AUTM San Diego Meeting

Perspectives on Gene Patents and Licensing

A view from the trenches – industry perspective

Saturday March 1, 2008

I. Background on InVivoScribe Technologies

- A. Introduction to the Company
- B. Founding – Brief Description of Company Beginnings
- C. Focus – Range of Products and Services
- D. IVS Business and Licensing Philosophies

II. Proprietary Interests

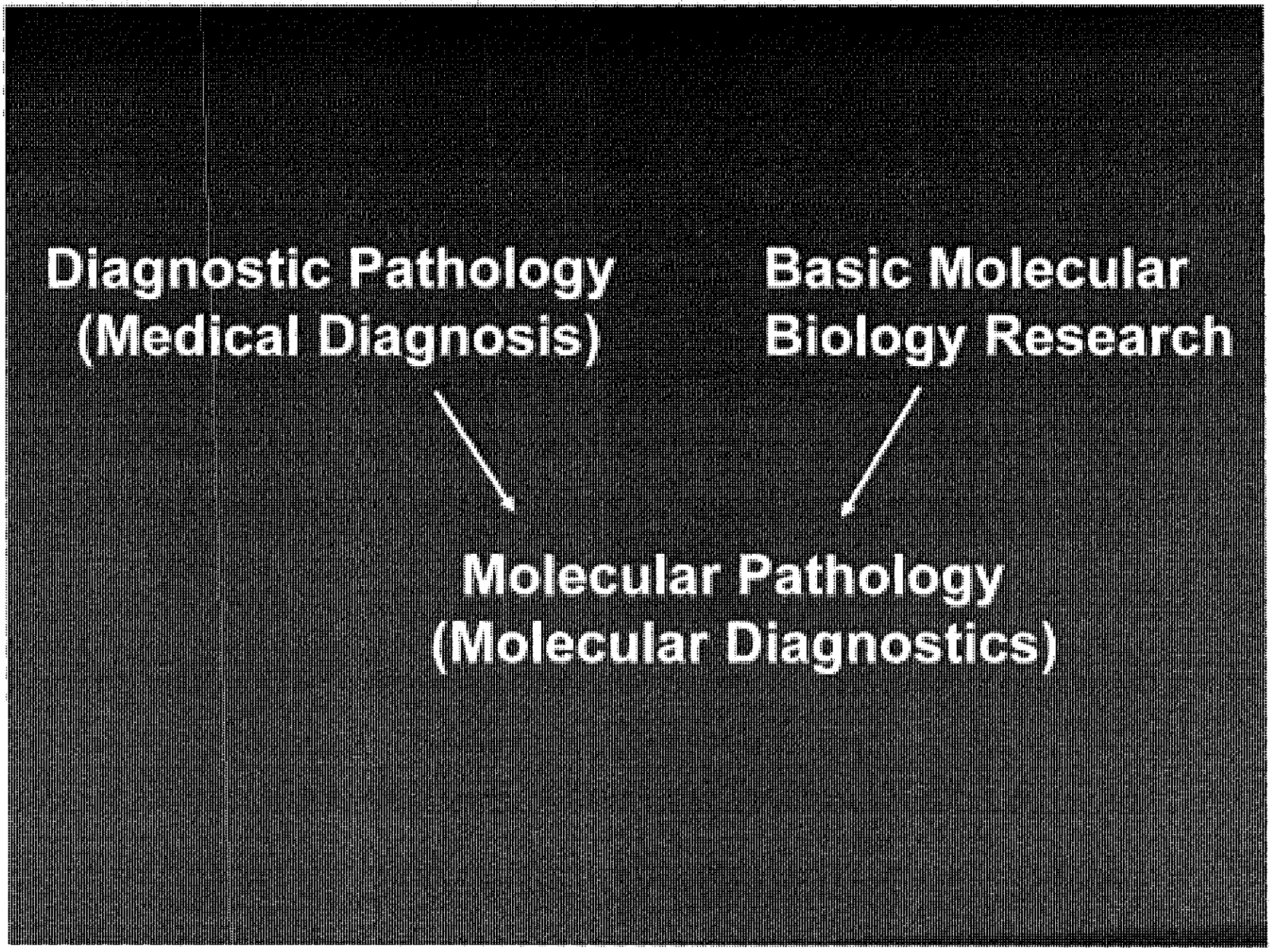
- A. Perspective on Patenting
- B. Technologies Developed In-House – Brief Descriptions
  - 1) In Vivo cDNA Synthesis Technologies
  - 2) Test Kits
- C. Technology In-Licensed – Respecting the Interests of the Patent Owner
  - 1) PCR-based testing of the Immunoglobulin and T cell Receptor Loci
  - 2) PCR-based testing of *FLT3* mutations

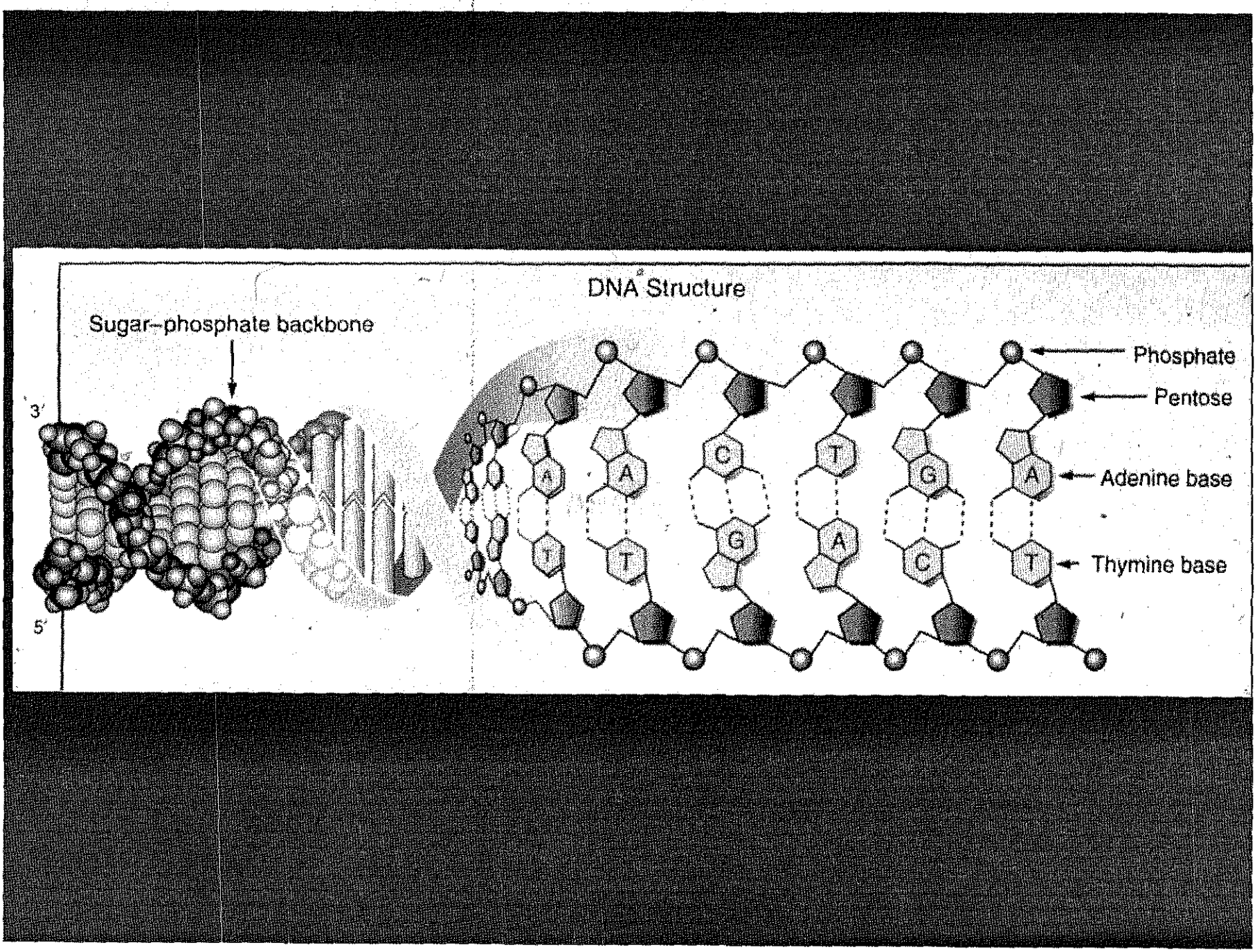
III. Technology Licensing Models

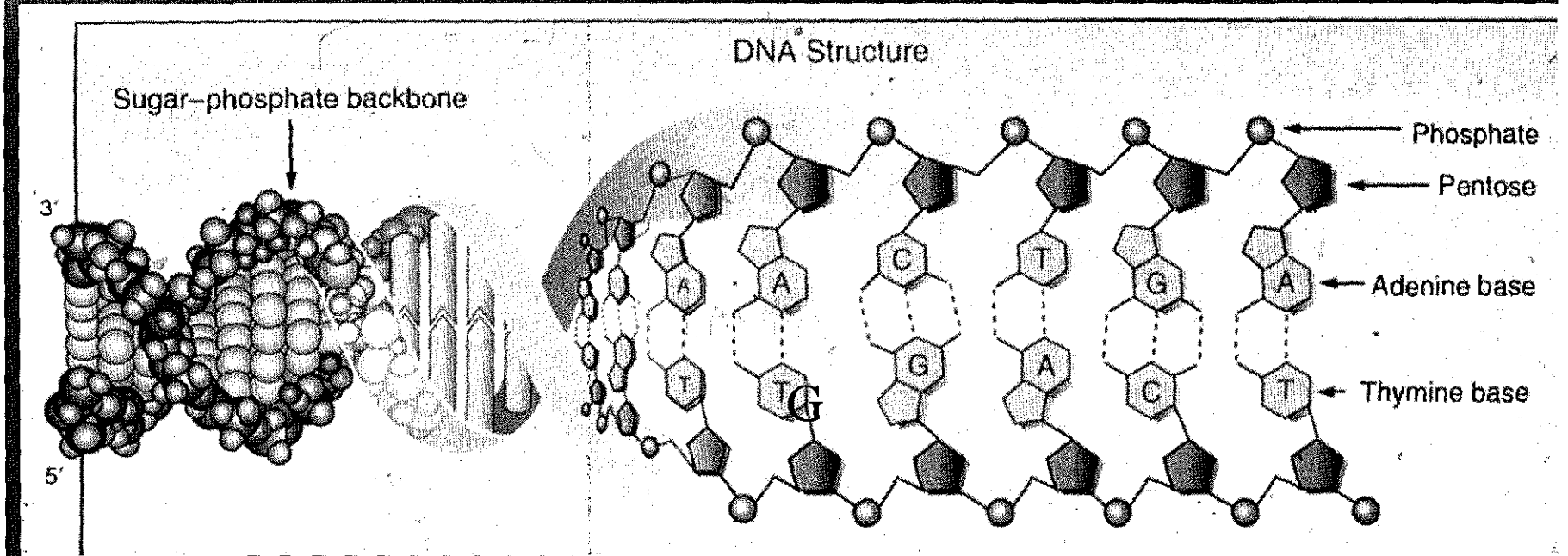
- A. Immunoglobulin and T-cell Receptor Clonality patents
- B. *FLT3* Mutation Detection patents

IV. In-House Testing

- A. PersonalMed Laboratories – Description and Range of Services


Diagnostic Pathology
(Medical Diagnosis)
Basic Molecular
Biology Research
Molecular Pathology
(Molecular Diagnostics)


DNA Structure
Sugar–phosphate backbone
3′
5′
Phosphate
Pentose
Adenine base
Thymine base
A
T
C
G
A
T
G
A
T
A
C
T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T
C
G

AREAS OF APPLICATION OF MOLECULAR PATHOLOGY

Infectious Disease
Neoplastic Disease
Genetic Disease
Identity Testing
HLA Typing
Pharmacogenetics

Board Certification in Molecular Diagnostics

(Recognized by the American Board of Medical Specialties)

AMERICAN BOARD OF MEDICAL GENETICS

Clinical Molecular Genetics

AMERICAN BOARD OF PATHOLOGY

Molecular Genetic Pathology

College of American Pathologists

Commission on Laboratory Accreditation

Inspection Checklist

MOLECULAR PATHOLOGY

Section: 12

CAP Laboratory Accreditation No: ☐☐☐☐☐☐-☐☐

Laboratory:

Section Name:

Address:

City: | State: | ZIP:

Laboratory Director:

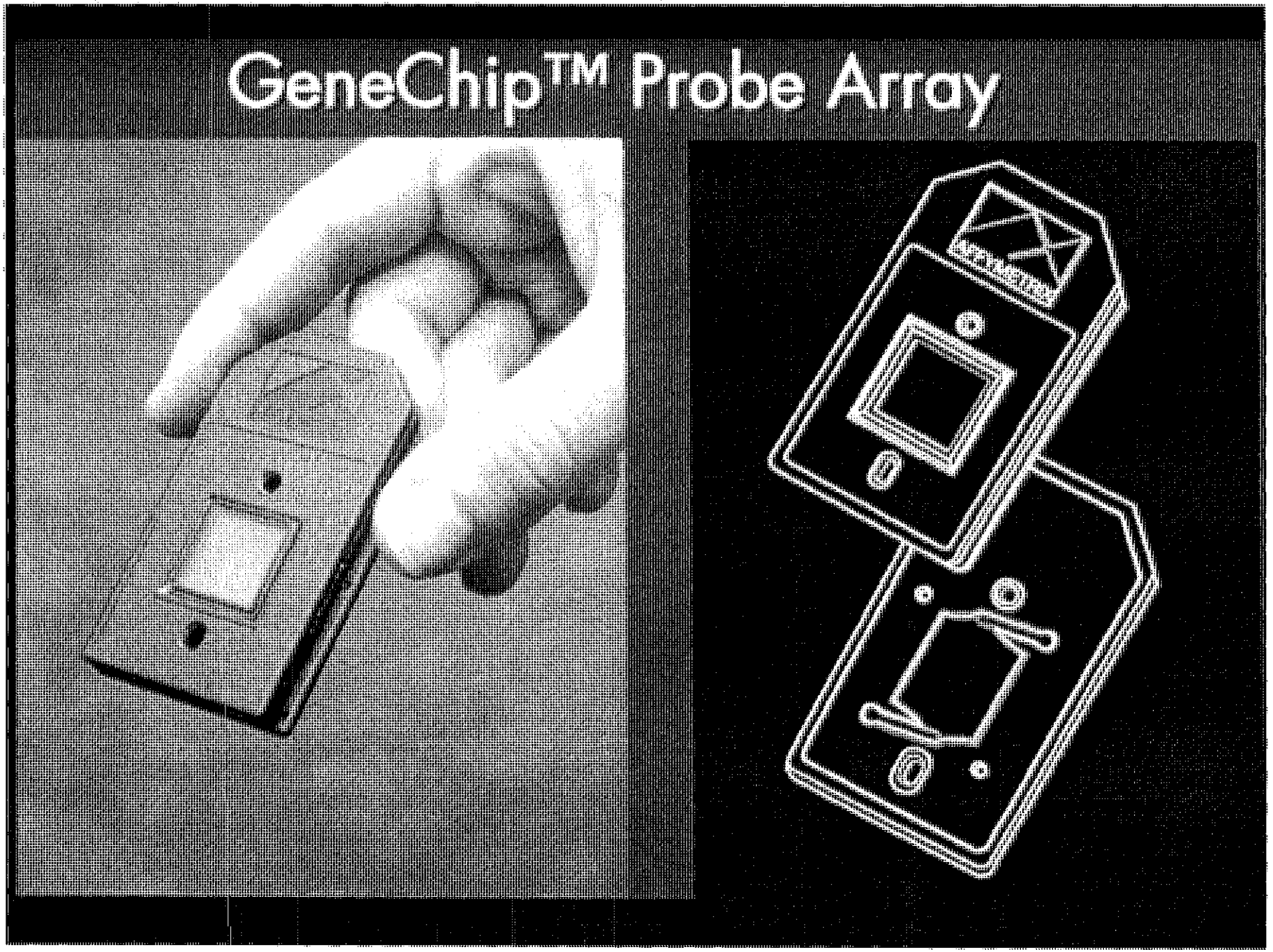
Inspector: | Inspection Date:

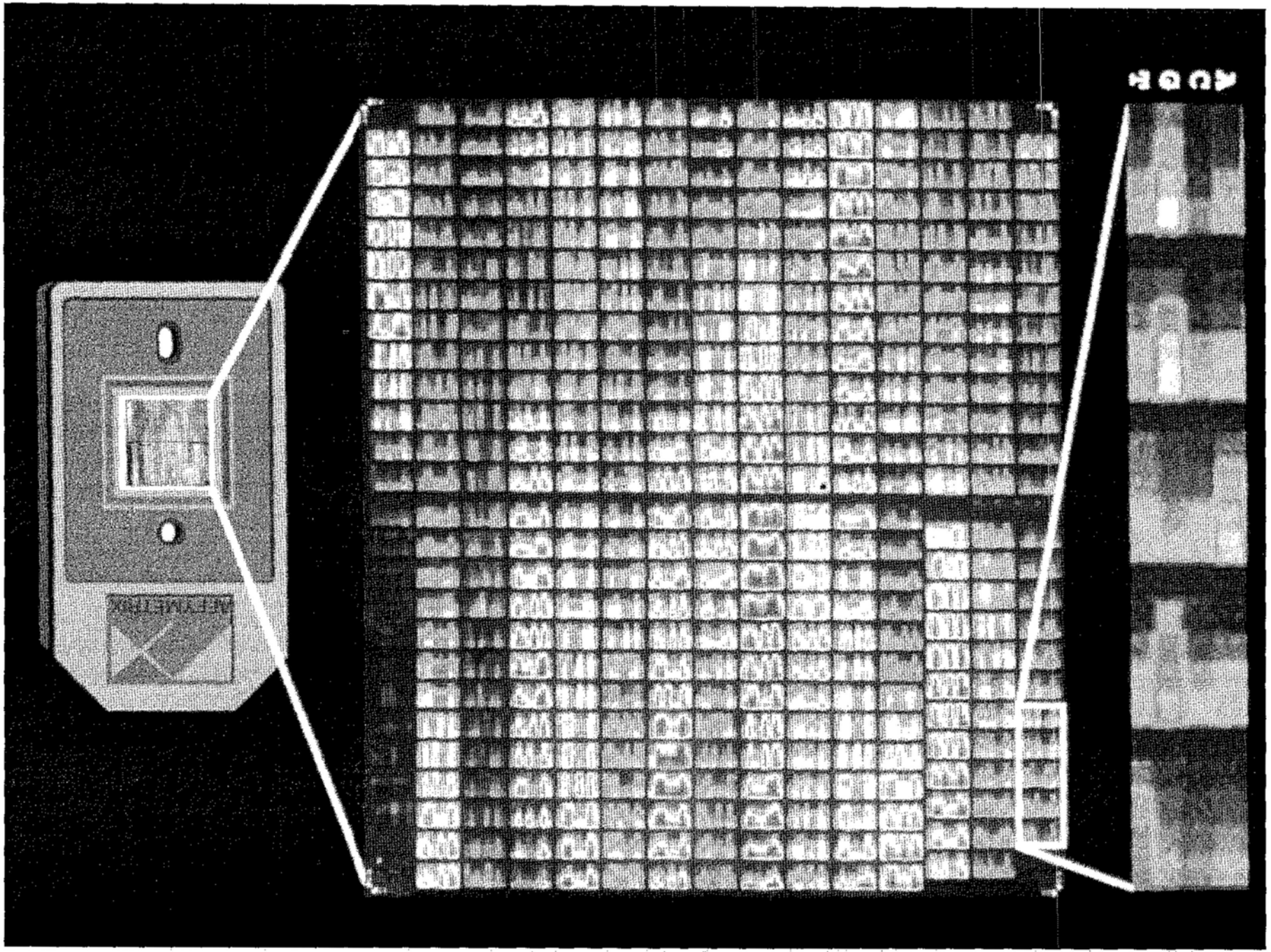
CAP Proficiency Testing Programs in Molecular Pathology

- Molecular Oncology (MO)
- In Situ Hybridization (ISH)
- Bacteria, Mycobacteria, Viruses (ID, HIV/HV2, HC5, HC6)
- Fluorescence In Situ Hybridization (CYF, CYG)
- Molecular Genetics (MGL)
- Forensic DNA Databases (DNA)
- Forensic Identity (FID)
- Parentage (PI)
- Molecular HLA-A,B,C Typing (ML)
- Molecular HLA-DR,DQ,DP Typing (DL)
- Bone Marrow Engraftment (ME)

Techniques Applied to Molecular Genetic Diagnosis

- Southern blot
- Dot blot/Reverse dot blot
- Northern blot
- Polymerase chain reaction
- SSCP/DGGE
- RT-PCR
- DNA sequencing
- TaqMan, real-time PCR
- Invader assay
- *In situ* hybridization
- Microarray hybridization


GeneChip™ Probe Array





1 array, 1 giant genomic step.

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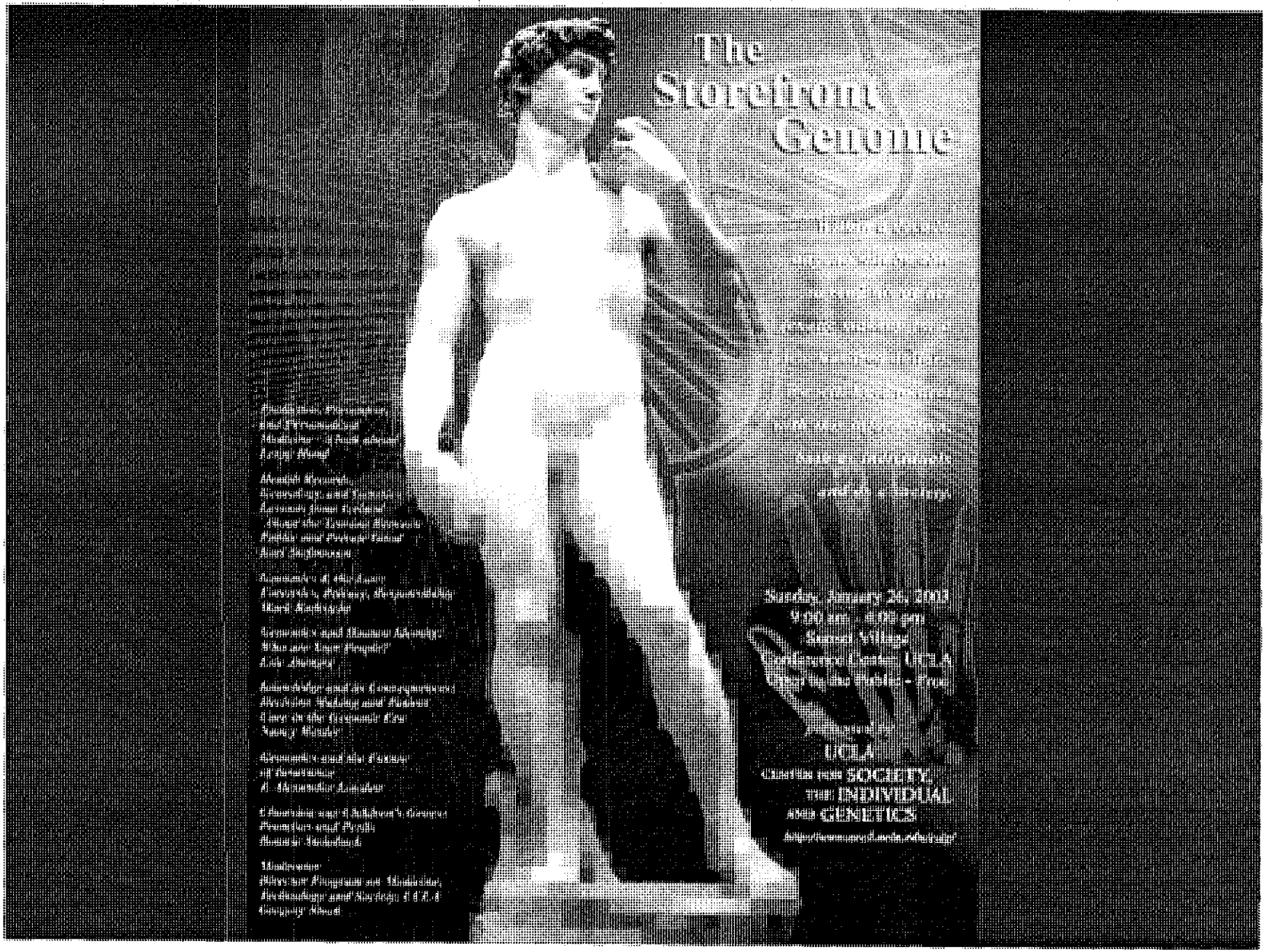
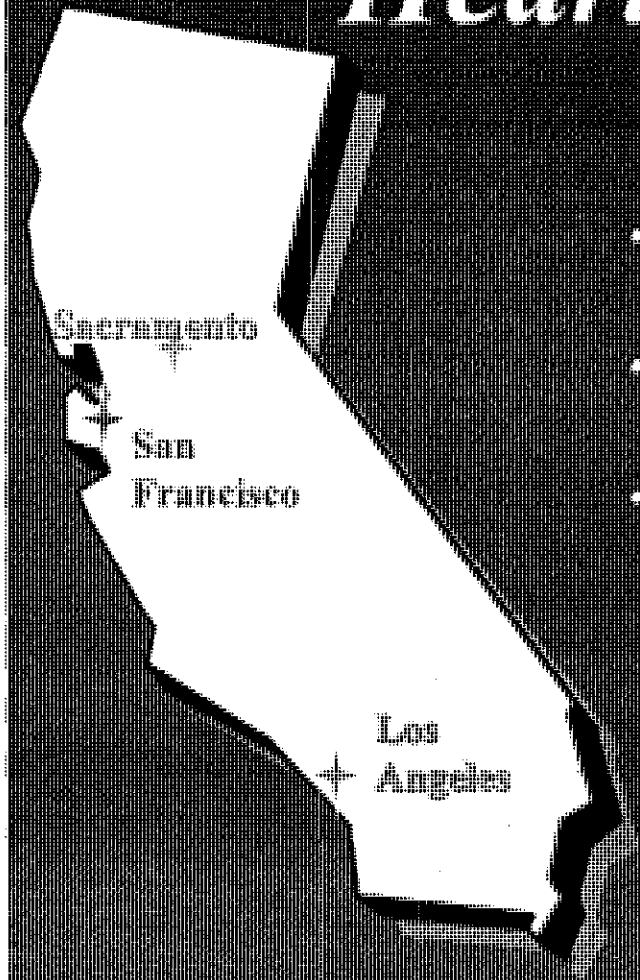

The
Stoerlotin
Genome
UCLA
SOCIETY,
INDIVIDUAL
GENETICS

"Cease and desist..."

- BCR-ABL mutations
- Spinocerebellar ataxia (types 1, 2, 3 and 6)
- Charcot-Marie-Tooth syndrome
- BRCA1&2 mutations (non-Ashkenazi)
- Hereditary hemochromatosis (home brew)
- Immunoglobulin & TCR gene rearrangements (home brew)
- Congenital hearing loss (Cnxn-26 and -30)

California Newborn Hearing Screening



- Mandated in 200 CCS-approved hospitals
- All infants screened before discharge
- 3 failed screens before referral to Audiology

Connexin-26 Sequence Variants

- Recessive mutations responsible for 50% of congenital nonsyndromic deafness
- Carrier frequency in general population is 3%

Carrier Frequencies of Common Connexin-26 Mutations

35delG	Caucasian	~1/33
167delT	Ashkenazi Jewish	~1/25
235delC	Asian	~1/100

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ACMG statement

Laboratory standards and guidelines for population-based cystic fibrosis carrier screening

Wayne W. Grody, MD, PhD[1], Garry R. Cutting, MD[2], Katherine W. Klinger, PhD[3], Carolyn Sue Richards, PhD[4], Michael S. Watson, PhD[5], and Robert J. Desnick, PhD, MD[6] (Subcommittee on Cystic Fibrosis Screening, Accreditation of Genetic Services Committee, ACMG)

RECOMMENDED CORE MUTATION PANEL FOR GENERAL POPULATION CF CARRIER SCREENING

ΔF508	ΔI507	G542X	G551D	W1282X	N1303K
R553X	621+1G>T	R117H	1717-1G>A	A455E	R560T
R1162X	G85E	R334W	R347P	711+1G>T	1898+1G>A
2184delA	1078delT	3849+10kbC>T	2789+5G>A	3659delC	1148T
3120+1G>A					

Genetic Testing Patents

- Claim covers the observation of an individual's genetic makeup at a disease-associated locus when done for diagnostic purposes
  - Includes (bars) all methods of looking at the locus
  - Permits monopolization of a medical practice
  - Permits "ownership" of a disease

Patenting of a Scientific *Concept*:

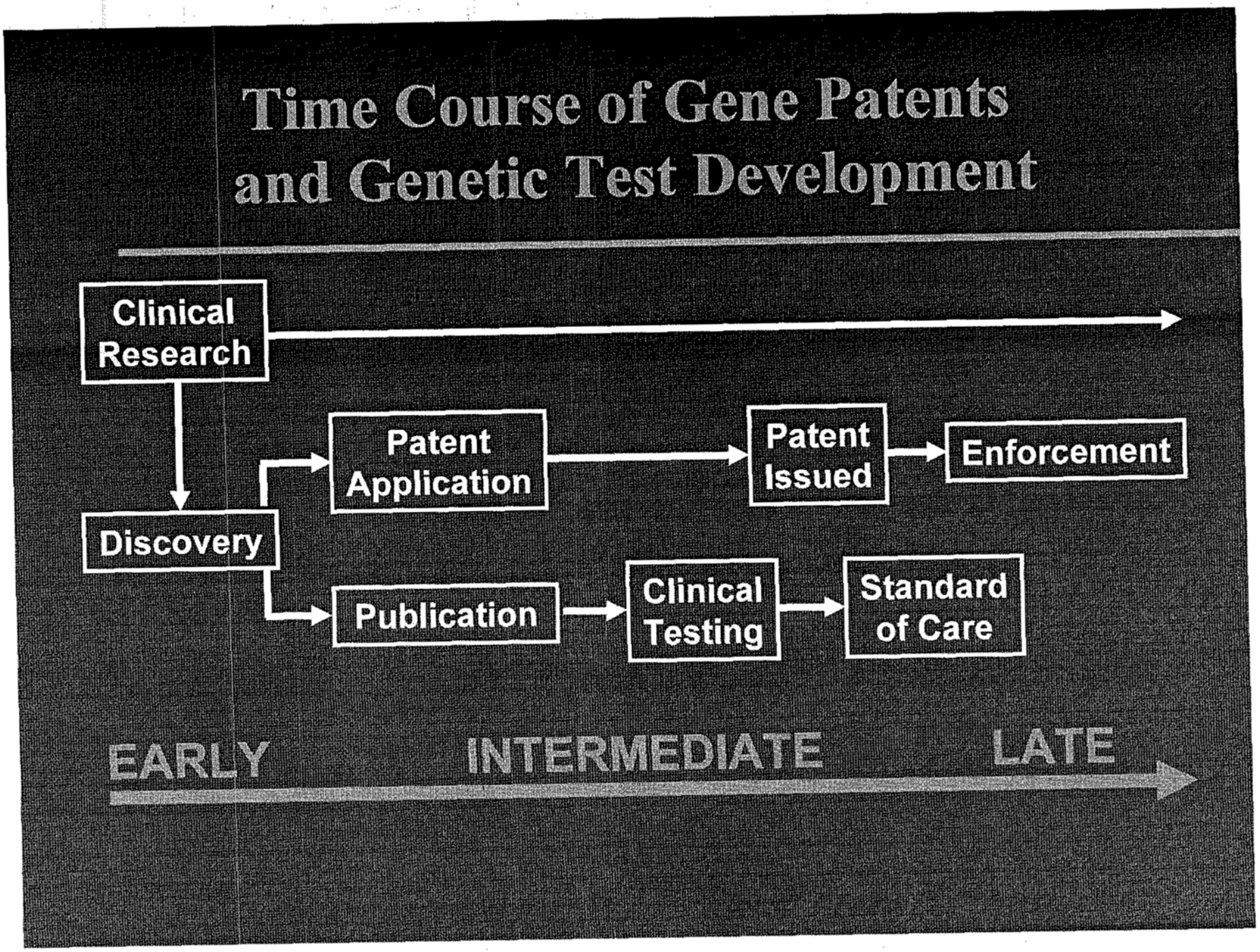
Metabolite *vs.* LabCorp

Clinical Genetic Testing is Vulnerable to Infringement

- ***Frist-Ganske Amendment*: Although diagnostic testing is the medical practice of the pathologist and geneticist, the broad protection given to medical procedures does not apply to diagnostic testing**

- ***Madey v. Duke*: Nonprofit nature of the institution not a defense**

- **Molecular diagnosticians in academic medical institutions use fundamental scientific knowledge to develop "home brew" tests and widely practice a diagnostic test before a patent is issued.**

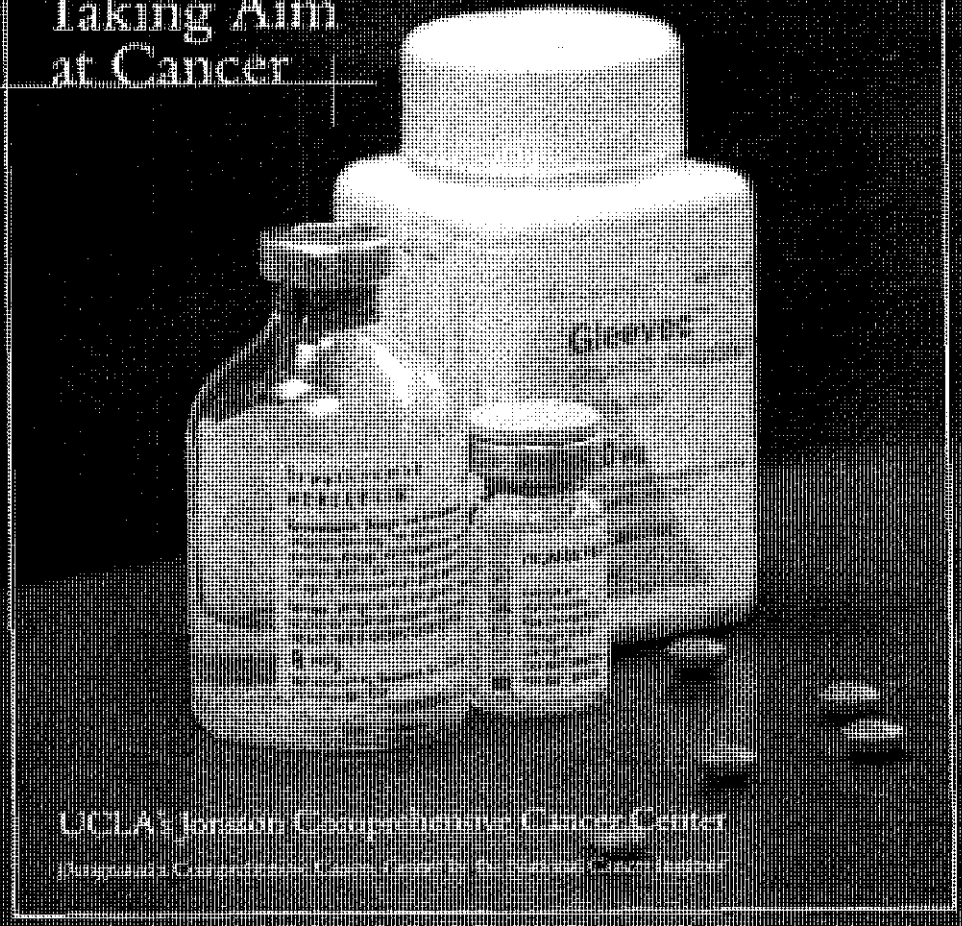

Time Course of Gene Patents and Genetic Test Development
Clinical Research
Discovery
Patent Application
Patent Issued
Enforcement
Publication
Clinical Testing
Standard of Care
EARLY
INTERMEDIATE
LATE

UCLA CANCER

Discoveries

2003–2004

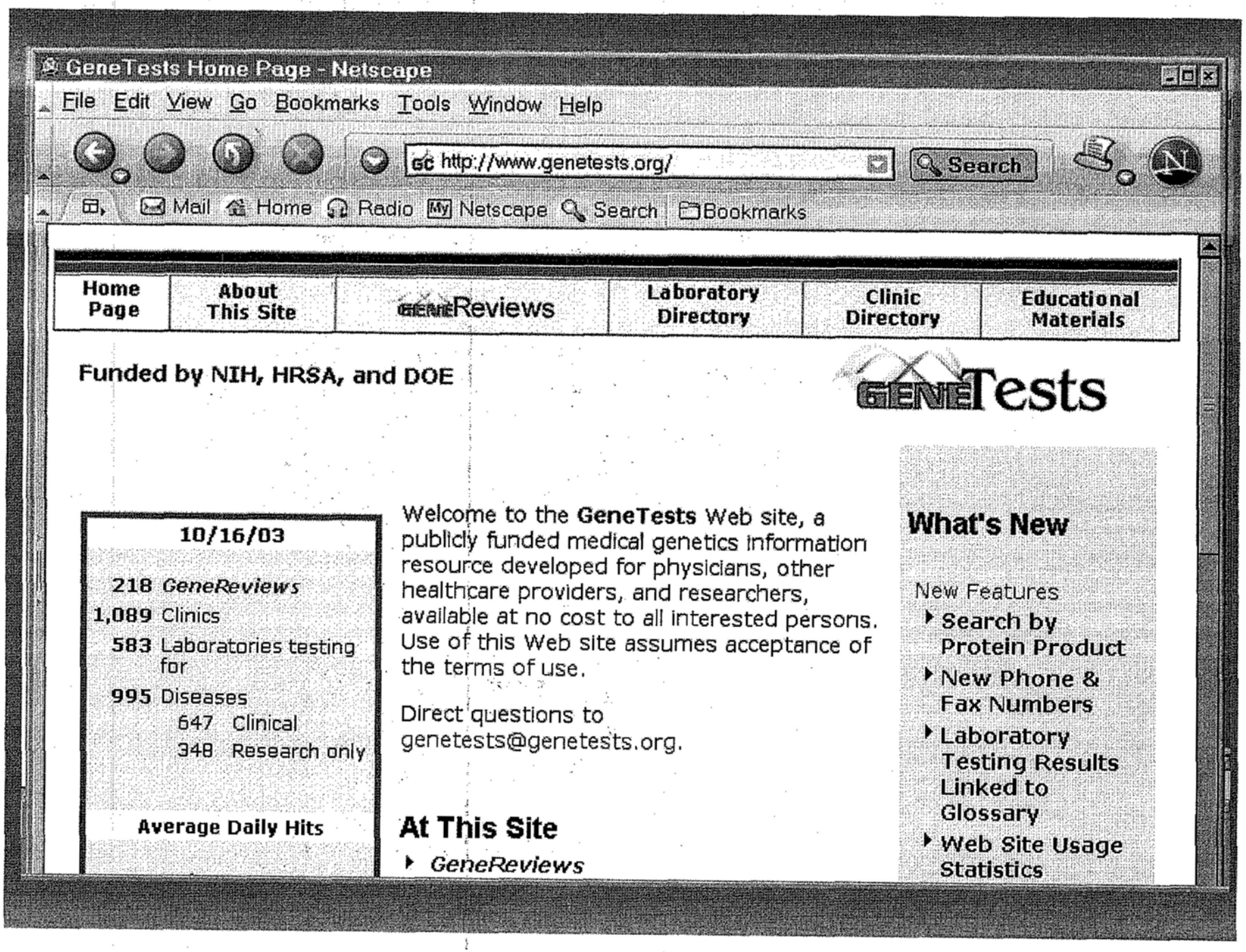
Taking Aim at Cancer



UCLA Jonsson Comprehensive Cancer Center

A Sample of Genetic Testing Patents

- 5,753,441 BRCA1
- 5,753,438 Hereditary hemochromatosis
- 5,741,645 Spinocerebellar ataxia Type 1
- 5,693,470 Non-polyposis colorectal cancer
- 5,691,144 CMT-X
- 5,686,240 Niemann-Pick disease
- 5,681,699 Ulcer. colitis and Crohn's disease
- 5,679,635 Canavan disease
- 5,670,320 Dystonia, Leber's optic neuro.
- 5,658,729 Premature atherosclerosis
- 5,654,138 Von Hippel-Lindau (VHL)
- 5,650,282 Williams syndrome
- 5,650,281 Colorectal cancer
- 5,645,995 Breast or ovarian cancer
- 5,645,993 HNLPP
- 5,639,614 Idiopathic dilated cardiomyopathy
- 5,639,607 Lead sensitivity
- 5,565,323 Sporadic Alzheimer disease
- 5,550,021 Compulsive disorder
- 5,541,060 Early-onset diabetes mellitus
- 5,518,880 XSCID
- 5,508,167 Alzheimer disease
- 5,506,101 Ototoxic deafness
- 5,500,343 Compulsive disorder (cocaine)
- 5,498,521 Retinal degenerative diseases
- 5,494,794 Alzheimer, Parkinson
- 5,492,808 Familial colon cancer (FCC)
- 5,429,923 Hypertrophic cardiomyopathy
- 5,387,506 Familial dysautonomia
- 5,374,525 Hypertension
- 5,306,616 CMT-1A
- 5,296,349 Myoclonic epilepsy
- 5,266,459 Gaucher disease
- 5,210,016 Compulsive disorder (alcohol)
- 5,045,449 Vascular aneurysms


GeneTests Home Page - Netscape
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995 Diseases
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What's New
New Features
Search by Protein Product
New Phone & Fax Numbers
Laboratory Testing Results Linked to Glossary
Web Site Usage Statistics

Gene Patent-Holder Marketing Strategies - 1

- Monopoly: exclusive licensing, single provider
  - BRCA1/2 (full sequencing)
  - Alzheimer's disease
  - Congenital hearing loss
  - Neurogenetic disorders
  - Canavan disease
  - BCR-ABL mutations

Gene Patent-Holder Marketing Strategies - 2

- Oligopoly: limited sublicensing to selected labs
  - BRCA1/2 (Ashkenazi mutation panel)
  - Hereditary hemochromatosis

Gene Patent-Holder Marketing Strategies - 3

- **Broad licensing: Nonexclusive royalty-bearing sublicenses to all labs that perform test**
  - **Cystic fibrosis (?)**
  - **Immunoglobulin gene rearrangements in lymphomas**
  - **Short tandem repeat polymorphisms**
  - ***All noncoding sequences (?)***

Impact on Healthcare

- Limited access and noncompetitive pricing
- Increased healthcare costs
- Lack of peer review and comparison
- Hampered quality assurance
- Potential undetected systematic errors
- Interference with medical training
- Restricted opportunity and incentive for test improvements and advancement of the field

Impact on Research

- Diagnostic test development is dependent upon clinical research and service
- Clinical research and service often admixed
  - Generation of mutation databases
  - Study of genotype-phenotype correlations
- Therapeutic research also impeded (development of drugs or gene therapy based on the gene sequence)
- *Madey v. Duke*: even noncommercial research may be restricted

Potential Solutions

- "Best Practices" to encourage dissemination of publicly funded enabling technologies
- Nonexclusive licensing
- Consortia, patent pools
- Expand *Frist-Ganske* to explicitly include diagnostic testing in the broad protection provided to medical procedures
- Consider compulsory sublicenses for public health imperatives
- Reasonable royalty rates for direct patient care applications

Why should a gene be patented, anyway?

PATENT CRITERIA

Originality
Utility
Non-obviousness
Created by the hand of man