cells that are permissive for adenovirus replication with an adenovirus vector, with nucleic acid encoding said chimeric adenovirus spike protein and with nucleic acid encoding at least one adenovirus E3 region protein or a functional part, derivative and/or analogue thereof, said method further comprising culturing said permissive cells to allow for at least one replication cycle of said adenovirus virus and harvesting said adenovirus particle.

[52] US Class:

[51] Int'l Class: C12N000510 C12N0015861

[52] ECLA: C07K0014075 C07K001414 C12N0015861T M07K031974 M12N071019A M12N075002 M12N081060E

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WO2007059473A2 MicroPatent Report

METHODS FOR THE PRODUCTION AND PURIFICATION OF ADENOVIRAL VECTORS

[71] Applicant: INTROGEN THERAPEUTICS INC; ZHANG SHUYUAN; PHAM HAI; SONG . . .

[72] Inventors: ZHANG, Shuyuan; PHAM, Hai; SONG, Ping; CLARKE, Peter

[21] Application No.: NA

[22] Filed: 20061113

[43] Published: 20070524

[30] Priority: US US2005735614P 20051112 ...

Go to Fulltext

[No drawing]

[57] Abstract:

The present invention relates to compositions comprising and methods for producing adenovirus compositions wherein host cells are grown in a bioreactor and purified by size partitioning purification to provide purified adenovirus compositions.

[52] US Class:

[51] Int'l Class: C12N0015861 A61K004800 C12N000702

[52] ECLA: C12N000702 C12N0015861 M12N079902A61

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METHODS FOR THE PRODUCTION AND PURIFICATION OF ADENOVIRAL VECTORS

[71] Applicant: INTROGEN THERAPEUTICS INC; ZHANG SHUYUAN; PHAM HAI; SONG . . .

[72] Inventors: ZHANG, Shuyuan; PHAM, Hai; SONG, Ping; CLARKE, Peter

[21] Application No.: NA

[22] Filed: 20061113

[43] Published: 20071101

[30] Priority: US US2005735614P 20051112 ...

[No drawing]

Go to Fulltext

[57] Abstract:

The present invention relates to compositions comprising and methods for producing adenovirus compositions wherein host cells are grown in a bioreactor and purified by size partitioning purification to provide purified adenovirus compositions.

[52] US Class:

[51] Int'l Class: C12N0015861 A61K004800 C12N000702

[52] ECLA: C12N000702 C12N0015861 M12N079902A61

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ADENOVIRUS SEROTYPE 26 VECTORS, NUCLEIC ACID AND VIRUSES PRODUCED THEREBY

[71] Applicant: MERCK CO INC; BETT ANDREW J; CASIMIRO DANILO R; SHIVER JOHN W; . . .

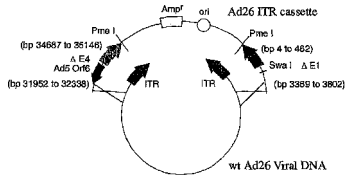
[72] Inventors: BETT, Andrew, J.; CASIMIRO, Danilo, R.; SHIVER, John, W.; EMINI, . . .

[21] Application No.: NA

[22] Filed: 20060207

[43] Published: 20060817

[30] Priority: US US2005652041P 20050211 ...



Go to Fulltext

[57] Abstract:

Adenoviral serotypes differ in their natural tropism. The various serotypes of adenovirus have been found to differ in at least their capsid proteins (e.g., penton-base and hexon proteins), proteins responsible for cell binding (e.g, fiber proteins), and proteins involved in adenovirus replication. This difference in tropism and capsid proteins among serotypes has led to many research efforts aimed at redirecting the adenovirus tropism by modification of the capsid proteins. The present invention bypasses such requirement for capsid protein modification as it presents a recombinant, replication-defective adenovirus of serotype 26, a rare adenoviral serotype, and methods for generating the alternative, recombinant adenovirus. Additionally, means of employing the recombinant adenovirus for delivery and expression of heterologous genes are provided.

[52] US Class:

[51] Int'l Class: C12Q000170

[52] ECLA: C12N0015861 A61K003921 C07K001416B C07K001416F C12N000700 K61K0039525C

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WO2006108707A1 MicroPatent Report

VIRUS PURIFICATION USING ULTRAFILTRATION

[71] Applicant: CRUCELL HOLLAND BV; WEGGEMAN MIRANDA

[72] Inventors: WEGGEMAN, Miranda

[21] Application No.: NA

[22] Filed: 20060411

[43] Published: 20061019

[30] Priority: EP EP2005102842A 20050411 ...

Go to Fulltext

[No drawing]

[57] Abstract:

The invention provides a method for the purification, of a virus comprising a step of ultrafiltration wherein the reteniate contains the virus, wherein back pressure of at least 5 kPa is applied on the permeate side. Th ivention also provides a method for purification of a recombinant adenovirus, said m ethod consisting essentially of: a) culturing cells that are infected with said recombinant adenovirus, b) lysing said cells and removing free nucleic acid, to provide a lysate comprising the recombinant adenovirus, c) clarifying the lysate to obtain an adenovirus preparation, d) subject the adenovirus preparation to ultrafiltration, wherein the adenovirus preparation is in the retentate, to concentrate the adenovirus preparation, e) subjecting the adenovirus preparation of step d) to ultrafiltration, wherein the adenovirus preparation is in the retenate and exchanging it with at least 5 diafiltration volumes (DFVs) of buffer, wherein in steps d) and e) back pressure of at least 5 kPa is applied on the permeate side.

[52] US Class:

[51] Int'l Class: C12N000702

[52] ECLA: C12N000702 M12N071019

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WO2006086357A2 MicroPatent Report

ADENOVIRUS SEROTYPE 36 VECTORS, NUCLEIC ACID AND VIRUSES PRODUCED THEREBY

[71] Applicant: MERCK CO INC; BETT ANDREW J; CASIMIRO DANILO R; SHIVER JOHN W; . . .

[72] Inventors: BETT, Andrew, J.; CASIMIRO, Danilo, R.; SHIVER, John, W.; EMINI, . . .

[21] Application No.: NA

[22] Filed: 20060206

[43] Published: 20060817

[30] Priority: US US2005651843P 20050210 ...

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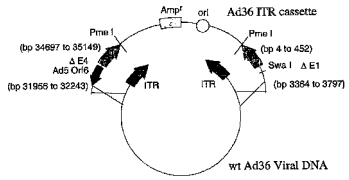

[57] Abstract:

Adenoviral serotypes differ in their natural tropism. The various serotypes of adenovirus have been found to differ in at least their capsid proteins (e.g., penton-base and hexon proteins), proteins responsible for cell binding (e.g, fiber proteins), and proteins involved in adenovirus replication. This difference in tropism and capsid proteins among serotypes has led to many research efforts aimed at redirecting the adenovirus tropism by modification of the capsid proteins. The present invention bypasses such requirement for capsid protein modification as it presents a recombinant, replication-defective adenovirus of serotype 36, a rare adenoviral serotype, and methods for generating the alternative, recombinant adenovirus. Additionally, means of employing the recombinant adenovirus for delivery and expression of heterologous genes are provided.

[52] US Class:

[51] Int'l Class: C12N0015861

[52] ECLA: A61K003921 C07K001416B C07K001416F C12N0015861

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ADENOVIRUS SEROTYPE 36 VECTORS, NUCLEIC ACID AND VIRUSES PRODUCED THEREBY

[71] Applicant: MERCK CO INC; BETT ANDREW J; CASIMIRO DANILO R; SHIVER JOHN W; . . .

[72] Inventors: BETT, Andrew, J.; CASIMIRO, Danilo, R.; SHIVER, John, W.; EMINI, . . .

[21] Application No.: NA

[22] Filed: 20060206

[43] Published: 20070201

[30] Priority: US US2005651843P 20050210 ...

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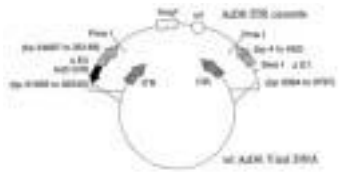

[57] Abstract:

Adenoviral serotypes differ in their natural tropism. The various serotypes of adenovirus have been found to differ in at least their capsid proteins (e.g., penton-base and hexon proteins), proteins responsible for cell binding (e.g, fiber proteins), and proteins involved in adenovirus replication. This difference in tropism and capsid proteins among serotypes has led to many research efforts aimed at redirecting the adenovirus tropism by modification of the capsid proteins. The present invention bypasses such requirement for capsid protein modification as it presents a recombinant, replication-defective adenovirus of serotype 36, a rare adenoviral serotype, and methods for generating the alternative, recombinant adenovirus. Additionally, means of employing the recombinant adenovirus for delivery and expression of heterologous genes are provided.

[52] US Class:

[51] Int'l Class: C12N001563 C12N001509

[52] ECLA: A61K003921 C07K001416B C07K001416F C12N0015861

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PROCESSES FOR ADENOVIRUS PURIFICATION USING CONTINUOUS FLOW CENTRIFUGATION

[71] Applicant: ALFA WASSERMANN INC

[72] Inventors: FORRESTER, Kathy

[21] Application No.: NA

[22] Filed: 20050225

[43] Published: 20061005

[30] Priority: US US2004789045A 20040227 ...

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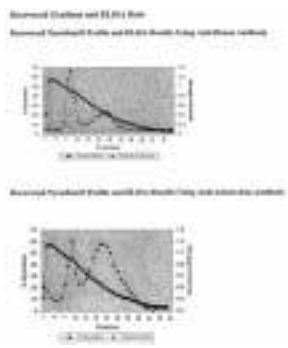

[57] Abstract:

The present invention relates to methods for the scalable preparation for adenoviral preparations comprising the steps of: culturing host cells comprising adenovirus; obtaining supernatants from the host cells; applying said supernatants to a centrifugal apparatus comprising a 50% w/v solution of non-ionic gradient; applying centrifugal force to said supernatants such that the flow is continuous and directed from bottom-to-top; separating the adenoviral particles according to their density; and obtaining high-yield fractions comprising active adenoviral particles.

[52] US Class:

[51] Int'l Class: C12N001586 C12N000700 B01D0017038

[52] ECLA: B01D001702H

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IMMUNIZATION REGIMEN WITH E4-DELETED ADENOVIRUS PRIME AND E1-DELETED ADENOVIRUS BOOST

[71] Applicant: TRUSTEES OF THE UNIVERSITY OF; WILSON JAMES M; ZHI YAN

[72] Inventors: WILSON, James, M.; ZHI, Yan

[21] Application No.: NA

[22] Filed: 20050427

[43] Published: 20060330

[30] Priority: US US2004565892P 20040428 ...

Go to Fulltext

[No drawing]

[57] Abstract:

An immunization regimen is provided which involves priming with an E1, E4-deleted adenovirus and boosting with an E1-deleted adenovirus. The second administered adenovirus has a capsid of a serotype which is not cross-reactive with the previously administered adenovirus. Further, a product containing the adenoviruses necessary to perform the immunization regimen is provided.

[52] US Class:

[51] Int'l Class: C12N0015861 A61K003900

[52] ECLA: A61K003912 C12N0015861 K61K0039525C K61K0039525D K61K0039545 K61K003957 M12N076003B

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IMMUNIZATION REGIMEN WITH E4-DELETED ADENOVIRUS PRIME AND E1-DELETED ADENOVIRUS BOOST

[71] Applicant: TRUSTEES OF THE UNIVERSITY OF; WILSON JAMES M; ZHI YAN

[72] Inventors: WILSON, James, M.; ZHI, Yan

[21] Application No.: NA

[22] Filed: 20050427

[43] Published: 20060615

[30] Priority: US US2004565892P 20040428 ...

Go to Fulltext

[No drawing]

[57] Abstract:

An immunization regimen is provided which involves priming with an E1, E4-deleted adenovirus and boosting with an E1-deleted adenovirus. The second administered adenovirus has a capsid of a serotype which is not cross-reactive with the previously administered adenovirus. Further, a product containing the adenoviruses necessary to perform the immunization regimen is provided.

[52] US Class:

[51] Int'l Class: C12N0015861 A61K003900

[52] ECLA: A61K003912 C12N0015861 K61K0039525C K61K0039525D K61K0039545 K61K003957 M12N076003B

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RECOMBINANT VECTORS AND METHODS FOR INDUCING AN IMMUNE RESPONSE

[71] Applicant: WISTAR INST; HENSLEY SCOTT E; ERTL HILDEGUND C J

[72] Inventors: HENSLEY, Scott, E.; ERTL, Hildegund, C., J.

[21] Application No.: NA

[22] Filed: 20050207

[43] Published: 20051013

[30] Priority: US US2004542431P 20040206 ...

Go to Fulltext

[No drawing]

[57] Abstract:

The present invention relates to recombinant vectors with additional, replacement, or modified viral-associated RNA nucleic acid sequences. Methods of using such vectors for modulating an immune response or for treating genetic or acquired diseases are also provided.

[52] US Class:

[51] Int'l Class: C12N IntClass::

[52] ECLA: C12N0015861 A61K003912 A61K0039235 K61K0039525C K61K004800 M12N071019A

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RECOMBINANT VECTORS AND METHODS FOR INDUCING AN IMMUNE RESPONSE

[71] Applicant: WISTAR INST; HENSLEY SCOTT E; ERTL HILDEGUND C J

[72] Inventors: HENSLEY, Scott, E.; ERTL, Hildegund, C., J.

[21] Application No.: NA

[22] Filed: 20050207

[43] Published: 20070308

[30] Priority: US US2004542431P 20040206 ...

Go to Fulltext

[No drawing]

[57] Abstract:

The present invention relates to recombinant vectors with additional, replacement, or modified viral-associated RNA nucleic acid sequences. Methods of using such vectors for modulating an immune response or for treating genetic or acquired diseases are also provided.

[52] US Class:

[51] Int'l Class: C12N000120 A61K003900 C12N001500

[52] ECLA: C12N0015861 A61K003912 A61K0039235 K61K0039525C K61K004800 M12N071019A

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CHIMPANZEE ADENOVIRUS VACCINE CARRIERS

[71] Applicant: ANGELETTI P IST RICHERCHE BIO; CIRILLO AGOSTINO; COLLOCA STEFANO; . . .

[72] Inventors: CIRILLO, Agostino; COLLOCA, Stefano; ERCOLE, Bruno, Bruni; MEOLA, . . .

[21] Application No.: NA

[22] Filed: 20050118

[43] Published: 20050804

[30] Priority: US US2004538799P 20040123 ...

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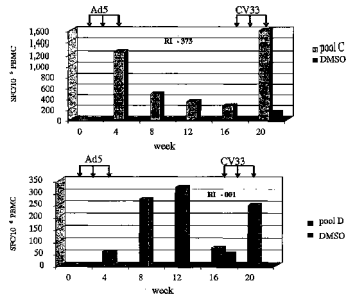

[57] Abstract:

The present invention provides recombinant replication-defective adenoviral vectors derived from chimpanzee adenoviruses and methods for generating recombinant adenoviruses in human E1-expressing cell lines. The invention also provides compositions and methods suitable for use for the delivery and expression of transgenes encoding immunogens against which a boosted immune response is desired. The invention further provides methods of generating clinical grade vector stocks suitable for use in humans. In a particular embodiment the invention contemplates the use of vectors comprising transgenes which encode tumor associated antigens in vaccines and pharmaceutical compositions for the prevention and treatment of cancer.

[52] US Class:

[51] Int'l Class: C12N0015861 C07K0014705 A61K004506 C07K001418 C12N000704 C12N000702 C07K0014075 C12N001586 C07K001416 A61K003900 A61K003800 A61K004800

[52] ECLA: A61K004506 C07K001416B C07K001418F4 C07K0014705B C12N000702 C12N000704A C12N0015861 K61K003800 K61K0039525C M07K022104 M12N081060

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CHIMPANZEE ADENOVIRUS VACCINE CARRIERS

[71] Applicant: ANGELETTI P IST RICHERCHE BIO; CIRILLO AGOSTINO; COLLOCA STEFANO; . . .

[72] Inventors: CIRILLO, Agostino; COLLOCA, Stefano; ERCOLE, Bruno, Bruni; MEOLA, . . .

[21] Application No.: NA

[22] Filed: 20050118

[43] Published: 20060330

[30] Priority: US US2004538799P 20040123 ...

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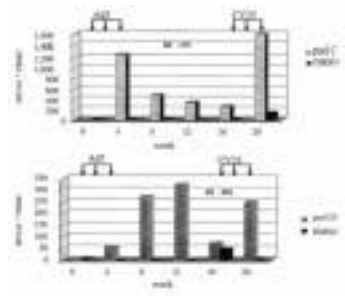

[57] Abstract:

The present invention provides recombinant replication-defective adenoviral vectors derived from chimpanzee adenoviruses and methods for generating recombinant adenoviruses in human E1-expressing cell lines. The invention also provides compositions and methods suitable for use for the delivery and expression of transgenes encoding immunogens against which a boosted immune response is desired. The invention further provides methods of generating clinical grade vector stocks suitable for use in humans. In a particular embodiment the invention contemplates the use of vectors comprising transgenes which encode tumor associated antigens in vaccines and pharmaceutical compositions for the prevention and treatment of cancer.

[52] US Class:

[51] Int'l Class: C12N0015861 C07K0014705 C07K0014075 C07K001418 A61K004506 C12N000704 C12N000702 A61K004800 C12N001586 C07K001416 A61K003900 A61K003800

[52] ECLA: A61K004506 C07K001416B C07K001418F4 C07K0014705B C12N000702 C12N000704A C12N0015861 K61K003800 K61K0039525C M07K022104 M12N081060

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IDENTIFICATION OF ENDOGENOUS TRIMERIZATION DOMAINS IN THE ADENOVIRUS FIBER PROTEIN THAT ALLOW DETARGETING AND RETARGETING OF VIRAL

[71] Applicant: SCRIPPS RESEARCH INST; NEMEROW GLEN R; LI ERGUANG

[72] Inventors: NEMEROW, Glen, R.; LI, Erguang

[21] Application No.: NA

[22] Filed: 20041229

[43] Published: 20050818

[30] Priority: US US2004535199P 20040109 ...

Go to Fulltext

[No drawing]

[57] Abstract:

Detargeted and retargeted adenovirus particles and vectors are provided. In particular, modified fibers for incorporation into adenovirus particles and the resulting detargeted and retargeted particles are provided. The modified fiber proteins, adenoviral particles and vectors comprising the modified fiber proteins, compositions, and methods of preparation and use of the modified fiber proteins and vectors for gene therapy are provided.

[52] US Class:

[51] Int'l Class: C12N0015861 C07K0014075

[52] ECLA: C07K0014075 C12N0015861T M12N071019A M12N081085

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COMBINATION APPROACHES FOR GENERATING IMMUNE RESPONSES

[71] Applicant: CHIRON CORP; NAT INST OF HEALTH NAT CANCER; BARNETT SUSAN W; GOMEZ- . . .

[72] Inventors: BARNETT, Susan, W.; GÓMEZ-ROMÁN, Victor, Raúl c/o National Institutes of . . .

[21] Application No.: NA

[22] Filed: 20040915

[43] Published: 20050331

[30] Priority: US US2003503617P 20030915 ...

Go to Fulltext

[No drawing]

[57] Abstract:

The present invention relates to methods, polynucleotides, and polypeptides encoding immunogenic HIV polypeptides derived from different strains within an HIV subtype and/or immunogenic HIV polypeptides from different subtypes. Uses of the polynucleotides and polypeptides in combination approaches for generating immune responses are described. The combination approaches described herein have been shown to induce broad and potent neutralizing activity against diverse HIV strains from multiple strains within a given subtype and against diverse subtypes. Formulations of compositions for generating immune responses and methods of use for such compositions are also disclosed.

[52] US Class:

[51] Int'l Class: A61K

[52] ECLA: A61K003921 K61K003953 M12N074003F

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THERAPEUTIC IMMUNIZATION OF HIV-INFECTED INDIVIDUALS

[71] Applicant: MERCK CO INC; EMINI EMILIO A; SHIVER JOHN W; CASIMIRO DANILO R; . . .

[72] Inventors: EMINI, Emilio, A.; SHIVER, John, W.; CASIMIRO, Danilo, R.; HAZUDA, Daria; . . .

[21] Application No.: NA

[22] Filed: 20040914

[43] Published: 20050331

[30] Priority: US US2003504522P 20030918 ...

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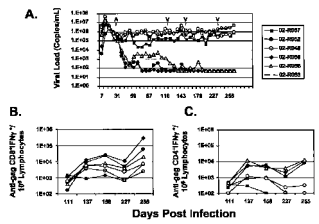

[57] Abstract:

The present invention provides an improved method for eliciting a therapeutic immune response in an individual infected with human immunodeficiency virus (“HIV”). The method comprises administering an adenoviral vaccine composition expressing an HIV antigen to an individual with controlled viremia. Immunization of infected individuals in this manner elicits a cellular-mediated immune response against the virus that is significant both in the level of the response and the breadth of the response. The therapeutic immune response that ensues is capable of effectively maintaining low titers of virus and, thus, offers the prospect of reducing individual dependency on antiviral therapy.

[52] US Class:

[51] Int'l Class: A61K

[52] ECLA:

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THERAPEUTIC IMMUNIZATION OF HIV-INFECTED INDIVIDUALS

[71] Applicant: MERCK CO INC; EMINI EMILIO A; SHIVER JOHN W; CASIMIRO DANILO R; . . .

[72] Inventors: EMINI, Emilio, A.; SHIVER, John, W.; CASIMIRO, Danilo, R.; HAZUDA, Daria; . . .

[21] Application No.: NA

[22] Filed: 20040914

[43] Published: 20070816

[30] Priority: US US2003504522P 20030918 ...

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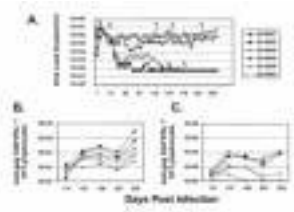

[57] Abstract:

The present invention provides an improved method for eliciting a therapeutic immune response in an individual infected with human immunodeficiency virus (“HIV”). The method comprises administering an adenoviral vaccine composition expressing an HIV antigen to an individual with controlled viremia. Immunization of infected individuals in this manner elicits a cellular-mediated immune response against the virus that is significant both in the level of the response and the breadth of the response. The therapeutic immune response that ensues is capable of effectively maintaining low titers of virus and, thus, offers the prospect of reducing individual dependency on antiviral therapy.

[52] US Class:

[51] Int'l Class: A01N006500 A01N006300 A01N004304 A61K003170

[52] ECLA:

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MODIFIED ADENOVIRAL VECTORS FOR USE IN VACCINES AND GENE THERAPY

[71] Applicant: CRUCELL HOLLAND BV; KOSTENSE STEFAN; OPHORST OLGA JOHANNA ALBERDINA; . . .

[72] Inventors: KOSTENSE, Stefan; OPHORST, Olga, Johanna, Alberdina, Elisa; HAVENGA, . . .

[21] Application No.: NA

[22] Filed: 20020920

[43] Published: 20040401

[30] Priority: NL WO2002NL608A 20020920

Go to Fulltext

[No drawing]

[57] Abstract:

The present invention provides novel methods and means for influencing the CTL-sensitivity of antigen presenting cells such as dendritic cells upon viral infections. The invention provides novel gene delivery vehicles that are useful in different therapeutic settings such as vaccination and/or gene therapy.

[52] US Class:

[51] Int'l Class: C12N000506 A61K003857 C12N000522 C12N0015861 A61K004800

[52] ECLA: A61K003857 C12N000506B11B C12N000506B11D C12N0015861 K61K0039525C K61K004800 M12N081060A1

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MIP-1α AND GM-CSF AS ADJUVANTS OF IMMUNE RESPONSE

[71] Applicant: BETH ISRAEL HOSPITAL; MCKAY PAUL; BAROUCH DAN; LETVIN NORMAN

[72] Inventors: MCKAY, Paul; BAROUCH, Dan; LETVIN, Norman

[21] Application No.: NA

[22] Filed: 20031107

[43] Published: 20040527

[30] Priority: US US2002424658P 20021107 ...

Go to Fulltext

[No drawing]

[57] Abstract:

The present invention features methods to substantially increase the immunogenicity of a vaccine, preferably a DNA vaccine, and involves providing a mammal with a vaccine regimen, which include at least one immunogen, GM-CSF, and MIP- I α in the absence of exogenous IL-4. The methods of the present invention are useful for the prevention, treatment, and reduction of various pathological states, including for example, cancer, microbial infections, autoimmune diseases, tissue rejection, and allergic reactions.

[52] US Class:

[51] Int'l Class: A61K003939

[52] ECLA: A61K003939 K61K0039555B2

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MIP-1α AND GM-CSF AS ADJUVANTS OF IMMUNE RESPONSE

[71] Applicant: BETH ISRAEL HOSPITAL; MCKAY PAUL; BAROUCH DAN; LETVIN NORMAN

[72] Inventors: MCKAY, Paul; BAROUCH, Dan; LETVIN, Norman

[21] Application No.: NA

[22] Filed: 20031107

[43] Published: 20051006

[30] Priority: US US2002424658P 20021107 ...

[No drawing]

Go to Fulltext

[57] Abstract:

The present invention features methods to substantially increase the immunogenicity of a vaccine, preferably a DNA vaccine, and involves providing a mammal with a vaccine regimen, which include at least one immunogen, GM-CSF, and MIP-I α in the absence of exogenous IL-4. The methods of the present invention are useful for the prevention, treatment, and reduction of various pathological states, including for example, cancer, microbial infections, autoimmune diseases, tissue rejection, and allergic reactions.

[52] US Class:

[51] Int'l Class: A61K003939

[52] ECLA: A61K003939 K61K0039555B2

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MIP-1ALPHA AND GM-CSF AS ADJUVANTS OF IMMUNE RESPONSE

[71] Applicant: BETH ISRAEL HOSPITAL; MCKAY PAUL; BAROUCH DAN; LETVIN NORMAN

[72] Inventors: MCKAY PAUL; BAROUCH DAN; LETVIN NORMAN

[21] Application No.: NA

[22] Filed: 20031107

[43] Published: 20040819

[30] Priority: US US2002424658P 20021107 ...

[No drawing]

Go to Fulltext

[57] Abstract:

The present invention features methods to substantially increase the immunogenicity of a vaccine, preferably a DNA vaccine, and involves providing a mammal with a vaccine regimen, which include at least one immunogen, GM-CSF, and MIP- I alpha in the absence of exogenous IL-4. The methods of the present invention are useful for the prevention, treatment, and reduction of various pathological states, including for example, cancer, microbial infections, autoimmune diseases, tissue rejection, and allergic reactions.

[52] US Class:

[51] Int'l Class: A61K003939

[52] ECLA: A61K003939 K61K0039555B2

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LARGE SCALE METHODS OF PRODUCING ADENOVIRUS AND ADENOVIRUS SEED STOCKS

[71] Applicant: MERCK CO INC; ZHOU WEICHANG; XIE LIANGZHI; ALTARAS NEDIM EMIL; AUNINS . . .

[72] Inventors: ZHOU, Weichang; XIE, Liangzhi; ALTARAS, Nedim Emil; AUNINS, John, . . .

[21] Application No.: NA

[22] Filed: 20030327

[43] Published: 20031016

[30] Priority: US US2002368706P 20020329 ...

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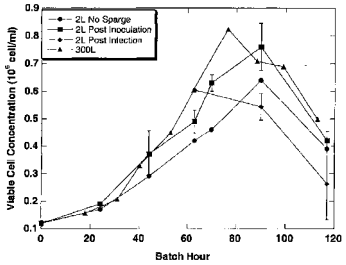

[57] Abstract:

A process for large scale virus production is disclosed, especially large scale adenovirus production. The methods described are preferably adapted to suspension culture of mammalian host cells in a large scale bioreactor where gas sparging becomes essential to provide adequate aeration through the duration of the culture. This methodology includes an elevated concentration of a compound which protects host cells from the shearing effects of gas sparging and agitation as well as utilizing virus seed stocks which have been generated free of cell lysis reagents. The invention also relates to methods of producing these virus seed stocks, which are scaleable and the resultant unclarified virus seed stocks which are concentrated to reduce storage volume for infection of large scale culture and which are free of cell lysis components, such as the detergent Triton X-100 or Polysorbate 80.

[52] US Class:

[51] Int'l Class: A61K004800 A61K0031395 C12N000700 C12Q000170 C12N000500 C12N000701 C12N000702

[52] ECLA: C12N000700 A61K0031395 A61K004800J C12N000500M M12N050050 M12N071019

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LARGE SCALE METHODS OF PRODUCING ADENOVIRUS AND ADENOVIRUS SEED STOCKS

[71] Applicant: MERCK CO INC; ZHOU WEICHANG; XIE LIANGZHI; ALTARAS NEDIM EMIL; AUNINS . . .

[72] Inventors: ZHOU, Weichang; XIE, Liangzhi; ALTARAS, Nedim Emil; AUNINS, John, . . .

[21] Application No.: NA

[22] Filed: 20030327

[43] Published: 20031120

[30] Priority: US US2002368706P 20020329 ...

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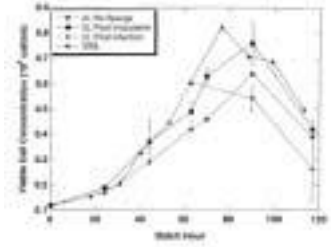

[57] Abstract:

A process for large scale virus production is disclosed, especially large scale adenovirus production. The methods described are preferably adapted to suspension culture of mammalian host cells in a large scale bioreactor where gas sparging becomes essential to provide adequate aeration through the duration of the culture. This methodology includes an elevated concentration of a compound which protects host cells from the shearing effects of gas sparging and agitation as well as utilizing virus seed stocks which have been generated free of cell lysis reagents. The invention also relates to methods of producing these virus seed stocks, which are scaleable and the resultant unclarified virus seed stocks which are concentrated to reduce storage volume for infection of large scale culture and which are free of cell lysis components, such as the detergent Triton X-100 or Polysorbate 80.

[52] US Class:

[51] Int'l Class: C12N000701 A61K0031395 C12N000700 C12N000702 C12Q000170

[52] ECLA: C12N000700 A61K0031395 A61K004800J C12N000500M M12N050050 M12N071019

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WO2002031170A1 MicroPatent Report

METHOD FOR CIRCULARIZING ADENOVIRAL NUCLEIC ACID VIA HOMOLOGOUS RECOMBINATION

[71] Applicant: MERCK CO INC; YOUIL RIMA

[72] Inventors: YOUIL, Rima

[21] Application No.: NA

[22] Filed: 20011005

[43] Published: 20020418

[30] Priority: US US2000239547P 20001010 ...

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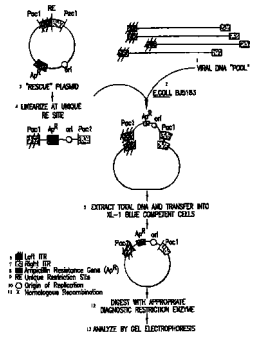

[57] Abstract:

Applicants have identified a process which exploits the bacterial homologous recombination system to convert double-stranded linear adenovirus genome into circularized plasmid form (See Figure 4). The system functions via adenoviral terminal fragments present on the plasmid that are less than 500 basepairs each. The result is a plasmid which is more readily analyzed by restriction digestion, PCR, DNA sequencing or used in transient transfection studies. The adenovirus plasmids that are generated can be rescued back into virus form. The entire procedure takes 4 days or less instead of the weeks required of plaque purification or dilution cloning isolation techniques. An additional plus of the instant invention is that the disclosed method does not require the use of tissue culture materials or facilities. The disclosed method allows for a more extensive and thorough examination of a viral preparation, in that it allows for the detection of variants incapable of propagation without the assistance of co-infecting intact adenoviral genomes. Under standard conditions of plaque purification, these variant genomes are not detected. It is predicted that far more variant genomes will be observed using the rapid method than would otherwise be detected by standard plaque purification methods.

[52] US Class:

[51] Int'l Class: C12N001564 C12N000701 C12N001509 C12N0015861

[52] ECLA: C12N001564 C12N0015861 M12N051000

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WO2002032943A2 MicroPatent Report

MODIFICATIONS OF HIV ENV, GAG, AND POL ENHANCE IMMUNOGENICITY FOR GENETIC IMMUNIZATION

[71] Applicant: US GOVERNMENT; CHADRABARTI BIMAL K; NABEL GARY J; HUANG YUE

[72] Inventors: NABEL, Gary, J.; HUANG, Yue

[21] Application No.: NA

[22] Filed: 20010814

[43] Published: 20020425

[30] Priority: US US2000225097P 20000814 ...

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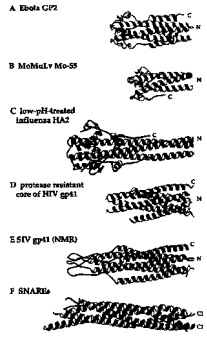

[57] Abstract:

Modified HIV Env, Gag, Pol, or Nef DNA with improved ability to elicit antibody and CTL responses to HIV antigens have been identified as prototype immunogens for the treatment and prevention of HIV infections.

[52] US Class:

[51] Int'l Class: C07K0014155 A61K00317088 A61K000908 C12N001509 A61P003118 A61K003800 C12N001549 C07K001416 A61K003900 A61K003939

[52] ECLA: C07K001416D K61K003800 K61K003953 K61K0039555B2 M07K031900

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MODIFICATIONS OF HIV ENV, GAG, AND POL ENHANCE IMMUNOGENICITY FOR GENETIC IMMUNIZATION

[71] Applicant: US GOVERNMENT; NABEL GARY J; CHADRABARTI BIMAL K; HUANG YUE

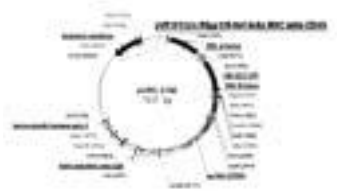
[72] Inventors: NABEL, Gary, J.; HUANG, Yue

[21] Application No.: NA

[22] Filed: 20010814

[43] Published: 20030109

[30] Priority: US US2000225097P 20000814 ...



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[57] Abstract:

Modified HIV Env, Gag, Pol, or Nef DNA with improved ability to elicit antibody and CTL responses to HIV antigens have been identified as prototype immunogens for the treatment and prevention of HIV infections.

[52] US Class:

[51] Int'l Class: C07K0014155 A61K00317088 A61K000908 C12N001509 A61P003118 A61K003800 C12N001549 C07K001416 A61K003900 A61K003939

[52] ECLA: C07K001416D K61K003800 K61K003953 K61K0039555B2 M07K031900

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MODIFICATIONS OF HIV ENV, GAG, AND POL ENHANCE IMMUNOGENICITY FOR GENETIC IMMUNIZATION

[71] Applicant: US GOVERNMENT; NABEL GARY J; CHADRABARTI BIMAL K; HUANG YUE

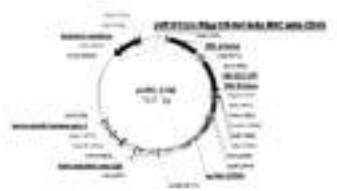
[72] Inventors: NABEL GARY J; HUANG YUE

[21] Application No.: NA

[22] Filed: 20010814

[43] Published: 20030904

[30] Priority: US US2000225097P 20000814 ...



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[57] Abstract:

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[52] US Class:

[51] Int'l Class: C07K0014155 A61K00317088 A61K000908 C12N001509 A61P003118 A61K003800 C12N001549 C07K001416 A61K003900 A61K003939

[52] ECLA: C07K001416D K61K003800 K61K003953 K61K0039555B2 M07K031900

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WO2002040693A1 MicroPatent Report

ADENOVIRAL REPLICONS

[71] Applicant: CRUCELL HOLLAND BV; HAVENGA MENZO JANS EMCO; BRUS RONALD HENDRIK PETER

[72] Inventors: HAVENGA, Menzo, Jans, Emco; BRUS, Ronald, Hendrik, Peter

[21] Application No.: NA

[22] Filed: 20011119

[43] Published: 20020523

[30] Priority: EP EP2000204097A 20001120 ...

Go to Fulltext

[No drawing]

[57] Abstract:

The invention provides a method for identifying an adenoviral replicon capable of eliminating a target cell, comprising contacting a representative cell with said adenoviral replicon and observing any detrimental effect. Once said replicon has been identified, it can be used to specifically eliminate certain cells involved in disease, for instance tumor cells. Preferably, said replicon contacts, enters and replicates predominantly in diseased cells, causing a detrimental effect in said cells, while in non-diseased cells no or a tolerable detrimental effect is induced. Preferably, said adenoviral replicon comprises a recombinant adenovirus with a fusion between DNA from Ad5 and subgroup B adenoviral DNA. Methods for producing and purifying a replicon according to the invention is also herewith provided.

[52] US Class:

[51] Int'l Class: C12N0015861 A61K004800

[52] ECLA: A61K004800J C12N0015861 C12N0015861C C12N0015861T M12N081060A1

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WO2001098513A2 MicroPatent Report

METHODS AND MEANS FOR THE COMPLEMENTATION OF VIRAL PROTEIN EXPRESSION IN STABLE CELL LINES

[71] Applicant: VERENIGING VOOR CHRISTELIJK WE; BEUSECHEM VICTOR WILLEM VAN; ...

[72] Inventors: VAN BEUSECHEM, Victor, Willem; GERRITSEN, Willem- Ronald

[21] Application No.: NA

[22] Filed: 20010618

[43] Published: 20011227

[30] Priority: EP EP2000202204A 20000623 ...

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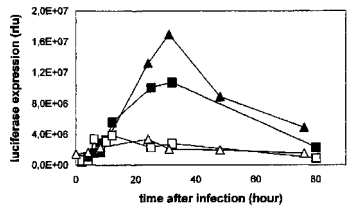

[57] Abstract:

Method for the propagation of recombinant virus in packaging cells, comprising the steps of: culturing the packaging cells free of virus introduction of the virus in the packaging cells propagation of the virus within the packaging cells isolating the virus from the packaging cells, wherein at least one gene of the virus, the expression of which leads to a product, being essential for the replication of the virus within the packaging cells is modified to be not functional or at least partly deleted from the said virus, the packaging cells comprise a stably replicating complementing gene, coding for a function complementing for the said essential product, the product being toxic to the said packaging cells, the expression of the said complementing gene being under the control of a transactivator responsive element (TRE), the gene encoding the corresponding transactivator being present in the recombinant virus genome and being expressible in the packaging cells upon infection thereof by the said virus.

[52] US Class:

[51] Int'l Class: C12N001586 C12N001534 C12N000510 C12N0015861

[52] ECLA: C12N000510T C12N001586 C12N0015861 M12N081060A1 M12N083000A1A

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METHODS AND MEANS FOR THE COMPLEMENTATION OF VIRAL PROTEIN EXPRESSION IN STABLE CELL LINES

[71] **Applicant:** VERENIGING VOOR CHRISTELIJK WE; BEUSECHEM VICTOR WILLEM VAN; . . .

[72] **Inventors:** VAN BEUSECHEM, Victor, Willem; GERRITSEN, Willem- Ronald

[21] **Application No.:** NA

[22] **Filed:** 20010618

[43] **Published:** 20020411

[30] **Priority:** EP EP2000202204A 20000623 ...

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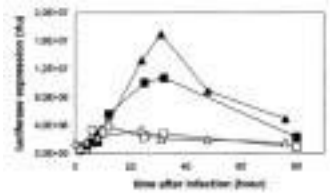

[57] **Abstract:**

Method for the propagation of recombinant virus in packaging cells, comprising the steps of: culturing the packaging cells free of virus introduction of the virus in the packaging cells propagation of the virus within the packaging cells isolating the virus from the packaging cells, wherein at least one gene of the virus, the expression of which leads to a product, being essential for the replication of the virus within the packaging cells is modified to be not functional or at least partly deleted from the said virus, the packaging cells comprise a stably replicating complementing gene, coding for a function complementing for the said essential product, the product being toxic to the said packaging cells, the expression of the said complementing gene being under the control of a transactivator responsive element (TRE), the gene encoding the corresponding transactivator being present in the recombinant virus genome and being expressible in the packaging cells upon infection thereof by the said virus.

[52] **US Class:**

[51] **Int'l Class:** C12N001586 C12N001534 C12N000510 C12N0015861

[52] **ECLA:** C12N000510T C12N001586 C12N0015861 M12N081060A1 M12N083000A1A

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ADENOVIRUS FORMULATIONS

[71] **Applicant:** MERCK CO INC; EVANS ROBERT K; VOLKIN DAVID B

[72] **Inventors:** EVANS, Robert, K.; VOLKIN, David, B.

[21] **Application No.:** NA

[22] **Filed:** 20010306

[43] **Published:** 20010913

[30] **Priority:** US US2000187440P 20000307 ...

Go to Fulltext

[No drawing]

[57] **Abstract:**

The invention relates to viral formulations and related pharmaceutical products for use in gene therapy and/or vaccine applications. Especially preferred viral formulations disclosed herein are liquid adenovirus formulations, which show improved stability when stored in about the 2-8°C range while also being compatible with parenteral administration. These formulations comprise a buffer, a sugar, a salt, a divalent cation, a non-ionic detergent, as well as a free radical scavenger and/or a chelating agent to inhibit free radical oxidation.

[52] **US Class:**

[51] **Int'l Class:** A61K004800 A61K004718 A61K003576 A61K000900 A61K000908 A61P004300 A61K004710 A61K0039235 A61K004734 A61P003112 A61K004726 A61K004700 A61K004746 A61K004702

[52] **ECLA:** A61K000900M5 K61K0039525 K61K004800

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METHODS AND COMPOSITIONS FOR THE MANUFACTURE OF REPLICATION INCOMPETENT ADENOVIRUS

[71] **Applicant:** GENOVO INC; HIMES VAUGHN B; RASTY SIYAMAK; PELUSO RICHARD W

[72] **Inventors:** HIMES, Vaughn, B.; RASTY, Siyamak; PELUSO, Richard, W.

[21] **Application No.:** NA

[22] **Filed:** 20001207

[43] **Published:** 20010621

[30] **Priority:** US US1999170550P 19991214 ...

Go to Fulltext

[No drawing]

[57] **Abstract:**

The present invention relates to complementing cell lines for the production of replication incompetent viruses, which significantly reduce or eliminate the presence of replication competent viruses. Methods to make and use the complementing cell lines are also provided, as are nucleic acid molecules, polynucleotides, and vectors for making the cell lines. In particular, the present invention relates to complementing cell lines for the production of replication incompetent adenoviruses (Ad), which significantly reduce or eliminate the presence of replication competent Ad (RCA) and can serve for the large scale production of infectious replication incompetent adenovirus particles that may be used for the treatment of human patients as for example in gene therapy. The present invention further relates to an assay for detecting the presence of replication competent virus particles, in particular RCA, in a stock of infectious replication incompetent virus particles, in particular replication incompetent adenovirus particles, which employs a real time quantitative PCR assay with a sensitivity level to detect one replication competent virus particle per ≥ 10^9 replication incompetent virus particles.

[52] **US Class:**

[51] **Int'l Class:** C12Q000168 C12N000119 C12N000115 G01N003353 C12N0015861 C12N000121 G01N0033569 G01N0033566 C12N000510 C12N001509

[52] **ECLA:** C12N0015861 M12N083044 M12N084020A

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METHODS AND COMPOSITIONS FOR THE MANUFACTURE OF REPLICATION INCOMPETENT ADENOVIRUS

[71] **Applicant:** GENOVO INC; HIMES VAUGHN B; RASTY SIYAMAK; PELUSO RICHARD W

[72] **Inventors:** HIMES, Vaughn, B.; RASTY, Siyamak; PELUSO, Richard, W.

[21] **Application No.:** NA

[22] **Filed:** 20001207

[43] **Published:** 20011129

[30] **Priority:** US US1999170550P 19991214 ...

Go to Fulltext

[No drawing]

[57] **Abstract:**

The present invention relates to complementing cell lines for the production of replication incompetent viruses, which significantly reduce or eliminate the presence of replication competent viruses. Methods to make and use the complementing cell lines are also provided, as are nucleic acid molecules, polynucleotides, and vectors for making the cell lines. In particular, the present invention relates to complementing cell lines for the production of replication incompetent adenoviruses (Ad), which significantly reduce or eliminate the presence of replication competent Ad (RCA) and can serve for the large scale production of infectious replication incompetent adenovirus particles that may be used for the treatment of human patients as for example in gene therapy. The present invention further relates to an assay for detecting the presence of replication competent virus particles, in particular RCA, in a stock of infectious replication incompetent virus particles, in particular replication incompetent adenovirus particles, which employs a real time quantitative PCR assay with a sensitivity level to detect one replication competent virus particle per ≥ 10^9 replication incompetent virus particles.

[52] **US Class:**

[51] **Int'l Class:** C12Q000168 C12N000119 C12N000115 G01N003353 C12N0015861 C12N000121 G01N0033569 G01N0033566 C12N000510 C12N001509

[52] **ECLA:** C12N0015861 M12N083044 M12N084020A

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ADENOVIRUS VECTORS WITH KNOBLESS FIBERS, AND THEIR USES

[71] Applicant: CRUCELL HOLLAND BV; VRIJE UNIVERSITEIT MEDISCH CT; ES HELMUTH . . .

[72] Inventors: VAN ES, Helmuth, Hendrikus, Gerardus; VAN BEUSECHEM, Victor, Willem

[21] Application No.: NA

[22] Filed: 20010426

[43] Published: 20011101

[30] Priority: US US2000200160P 20000426 ...

Go to Fulltext

[No drawing]

[57] Abstract:

The present invention provides novel adenoviral vectors, in which the knob of the fiber protein has been removed and replaced with a binding ligand. The invention also provides methods of constructing such vectors and provides uses for such vectors. A modified knobless adenovirus comprising a new binding ligand according to the invention has improved capabilities of entry into specific cell types.

[52] US Class:

[51] Int'l Class: C12N0015861 C07K001415 C07K0014075

[52] ECLA: C07K0014075 C07K001415 C12N0015861T M07K031900 M12N081060 M12N081060D1 M12N081080 M12N081085D M12N081085G

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ADENOVIRUS VECTORS WITH KNOBLESS FIBERS, AND THEIR USES

[71] Applicant: CRUCELL HOLLAND BV; VRIJE UNIVERSITEIT MEDISCH CT; ES HELMUTH . . .

[72] Inventors: VAN ES, Helmuth, Hendrikus, Gerardus; VAN BEUSECHEM, Victor, Willem

[21] Application No.: NA

[22] Filed: 20010426

[43] Published: 20020613

[30] Priority: US US2000200160P 20000426 ...

Go to Fulltext

[No drawing]

[57] Abstract:

The present invention provides novel adenoviral vectors, in which the knob of the fiber protein has been removed and replaced with a binding ligand. The invention also provides methods of constructing such vectors and provides uses for such vectors. A modified knobless adenovirus comprising a new binding ligand according to the invention has improved capabilities of entry into specific cell types.

[52] US Class:

[51] Int'l Class: C12N0015861 C07K001415 C07K0014075

[52] ECLA: C07K0014075 C07K001415 C12N0015861T M07K031900 M12N081060 M12N081060D1 M12N081080 M12N081085D M12N081085G

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IDENTIFICATION OF PEPTIDES THAT FACILITATE UPTAKE AND CYTOPLASMIC AND/OR NUCLEAR TRANSPORT OF PROTEINS, DNA AND VIRUSES

[71] Applicant: UNIV PITTSBURGH

[72] Inventors: ROBBINS, Paul, D.; MI, Zhibao; FRIZZELL, Raymond; GLORIOSO, Joseph, . . .

[21] Application No.: NA

[22] Filed: 20000831

[43] Published: 20010308

[30] Priority: US US1999151980P 19990901 ...

Go to Fulltext

[No drawing]

[57] Abstract:

The present invention relates to internalizing peptides which facilitate the uptake and transport of cargo into the cytoplasm and nuclei of cells as well as methods for the identification of such peptides. The internalizing peptides of the present invention are selected for their ability to efficiently internalize cargo into a wide variety of cell types both in vivo and in vitro. The method for identification of the internalizing peptides of the present invention comprises incubating a target cell with a peptide display library, isolating peptides with internalization characteristics and determining the ability of said peptide to internalize cargo into a cell.

[52] US Class:

[51] Int'l Class: C40B004002 A61K004748 C12N001510 C07K000706 C07K000708 A61K003900 A61K003800 A61K004800

[52] ECLA: C40B004002 A61K004748R C07K000706A C07K000708A C12N001510C1 G01N003368A8 K61K003800 K61K003900 M07K020700 M07K031900 K61K004800

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IDENTIFICATION OF PEPTIDES THAT FACILITATE UPTAKE AND CYTOPLASMIC AND/OR NUCLEAR TRANSPORT OF PROTEINS, DNA AND VIRUSES

[71] Applicant: UNIV PITTSBURGH

[72] Inventors: ROBBINS, Paul, D.; MI, Zhibao; FRIZZELL, Raymond; GLORIOSO, Joseph, . . .

[21] Application No.: NA

[22] Filed: 20000831

[43] Published: 20020124

[30] Priority: US US1999151980P 19990901 ...

Go to Fulltext

[No drawing]

[57] Abstract:

The present invention relates to internalizing peptides which facilitate the uptake and transport of cargo into the cytoplasm and nuclei of cells as well as methods for the identification of such peptides. The internalizing peptides of the present invention are selected for their ability to efficiently internalize cargo into a wide variety of cell types both in vivo and in vitro. The method for identification of the internalizing peptides of the present invention comprises incubating a target cell with a peptide display library, isolating peptides with internalization characteristics and determining the ability of said peptide to internalize cargo into a cell.

[52] US Class:

[51] Int'l Class: C40B004002 A61K004748 C12N001510 C07K000706 C07K000708 A61K003900 A61K003800 A61K004800

[52] ECLA: C40B004002 A61K004748R C07K000706A C07K000708A C12N001510C1 G01N003368A8 K61K003800 K61K003900 M07K020700 M07K031900 K61K004800

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PROPAGATION METHOD

[71] Applicant: GLAXO GROUP LTD; FORD MARTIN JAMES; HISSEY PAUL HENRY; PATEMAN TONY ...

[72] Inventors: FORD, Martin, James; HISSEY, Paul, Henry; PATEMAN, Tony, James

[21] Application No.: NA

[22] Filed: 20000602

[43] Published: 20010111

[30] Priority: GB GB199915413A 19990701 ...

Go to Fulltext

[No drawing]

[57] Abstract:

The present invention provides a method for the propagation of lytic organisms which comprises the infection of the cells of a stable cell line within a hollow fibre bioreactor with a lytic organism, wherein after said infection, said organism multiplies within the cells and can be harvested, characterised in that the cell line can survive for at least ten days after said infection. The invention further provides a method as herein described wherein after harvest, the cell line is allowed to re-populate the bioreactor, and at least one subsequent harvest may be taken, with the cell line being able to re-populate the bioreactor after each harvest.

[52] US Class:

[51] Int'l Class: C12N000700 A61K003576

[52] ECLA: A61K003576 C12N000700 M12N071019

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METHODS FOR THE PROPAGATION OF LYTIC ORGANISMS

[71] Applicant: GLAXO GROUP LTD; FORD MARTIN JAMES; HISSEY PAUL HENRY; PATEMAN TONY ...

[72] Inventors: FORD, Martin, James; HISSEY, Paul, Henry; PATEMAN, Tony, James

[21] Application No.: NA

[22] Filed: 20000602

[43] Published: 20010712

[30] Priority: GB GB199915413A 19990701 ...

Go to Fulltext

[No drawing]

[57] Abstract:

The present invention provides a method for the propagation of lytic organisms which comprises the infection of the cells of a stable cell line within a hollow fibre bioreactor with a lytic organism, wherein after said infection, said organism multiplies within the cells and can be harvested, characterised in that the cell line can survive for at least ten days after said infection. The invention further provides a method as herein described wherein after harvest, the cell line is allowed to re-populate the bioreactor, and at least one subsequent harvest may be taken, with the cell line being able to re-populate the bioreactor after each harvest.

[52] US Class:

[51] Int'l Class: C12N000700 A61K003576

[52] ECLA: A61K003576 C12N000700 M12N071019

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RECOMBINANT PROTEIN PRODUCTION IN A HUMAN CELL

[71] Applicant: INTROGENE BV; HATEBOER GUUS; VERHULST KARINA CORNELIA; SCHOUTEN ...

[72] Inventors: HATEBOER, Guus; VERHULST, Karina, Cornelia; SCHOUTEN, Govert, Johan; ...

[21] Application No.: NA

[22] Filed: 20000417

[43] Published: 20001026

[30] Priority: EP EP1999201176A 19990415 ...

Go to Fulltext

[No drawing]

[57] Abstract:

The present invention provides methods and compositions for the production of recombinant proteins in a human cell line. The methods and compositions are particularly useful for generating stable expression of human recombinant proteins of interest that are modified post-translationally, e.g. by glycosylation. Such proteins may have advantageous properties in comparison with their counterparts produced in non-human systems like Chinese Hamster Ovary (CHO) cells.

[52] US Class:

[51] Int'l Class: C12N000510 A61K0039395 A61K0039145 A61K0039125 C12N001509 C12P002102 A61K003929 A61K003921 C07K0014075 C12N001585 A61P003112 A61K003923 C07K0014505 A61K0039245 C12R000191

[52] ECLA: C12N001585 M12N080010E M12N083000 M12N083015 M12N083060 M12N084020

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RECOMBINANT PROTEIN PRODUCTION IN A HUMAN CELL USING SEQUENCES ENCODING ADENOVIRUS E1 PROTEIN

[71] Applicant: INTROGENE BV; HATEBOER GUUS; VERHULST KARINA CORNELIA; SCHOUTEN ...

[72] Inventors: HATEBOER, Guus; VERHULST, Karina, Cornelia; SCHOUTEN, Govert, Johan; ...

[21] Application No.: NA

[22] Filed: 20000417

[43] Published: 20010215

[30] Priority: EP EP1999201176A 19990415 ...

Go to Fulltext

[No drawing]

[57] Abstract:

The present invention provides methods and compositions for the production of recombinant proteins in a human cell line, using sequences encoding at least one E1 protein of an adenovirus where the cells does not encode a structural adenoviral protein from its genome. The methods and compositions are particularly useful for generating stable expression of human recombinant proteins of interest that are modified post-translationally, e.g. by glycosylation. Such proteins may have advantageous properties in comparison with their counterparts produced in non-human systems like Chinese Hamster Ovary (CHO) cells.

[52] US Class:

[51] Int'l Class: C12N000510 A61K0039395 A61K0039145 A61K0039125 C12N001509 C12P002102 A61K003929 A61K003921 C07K0014075 C12N001585 A61P003112 A61K003923 C07K0014505 A61K0039245 C12R000191

[52] ECLA: C12N001585 M12N080010E M12N083000 M12N083015 M12N083060 M12N084020

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COMPOSITIONS AND METHODS USEFUL FOR PRODUCTION OF RECOMBINANT VIRUSES WHICH REQUIRE HELPER VIRUSES

[71] Applicant: UNIV PENNSYLVANIA; XIAO WEIDONG; WILSON JAMES M

[72] Inventors: XIAO, Weidong; WILSON, James, M.

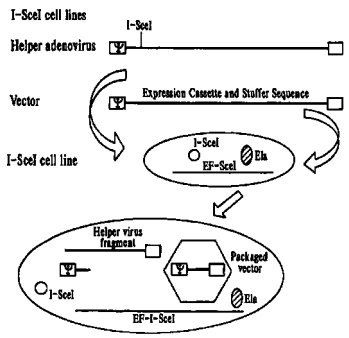
[21] Application No.: NA

[22] Filed: 20000107

[43] Published: 20001214

[30] Priority: US US1999137105P 19990602 ...

Go to Fulltext



[57] Abstract:

A method of producing recombinant viruses which require helper viruses for packaging is provided. The method uses a recombinant helper virus which has been designed to contain at least one rare-cutting restriction site (e.g., for I-SceI), a viral vector which is helper-dependent for packaging, and a recombinant host cell which is capable of expressing a rare-cutting restriction enzyme (e. g., I-SceI). The method involves transfecting or infecting the host cell with the helper virus and viral vector and incubating the cell under conditions which permit encapsidation of the viral vector in an adenovirus capside. Thereafter, the I-SceI expressed by the host cell digests the helper virus, permitting ready separation of the digested fragments of the helper virus from the packaged recombinant virus.

[52] US Class:

[51] Int'l Class: C12N000700 C12N000510 C12N001509 C12N000701 C12N0015861

[52] ECLA: C12N000510T C12N0015861 M12N080080

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COMPOSITIONS AND METHODS FOR PRODUCTION OF RECOMBINANT VIRUS USING A CARRIER VECTOR DERIVED FROM A NONMAMMALIAN VIRUS

[71] Applicant: GENOVO INC; RASTY SIYAMAK; GONDA MATTHEW A; CHEN HAIFENG

[72] Inventors: RASTY, Siyamak; GONDA, Matthew, A.; CHEN, Haifeng

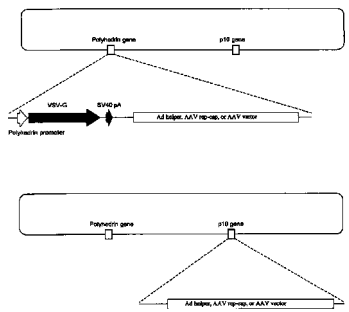
[21] Application No.: NA

[22] Filed: 20000525

[43] Published: 20001207

[30] Priority: US US1999136650P 19990527 ...

Go to Fulltext



[57] Abstract:

This invention relates to nonmammalian carrier vectors and viruses useful in the production of high titers of recombinant viruses which may contain foreign DNA inserts or which may be point-mutated or deleted viruses, and methods of producing those viruses. The nonmammalian carrier vector ("carrier vector") is a chimeric vector which includes those portions of a nonmammalian virus backbone which allow replication in a nonmammalian host cell. The carrier vector includes various nucleic acid cassettes, which may include an embedded recombinant viral genome containing a desired transgene, components necessary for production of a replication-defective recombinant virus containing the transgene, and domains that permit the carrier vector to bind to mammalian cells. The invention also provides methods of producing high concentrations of recombinant virus as a substantially homogeneous preparation, compositions to produce the recombinant virus, and recombinant viruses.

[52] US Class:

[51] Int'l Class: C12N0015866 A61K004800 A61K003576 C12N001509 C12N0015864 C12N000700 C12N000701 C12N000702 C12R000191

[52] ECLA: C12N0015864A C12N0015866 M12N080010E M12N083000 M12N083042 M12N083060 M12N084020 M12N084020A

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A NOVEL PACKAGING CELL LINE FOR THE RESCUE, PRODUCTION AND TITRATION OF HIGH-CAPACITY ADENOVIRUS AMPLICON VECTORS

[71] Applicant: SINAI SCHOOL MEDICINE; KROUGLIAK VALERI A; EISENSMITH RANDY C

[72] Inventors: KROUGLIAK, Valeri, A.; EISENSMITH, Randy, C.

[21] Application No.: NA

[22] Filed: 20000526

[43] Published: 20001207

[30] Priority: US US1999136481P 19990528 ...

Go to Fulltext

[No drawing]

[57] Abstract:

The present invention describes a method of producing adenovirus gutless amplicon viral vector substantially reduced in the content of helper virus. The invention also describes a system for the helper virus independent replication and packaging of adenovirus gutless vectors. A cell line for this system is also discussed.

[52] US Class:

[51] Int'l Class: C12N0015861 C12N001538 C12N000510

[52] ECLA: C12N000510T C12N0015861 M12N080010E M12N080030 M12N083000A1A M12N083038 M12N084020A

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A NOVEL PACKAGING CELL LINE FOR THE RESCUE, PRODUCTION AND TITRATION OF HIGH-CAPACITY ADENOVIRUS AMPLICON VECTORS

[71] Applicant: SINAI SCHOOL MEDICINE; KROUGLIAK VALERI A; EISENSMITH RANDY C

[72] Inventors: KROUGLIAK VALERI A; EISENSMITH RANDY C

[21] Application No.: NA

[22] Filed: 20000526

[43] Published: 20020418

[30] Priority: US US1999136481P 19990528 ...

Go to Fulltext

[No drawing]

[57] Abstract:

The present invention describes a method of producing adenovirus gutless amplicon viral vector substantially reduced in the content of helper virus. The invention also describes a system for the helper virus independent replication and packaging of adenovirus gutless vectors. A cell line for this system is also discussed.

[52] US Class:

[51] Int'l Class: C12N0015861 C12N001538 C12N000510

[52] ECLA: C12N000510T C12N0015861 M12N080010E M12N080030 M12N083000A1A M12N083038 M12N084020A

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WO2000046360A1 MicroPatent Report

IMPROVED HELPER DEPENDENT VECTOR SYSTEM FOR GENE THERAPY

[71] Applicant: MERCK CO INC; BETT ANDREW; SANDIG VOLKER; YOUIL RIMA

[72] Inventors: BETT, Andrew; SANDIG, Volker; YOUIL, Rima

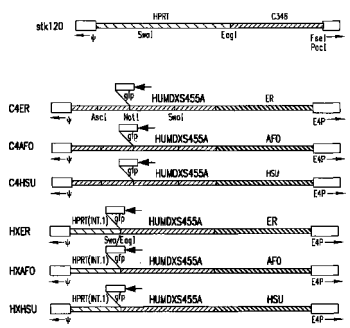
[21] Application No.: NA

[22] Filed: 20000131

[43] Published: 20000810

[30] Priority: US US1999118601P 19990204 ...

Go to Fulltext



[57] Abstract:

The present invention features helper-dependent adenoviral vector elements, and helper adenoviral elements, that enhance the production and isolation of helper-dependent adenoviral vectors. Such elements include a modified packaging signal having low homology to, and preferably less activity than, a wild-type packaging signal, an E4 non-coding segment directly joined to the 5' ITR that confers a selective advantage, and stuffer region(s) that provide a helper-dependent adenoviral vector with a GC content of about 50 % to about 60 %. The modified packaging signal is preferably used in a helper virus to decrease recombination and generation of the virus. The E4 non-coding segment and the stuffer region(s) are preferably used in a helper-dependent adenoviral vector to provide the vector with a growth advantage over a helper virus.

[52] US Class:

[51] Int'l Class: A61K004800 A61K003576 C12N001509 C12N0015861 A61P004300 C12N000510 C12N000700

[52] ECLA: C12N0015861C

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WO2000042208A1 MicroPatent Report

ADENOVIRUS VECTORS, PACKAGING CELL LINES, COMPOSITIONS, AND METHODS FOR PREPARATION AND USE

[71] Applicant: NOVARTIS AG; NOVARTIS ERFIND VERWALT GMBH; SCRIPPS RESEARCH ...

[72] Inventors: SKRIPCHENKO, Yelena

[21] Application No.: NA

[22] Filed: 20000114

[43] Published: 20000720

[30] Priority: US US1999115920P 19990114 ...

Go to Fulltext

[No drawing]

[57] Abstract:

The present invention relates to methods for gene therapy, especially to adenovirus-based gene therapy, and related cell lines and compositions. In particular, novel nucleic acid constructs and packaging cell lines are disclosed, for use in facilitating the development of high-capacity and targeted vectors. The invention also discloses a variety of high-capacity adenovirus vectors and related compositions and kits including the disclosed cell lines and vectors. Finally, the invention discloses methods of preparing and using the disclosed vectors, cell lines and kits.

[52] US Class:

[51] Int'l Class: C12N001509 A61K004800 A61K003576 G01N003353 C12N000700 A61P003500 C12Q000168 C12N0015861 A61P004300 G01N0033566 C12N000510

[52] ECLA: C12N000510T C12N0015861 C12N0015861T K61K004800 M12N080030 M12N081060A1 M12N080010E M12N083048

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ADENOVIRUS VECTORS, PACKAGING CELL LINES, COMPOSITIONS, AND METHODS FOR PREPARATION AND USE

[71] Applicant: SCRIPPS RESEARCH INST; NOVARTIS AG; NOVARTIS ERFIND VERWALT GMBH

[72] Inventors: NEMEROW GLEN ROBERT; VON SEGGERN DANIEL J; HALLENBECK PAUL L; . . .

[21] Application No.: NA

[22] Filed: 20000114

[43] Published: 20020510

[30] Priority: US US1999115920P 19990114 ...

Go to Fulltext

[No drawing]

[57] Abstract:

The present invention relates to methods for gene therapy, especially to adenovirus-based gene therapy, and related cell lines and compositions. In particular, novel nucleic acid constructs and packaging cell lines are disclosed, for use in facilitating the development of high-capacity and targeted vectors. The invention also discloses a variety of high-capacity adenovirus vectors and related compositions and kits including the disclosed cell lines and vectors. Finally, the invention discloses methods of preparing and using the disclosed vectors, cell lines and kits.

[52] US Class:

[51] Int'l Class: C12N001509 A61K004800 A61K003576 G01N003353 C12N000700 A61P003500 C12Q000168 C12N0015861 A61P004300 G01N0033566 C12N000510

[52] ECLA: C12N000510T C12N0015861 C12N0015861T K61K004800 M12N080030 M12N081060A1 M12N080010E M12N083048

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A RECOMBINANT VECTOR EXPRESSING MULTIPLE COSTIMULATORY MOLECULES AND USES THEREOF

[71] Applicant: US HEALTH; THERION BIOLOG CORP; SCHLOM JEFFREY; HODGE JAMES; PANICALI . . .

[72] Inventors: SCHLOM, Jeffrey; HODGE, James; PANICALI, Dennis

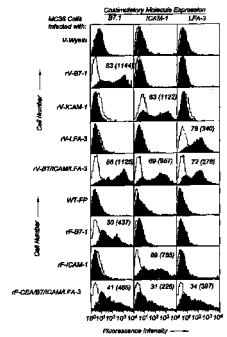
[21] Application No.: NA

[22] Filed: 19991112

[43] Published: 20000615

[30] Priority: US US1998111582P 19981209 ...

Go to Fulltext



[57] Abstract:

The present invention is a recombinant vector encoding and expressing at least three or more costimulatory molecules. The recombinant vector may additionally contain a gene encoding one or more target antigens or immunological epitope thereof. The synergistic effect of these costimulatory molecules on the enhanced activation of T cells is demonstrated. The degree of T-cell activation using recombinant vectors containing genes encoding three costimulatory molecules was far greater than the sum of recombinant vector constructs containing one costimulatory molecule and greater than the use of two costimulatory molecules. Results employing the triple costimulatory vectors were most dramatic under conditions of either low levels of first signal or low stimulator to T-cell ratios. This phenomenon was observed with both isolated $CD4^+$ and $CD8^+$ T cells. The recombinant vectors of the present invention are useful as immunogenes and vaccines against cancer and pathogenic micro-organisms, and in providing host cells, including dendritic cells and splenocytes with enhanced antigen-presenting functions.

[52] US Class:

[51] Int'l Class: A61K0039275 C07K0014705 A61K0039125 C12N000700 A61P003112 A61K003574 C12N000115 A61K003512 A61P003500 G01N003353 C12N000119 A61P003110 A61K004800 C12Q000102 C12N001502 C12N000510 A61K003912 C12N0015863 A61K003576 A61K0039235 A61K003929 A61P003706 A61P003104 A61P000104 A61K003921 A61K003800 C12N000121 A61P003702 A61K0039245 A61K003900

[52] ECLA: C07K0014705B C07K0014705B20 C07K0014705B22 C07K0014705B24 C12N0015863 K61K003512 K61K003900 K61K003957 K61K004800 M07K020700 M07K022100

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METHODS OF AUGMENTING MUCOSAL IMMUNITY THROUGH SYSTEMIC PRIMING AND MUCOSAL BOOSTING

[71] Applicant: WISTAR INST

[72] Inventors: ERTL, Hildegund, C. , J.

[21] Application No.: NA

[22] Filed: 19990819

[43] Published: 20000302

[30] Priority: US US199897185P 19980820 ...

[No drawing]

Go to Fulltext

[57] Abstract:

A method for inducing and enhancing mammalian mucosal immunity includes the steps of first administering to a mammal via a non-mucosal route a suitable amount of a priming vaccine composition which comprises a DNA sequence encoding an antigen of a pathogen under the control of regulatory sequences directing expression thereof in a mammalian cell, and subsequently, administering intranasally a boosting vaccine composition which comprises the same antigen in protein form or a DNA sequence encoding the same antigen. A method to reduce the anti-viral immune response to a recombinant viral vaccine includes the steps of administering a similar priming DNA vaccine composition that lacks any viral protein and subsequently administering as a boosting vaccine, a recombinant virus containing a DNA sequence encoding the same antigen as encoded by the DNA vaccine, wherein upon said recombinant virus vaccine administration, the immune response to the antigen is enhanced and the immune response to the recombinant virus is reduced.

[52] US Class:

[51] Int'l Class: A61K003912

[52] ECLA: A61K003912 K61K003953 K61K003954 K61K003954A K61K0039545 K61K0039555B2

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ADENOVIRAL BASED PROMOTER ASSAY

[71] Applicant: MERCK CO INC; RICHARDS KAREN; RUSHMORE THOMAS H; MORSY MANAL A

[72] Inventors: RICHARDS, Karen; RUSHMORE, Thomas, H.; MORSY, Manal, A.

[21] Application No.: NA

[22] Filed: 19990709

[43] Published: 20000127

[30] Priority: US US199892777P 19980714 ...

[No drawing]

Go to Fulltext

[57] Abstract:

Adenoviral vectors are used to transfer a promoter/reporter gene construct to mammalian cell cultures. The promoter/reporter gene construct is used to determine if a candidate inducing agent has promoter-inducing activity; or can be used to determine if a candidate promoter has activity in the presence of a known inducer.

[52] US Class:

[51] Int'l Class: C12N001509 C12N000510 G01N003350 G01N003315 C12N0015861 C12Q000168 C12Q000170

[52] ECLA: C12N0015861 C12Q000168P M12N083000A1 M12N083085

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NOVEL ADENOVIRAL VECTORS FOR GENE THERAPY

[71] Applicant: MERCK CO INC; MORSY MANAL A; SANDIG VOLKER

[72] Inventors: MORSY, Manal, A.; SANDIG, Volker

[21] Application No.: NA

[22] Filed: 19990604

[43] Published: 19991216

[30] Priority: US US199888605P 19980609 ...

Go to Fulltext

[No drawing]

[57] Abstract:

Helper dependent adenoviral vectors are suitable for use in gene therapy, as they are stable, contain only a very small amount less than about 0.5 % of helper virus contamination, and are less immunogenic than previous adenoviral vectors. The only viral DNA in the vectors are ITRs and packaging signals, and overall size is about 26-38 kb.

[52] US Class:

[51] Int'l Class: C12N0015861 A61K003822 A61K003576 C12N001509 C12N000700 A61K004800 C07K0014575 C12N000510

[52] ECLA: A61K003822K C07K0014575P C12N0015861 K61K004800 M07K020700 M12N080030 M12N083038

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CONSTRUCTION OF RETROVIRAL PRODUCER CELLS FROM ADENOVIRAL AND RETROVIRAL VECTORS

[71] Applicant: OKLAHOMA MED RES FOUND

[72] Inventors: LIN, Xinli; TANG, Jordan, J., N.

[21] Application No.: NA

[22] Filed: 19990429

[43] Published: 19991104

[30] Priority: US US199883511P 19980429 ...

Go to Fulltext

[No drawing]

[57] Abstract:

A combination of adenoviral and retroviral vectors used to construct second generation packaging cells that deliver marker genes to target cells is described. A vector based upon Moloney murine leukemia virus (MLV) was used to deliver marker genes, and an adenovirus-based delivery system was used to deliver MLV structural genes (gagpol and env) to cultured cells. The procedure transformed the cells into new retroviral producer cells, which generate replication-incompetent retroviral particles in the culture supernatant for transferring marker genes to target cells. The titer of the retroviral-containing supernatant generated from the second generation producer cells reached above 105 cfu/ml, which is comparable to the MLV-based producer cell lines currently used in human gene therapy trials. The vector and procedures are adaptable for experimental human gene therapy in which the new producer cells are transplanted into patients for continuous gene transfer.

[52] US Class:

[51] Int'l Class: C12N001586 C12N000510 C12N001509 C12N0015867

[52] ECLA: C12N0015867P C12N0015861C C12N0015867

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CONSTRUCTION OF RETROVIRAL PRODUCER CELLS FROM ADENOVIRAL AND RETROVIRAL VECTORS

[71] Applicant: OKLAHOMA MED RES FOUND

[72] Inventors: LIN XINLI; TANG JORDAN J N

[21] Application No.: NA

[22] Filed: 19990429

[43] Published: 20001214

[30] Priority: US US199883511P 19980429 ...

[No drawing]

Go to Fulltext

[57] Abstract:

A combination of adenoviral and retroviral vectors used to construct second generation packaging cells that deliver marker genes to target cells is described. A vector based upon Moloney murine leukemia virus (MLV) was used to deliver marker genes, and an adenovirus-based delivery system was used to deliver MLV structural genes (gagpol and env) to cultured cells. The procedure transformed the cells into new retroviral producer cells, which generate replication-incompetent retroviral particles in the culture supernatant for transferring marker genes to target cells. The titer of the retroviral-containing supernatant generated from the second generation producer cells reached above 105 cfu/ml, which is comparable to the MLV-based producer cell lines currently used in human gene therapy trials. The vector and procedures are adaptable for experimental human gene therapy in which the new producer cells are transplanted into patients for continuous gene transfer.

[52] US Class:

[51] Int'l Class: C12N001586 C12N000510 C12N001509 C12N0015867

[52] ECLA: C12N0015867P C12N0015861C C12N0015867

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EFFICIENT PURIFICATION OF ADENOVIRUS

[71] Applicant: GENVEC INC

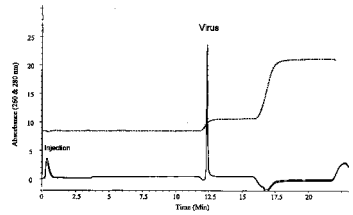
[72] Inventors: CARRIÓN, Miguel, E. ; MENGER, Marilyn; KOVESDI, Imre

[21] Application No.: NA

[22] Filed: 19990422

[43] Published: 19991028

[30] Priority: US US199882628P 19980422 ...



Go to Fulltext

[57] Abstract:

A method of enriching a solution of an adenovirus comprising applying a mixed solution comprising an adenovirus and at least one undesired type of biomolecule to an anion exchange chromatography resin containing a binding moiety selected from the group consisting of dimethylaminopropyl, dimethylaminobutyl, dimethylaminoisobutyl, and dimethylaminopentyl and eluting the adenovirus from the chromatography resin. Also provided is a method of purifying an adenovirus from adenovirus-infected cells comprising lysing such cells, applying the lysate to a single chromatography resin, eluting the adenovirus from the chromatography resin, and collecting a fraction containing adenovirus that is substantially as pure as triple CsC1 density gradient-purified adenovirus. The present method further provides a method of accurately quantifying the number of adenoviral particles in a solution of adenovirus comprising applying to and eluting from an anion exchange chromatography resin a sample solution of adenovirus, comparing the absorbance of the sample solution of adenovirus and the absorbance of a standard solution of adenovirus, and quantifying the number of adenoviral particles in the sample solution.

[52] US Class:

[51] Int'l Class: G01N003096 C12Q000106 B01D001536 G01N003348 G01N0033569 C12N000702 B01J0020285 G01N0033483 B01J004120 G01N003088 C07K0014075 B01D001534 G01N003062 G01N003006

[52] ECLA: B01D001536B4 B01J004120 C07K0014075 C12N000702 C12Q000106 G01N003096 L01D001534P M12N071019A S01N003006 S01N003062A2 S01N003088C1 S01N0333075

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WO1999054441A8 MicroPatent Report

EFFICIENT PURIFICATION OF ADENOVIRUS

[71] Applicant: GENVEC INC

[72] Inventors: CARRION MIGUEL E; MENGER MARILYN; KOVESDI IMRE

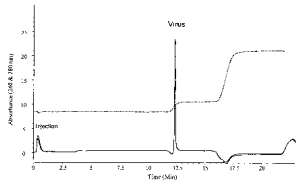
[21] Application No.: NA

[22] Filed: 19990422

[43] Published: 20000224

[30] Priority: US US199882628P 19980422 ...

Go to Fulltext



[57] Abstract:

A method of enriching a solution of an adenovirus comprising applying a mixed solution comprising an adenovirus and at least one undesired type of biomolecule to an anion exchange chromatography resin containing a binding moiety selected from the group consisting of dimethylaminopropyl, dimethylaminobutyl, dimethylaminoisobutyl, and dimethylaminopentyl and eluting the adenovirus from the chromatography resin. Also provided is a method of purifying an adenovirus from adenovirus-infected cells comprising lysing such cells, applying the lysate to a single chromatography resin, eluting the adenovirus from the chromatography resin, and collecting a fraction containing adenovirus that is substantially as pure as triple CsC1 density gradient-purified adenovirus. The present method further provides a method of accurately quantifying the number of adenoviral particles in a solution of adenovirus comprising applying to and eluting from an anion exchange chromatography resin a sample solution of adenovirus, comparing the absorbance of the sample solution of adenovirus and the absorbance of a standard solution of adenovirus, and quantifying the number of adenoviral particles in the sample solution.

[52] US Class:

[51] Int'l Class: G01N003096 C12Q000106 B01D001536 G01N003348 G01N0033569 C12N000702 B01J0020285 G01N0033483 B01J004120 G01N003088 C07K0014075 B01D001534 G01N003062 G01N003006

[52] ECLA: B01D001536B4 B01J004120 C07K0014075 C12N000702 C12Q000106 G01N003096 L01D001534P M12N071019A S01N003006 S01N003062A2 S01N003088C1 S01N0333075

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WO1999016466A2 MicroPatent Report

VACCINE COMPOSITIONS AND METHODS OF ENHANCING VACCINE EFFICACY

[71] Applicant: BETH ISRAEL HOSPITAL; LETVIN NORMAN L; BAROUCH DAN H

[72] Inventors: LETVIN, Norman, L.; BAROUCH, Dan, H.

[21] Application No.: NA

[22] Filed: 19980929

[43] Published: 19990408

[30] Priority: US US199760338P 19970929 ...

Go to Fulltext

[No drawing]

[57] Abstract:

The invention provides methods, vaccine compositions and plasmid constructs which enhance the immune response of a vaccine.

[52] US Class:

[51] Int'l Class: A61K003939 A61K003921 A61P003100 C07K001416 C07K001455 A61K003900

[52] ECLA: A61K003921+M A61K003939 C07K001416D C07K001455 K61K003900 K61K003951 K61K0039545 K61K0039555B2 K61K0039555B2L K61K0039555B2L2 K61K0039555B2L12 K61K0039555B5 M07K020700 M07K031900

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VACCINE COMPOSITIONS AND METHODS OF ENHANCING VACCINE EFFICACY

[71] Applicant: BETH ISRAEL HOSPITAL; LETVIN NORMAN L; BAROUCH DAN H

[72] Inventors: LETVIN NORMAN L; BAROUCH DAN H

[21] Application No.: NA

[22] Filed: 19980929

[43] Published: 19990603

[30] Priority: US US199760338P 19970929 ...

Go to Fulltext

[No drawing]

[57] Abstract:

The invention provides methods, vaccine compositions and plasmid constructs which enhance the immune response of a vaccine.

[52] US Class:

[51] Int'l Class: A61K003939 A61K003921 A61P003100 C07K001416 C07K001455 A61K003900

[52] ECLA: A61K003921+M A61K003939 C07K001416D C07K001455 K61K003900 K61K003951 K61K0039545 K61K0039555B2 K61K0039555B2L K61K0039555B2L2 K61K0039555B2L12 K61K0039555B5 M07K020700 M07K031900

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RECOMBINANT CELO AVIAN ADENOVIRUS AND USE AS VACCINATING VECTOR

[71] Applicant: VETERINAIRES ET ALIMENTAIRES C; LANGLOIS PATRICK

[72] Inventors: LANGLOIS, Patrick

[21] Application No.: NA

[22] Filed: 19980813

[43] Published: 19990225

[30] Priority: FR FR199710386A 19970814 ...

Go to Fulltext

[No drawing]

[57] Abstract:

The invention concerns methods for preparing recombinant CELO avian adenoviruses and their uses as vector for the expression of heterologous proteins for preparing vaccines, in particular for protecting avian species against common infectious diseases, or as vector for the expression of heterologous proteins involved in the metabolism.

[52] US Class:

[51] Int'l Class: C12N0015861 A61K003900

[52] ECLA: C12N0015861 K61K003900 M12N022104 M12N071019B M12N080030 M12N084020A

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WO1997038723A1 MicroPatent Report

TARGETED VIRAL VECTORS

[71] Applicant: IMMUSOL INC; MAMOUNAS MICHAEL; YU GANG; YANG QICHENG; LI QI XIANG; . . .

[72] Inventors: MAMOUNAS, Michael; YU, Gang; YANG, Qicheng; LI, Qi- Xiang; BARBER, Jack; . . .

[21] Application No.: NA

[22] Filed: 19970415

[43] Published: 19971023

[30] Priority: US US199615497P 19960416 ...

Go to Fulltext

[No drawing]

[57] Abstract:

Viral vectors are targeted to selected cell types by blocking the wild-type viral cell binding site and incorporating a targeting agent into the vector particle. The targeting agent binds to the selected cell type by binding a molecule on the surface of the cell, or by binding a second targeting agent which binds the selected cell. Parvovirus, retrovirus, Herpes virus and Ad virus based vectors are provided. Libraries of viral vectors having the targeting agent are provided. Methods of selecting recombinant viral vectors from the libraries are also provided. Polypeptide ligands isolated from libraries of phage or viral vectors are provided.

[52] US Class:

[51] Int'l Class: C12N001512 C07K001628 A61K004800 C12N001586 C12N0015864 C12N0015867

[52] ECLA: A61K004800 C07K001628Z C12N001586 C12N0015864A C12N0015867T K61K004800 M07K020700 M07K031900 M12N081040 M12N081085G

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WO1997031115A2 MicroPatent Report

SYNTHETIC HIV GENES

[71] Applicant: MERCK CO INC; SHIVER JOHN W; DAVIES MARY ELLEN; FREED DANIEL C; LIU . . .

[72] Inventors: SHIVER, John, W.; DAVIES, Mary-Ellen; FREED, Daniel, C.; LIU, Margaret, . . .

[21] Application No.: NA

[22] Filed: 19970218

[43] Published: 19970828

[30] Priority: US US199612082P 19960222 ...

Go to Fulltext

[No drawing]

[57] Abstract:

Synthetic DNA molecules encoding HIV genes and modifications of HIV genes are provided. The codons of the synthetic molecules use codons preferred by the projected host cell. The synthetic molecules may be used as a polynucleotide vaccine which provides effective immunoprophylaxis against HIV infection through neutralizing antibody and cell-mediated immunity.

[52] US Class:

[51] Int'l Class: C12N001500 A61P003100 A61K003170 A61K003100 C12N001509 C12Q000168 A61K004800 A61K00317088 C07K001416 C12N001549 A61P003118 A61K0031711 C12N000510 A61K003921 C12R000192

[52] ECLA: C07K001416D K61K003951 M07K020700 M07K031900

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WO1997031115A3 MicroPatent Report

SYNTHETIC HIV GENES

[71] Applicant: MERCK CO INC; SHIVER JOHN W; DAVIES MARY ELLEN; FREED DANIEL C; LIU ...

[72] Inventors: SHIVER JOHN W; DAVIES MARY-ELLEN; FREED DANIEL C; LIU MARGARET A; ...

[21] Application No.: NA

[22] Filed: 19970218

[43] Published: 19971009

[30] Priority: US US199612082P 19960222 ...

Go to Fulltext

[No drawing]

[57] Abstract:

[52] US Class:

[51] Int'l Class: C12N001500 A61P003100 A61K003170 A61K003100 C12N001509 C12Q000168 A61K004800 A61K00317088 C07K001416 C12N001549 A61P003118 A61K0031711 C12N000510 A61K003921 C12R000192

[52] ECLA: C07K001416D K61K003951 M07K020700 M07K031900

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WO1996022378A1 MicroPatent Report

CELLS FOR THE PRODUCTION OF RECOMBINANT ADENOVIRUSES

[71] Applicant: RHONE POULENC RORER SA; DEDIEU JEAN FRANCOIS; LATTA MARTINE; ...

[72] Inventors: DEDIEU, Jean François; LATTA, Martine; ORSINI, Cécile; ...

[21] Application No.: NA

[22] Filed: 19960119

[43] Published: 19960725

[30] Priority: FR FR1995747A 19950120 ...

Go to Fulltext



[57] Abstract:

The invention relates to cells usable for the production of defective adenoviruses comprising, inserted into their genome, a portion of the region E4 of an adenovirus genome carrying the reading phase ORF6 under the control of a functional promoter.

[52] US Class:

[51] Int'l Class: C12N0015861 C12N000510 C07K0014075 C12N001509 C12N001534 C12N000700 C12N0015864 C12N000704 C12N001500 C12R000192

[52] ECLA: C07K0014075 C12N000704A C12N0015861 C12N0015864A M07K020700 M12N083000A1

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COORDINATE (IN VIVO) GENE EXPRESSION

[71] Applicant: MERCK CO INC; LIU MARGARET A; SHIVER JOHN W; PERRY HELEN C

[72] Inventors: LIU, MARGARET, A., US; SHIVER, JOHN, W., US; PERRY, HELEN, C., US

[21] Application No.: NA

[22] Filed: 19950303

[43] Published: 19950914

[30] Priority: US US1994207526A 19940307 ...

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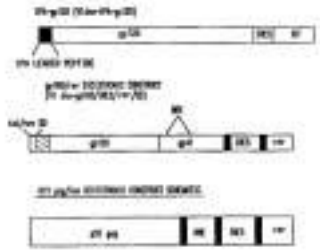

[57] Abstract:

Nucleic acids, including DNA constructs and RNA transcripts, capable of inducing coordinate expression of two to three cistrons upon direct introduction into animal tissues, are presented. Bi- or tri-cistronic polynucleotides of this invention include those encoding and co-expressing HIV gene products, genes encoding antigens unrelated to HIV, and immunostimulatory gene products, including but not limited to GM-CSF, interleukins, interferon and members of the B7 family of proteins which act as T-cell costimulatory elements. The methods and polynucleotides of this invention are generally applicable to co-ordinate expression (in vivo) of any two or more genes in a single cell.

[52] US Class:

[51] Int'l Class: A61P003704 A61K003921 A61K003170 A61K0009127 C12N001509 C07K001416 A61K003800 A61P003112 C07H002104 C12N001585 A61K004800 A61K003804 A61P003500 A61K003821 A61K003900

[52] ECLA: C07K001416 C12N001585 K61K003900 K61K004800 M07K020700 M12N083044 M12N083050 M12N084020A

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COORDINATE IN VIVO GENE EXPRESSION

[71] Applicant: MERCK CO INC; LIU MARGARET A; SHIVER JOHN W; PERRY HELEN C

[72] Inventors: LIU, Margaret, A.; SHIVER, John, W.; PERRY, Helen, C.

[21] Application No.: NA

[22] Filed: 19950303

[43] Published: 19951207

[30] Priority: US US1994207526A 19940307 ...

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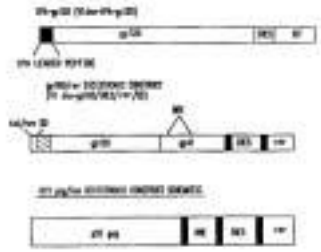

[57] Abstract:

Nucleic acids, including DNA constructs and RNA transcripts, capable of inducing coordinate expression of two to three cistrons upon direct introduction into animal tissues, are presented. Bi- or tri-cistronic polynucleotides of this invention include those encoding and co- expressing HIV gene products, genes encoding antigens unrelated to HIV, and immunostimulatory gene products, including but not limited to GM-CSF, interleukins, interferon and members of the B7 family of proteins which act as T-cell costimulatory elements. The methods and polynucleotides of this invention are generally applicable to co-ordinate expression in vivo of any two or more genes in a single cell.

[52] US Class:

[51] Int'l Class: A61P003704 A61K003921 A61K003170 A61K0009127 C12N001509 C07K001416 A61K003800 A61P003112 C07H002104 C12N001585 A61K004800 A61K003804 A61P003500 A61K003821 A61K003900

[52] ECLA: C07K001416 C12N001585 K61K003900 K61K004800 M07K020700 M12N083044 M12N083050 M12N084020A

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WO1995016772A1 MicroPatent Report

ADENOVIRUS GENE EXPRESSION SYSTEM

[71] Applicant: CORNELL RES FOUNDATION INC; FALCK PEDERSEN ERIK S

[72] Inventors: FALCK-PEDERSEN, Erik, S.

[21] Application No.: NA

[22] Filed: 19941214

[43] Published: 19950622

[30] Priority: US US1993166925A 19931214 ...

Go to Fulltext

[No drawing]

[57] Abstract:

The present invention provides a novel, highly efficient, recombinant adenovirus expression system for expression of a heterologous gene(s) and/or gene product(s) in a mammalian cell. The recombinant adenovirus was produced by cotransfecting a novel vector with the large fragment of the adenovirus-5 genome in 293 cells. Homologous recombination between these two DNA fragments resulted in the production of the recombinant adenovirus expression system. This vector, when converted to a recombinant virus has the unique capability of expressing one or more heterologous genes at very high levels. The novel vector, comprises, at least one cDNA insertion site for cloning a selected heterologous gene; a promoter sequence positioned upstream from the gene insertion site; the left end replication and packaging elements of the adenovirus-5 genome positioned upstream of the promoter; a highly efficient eukaryotic splice acceptor and splice donor site positioned immediately downstream of the promoter; and positioned downstream of the insertion site a strong polyadenylation sequence and the region for homologous recombination containing a portion of the adenovirus-5 genome. Between the packaging sequence and the CMV promoter are restriction sites for insertion of a second fully functional transcription unit.

[52] US Class:

[51] Int'l Class: C12N0015861 C07K001472 C07K001457

[52] ECLA: C07K001457 C07K001472B C12N0015861 M07K020700 M12N083038 M12N083044

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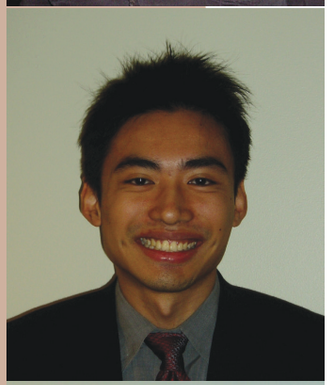
AUTHOR BIOGRAPHIES



YU-HUI SUNG, from Taiwan, is a J.D. candidate, class of 2009. Before going to Pierce Law, she worked for Top one hundred companies in Taiwan for eight years as an in-house patent engineer. She helped to prosecute patents in Taiwan, U.S., and China. She supported discovery procedures for several IP litigations in the US. Last year, she searched and reviewed over 1000 US and Japanese patents and applications for her summer job.



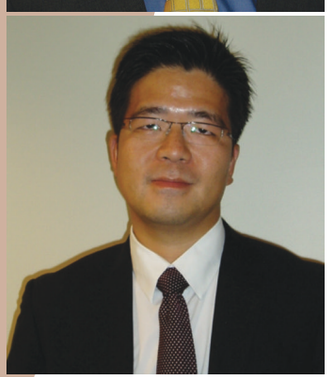
CYRIL CHAN, from Andover, Massachusetts, is a J.D. candidate, class of 2010. Mr. Chan graduated from the University of Illinois at Urbana-Champaign in 2007 with a B.S. degree in Materials Science & Engineering and a B.A. degree in English with distinction. Mr. Chan worked as a patent examiner intern at the U.S. Patent and Trademark Office in 2006 and 2007. He is interested in pursuing a career as a patent attorney.



EE MING YAP, from Los Angeles, CA, is a J.D. Candidate, class of 2009. Ms. Yap graduated from the University of California, Los Angeles in 2005 with a Bachelors of Arts in English. She spent much of her time there working in microbiology labs gaining experience in designing experiments and refining laboratory techniques. She worked as an intern for the in-house counsel at an electrical engineering company in El Segundo, CA. There she discovered her interest in intellectual property law. After graduation, she is excited to begin using her experience in technology and writing to advance a career in patent litigation.



TRISTAN CARRIER, from Winslow, Maine, is a J.D. candidate, class of 2010. Mr. Carrier graduated from Boston University in 2007 with a B.S. degree in Biomedical Engineering. He is interested in pursuing a career in patent litigation and prosecution. Mr. Carrier is an avid snowboarder, golfer, and rugby player.



BUMRAE CHO, from Seoul, South Korea, a J.D. candidate, class of 2009. Mr. Cho graduated from Yonsei University in 1996 with a B.S. degree in Food and Biotechnology, and a LL.M. degree in Intellectual Property Law. He has worked in a patent boutique in Korea for seven years as a patent engineer. During his work in the law firm, he has experienced diverse biotech patent litigations and freedom-to-operate searches for global pharmaceutical and biotech companies. He is interested in business development in biotech companies and law firms.



MICHELLE WINDOM, a native of New Orleans, Louisiana, is pursuing her J.D. degree and is currently a second year law student at Franklin Pierce Law Center. Ms. Windom graduated from Louisiana State University in 2002 with a Bachelor of Science degree in Biological Engineering, in 2004 from Tulane University with a Masters of Engineering in Biomedical Engineering, and in 2006 from Pierce Law Center with a Masters in Intellectual Property Law. She is interested in utilizing her science background to pursue a career in patent litigation and prosecution.



ALEX FERRE, from Richmond, Virginia, is a J.D. candidate, class of 2010. Mr Ferre graduated from Virginia Commonwealth University in 2007 with a B.S. in Biochemistry and a minor in Biology. He is interested in pursuing patent litigation career and eventually working in house in the biotechnology industry.



CONSTANCE A. ROGERS, from North Carolina, is a J.D., L.L.M. candidate, class of 2009. Ms. Rogers graduated from North Carolina State University in 2002 with a BS degree in Biochemistry and a Minor in Biological Sciences, and in 2004 from North Carolina State University with a Master's Degree in Biochemistry. She is interested in pursuing a career in patent litigation and prosecution.



TODD PRATT, from Eugene, Oregon, is a J.D. candidate, class of 2009. Mr. Pratt graduated from Southern Oregon University in 2006 with a B.S. degree in Biology – Biological Sciences. As a result of his scientific background, Todd is pursuing a career in patent prosecution and litigation in the coming year.

PROFESSORS:

JON R. CAVICCHI, J.D., LL.M.
(Intellectual Property)

STANLEY P. KOWALSKI, Ph.D, J.D.