United States District Court,
D. Massachusetts.

PIECZENIK and I.C,
v.
DYAX CORP.

No. CIV.A. 00-11370-RGS

Sept. 18, 2002.

Owner of patent for identification and production of monoclonal antibodies sued competitor for infringement. Construing claims, the District Court, Stearns, J., held that: (1) patent called for creation of peptide library of given size, and (2) "oligonucleotide" was compound created by condensation of typically fewer than 20 nucleotides.

Claims construed.

5,866,363. Construed.

Michael A. Nicodema, Morgan & Finnegan, New York, NY, Thomas J. Gallitano, Michael T. Sullivan, Conn, Kavanaugh, Rosenthal, Peisch & Ford, Boston, MA, Neil V. McKittrick, Hill & Barlow, A Professional Corp., Boston, MA, Barry Schindler, Dreier & Baritz LLP, New York, NY, for George Pieczenik, Plaintiff.

James F. Haley, Christopher J. Harnett, Robert B. Wilson, Lynnette Noblitt, Fish & Neave, New York, NY, Hallie Kostrinsky, Fish & Neave, New York, NY, Christine M. Roach, Roach & Carpenter, P.C., Boston, for Dyax Corporation, Defendant.

MEMORANDUM AND ORDER

STEARNS**, District Judge.**

This decision follows a hearing held under the directives of Markman v. Westview Instruments, Inc., 517 U.S. 370, 116 S.Ct. 1384, 134 L.Ed.2d 577 (1996). " *Markman* requires a trial judge in a patent case to construe and define the contested claims of a patent. The task committedto the judge is to explain what the protected invention is, and sometimes what it is not, ideally in language that will be accessible to a lay jury." Biogen, Inc. v. Amgen, Inc., 18 F.Supp.2d 105, 106 (D.Mass.1998).

As described by the inventor, Dr. George Pieczenik:

[t]he invention provides an efficient and convenient means for the identification and production of

monoclonal antibodies to any specific region of any antigen or hapten of interest. Monoclonal antibody production, according to the invention, does not require antigenic stimulation of a host animal. This is a critical concept of the present invention. Such antigenic stimulation can be employed to increase the frequency for cognate hybridoma formation, but there will be a member of an antibody population (of a sufficiently large number of members) which will recognize the particular epitope even in the absence of such stimulation.

The invention involves the antibody binding properties of a test species, e.g., a peptide, but is totally independent of the ability of the test species to induce an antigenic response in vivo. The invention permits the identification of the specific peptide sequence on a protein that is recognized by an antibody, i.e., the epitope. The specificity of antibodies recognizing distinct sequences, or epitopes, on the same antigen can be differentiated. In addition, the invention permits the characterization and the localization on a chromosome of the nucleotide sequence encoding the amino acid sequence recognized by an antibody.

'363 Patent, Col. 5, Ins. 29-50.

The utility of the invention, according to plaintiffs, derives from its "library" of peptide sequences, which allows an "antibody binding specificity to be determined without previous knowledge of antigenic sequences," and its recognition "that the size of the bindable universe (epitopic) and binding universe (antibody) is limited and thus can be enumerated, recognized and synthesized." Plaintiffs' Response, at 1. FN1 The invention has practical application in the development of pharmaceutical products like vaccines. The principal patent in dispute, U.S. Patent No. 5,866,363 (the '363 patent), "Method and Means for Sorting and Identifying Biological Information," contains two partially disputed independent claims, numbered 24 and 34. FN2

FN1. There were two rounds of briefing, which are designated in this Memorandum as Plaintiffs' Brief, Dyax Brief, Plaintiffs' Response, and Dyax Reply.

FN2. The '363 patent is a continuation-in-part of two earlier applications, the earliest of which was filed on August 28, 1985. Both of the earlier applications were ultimately abandoned.

The Disputed Claims

Claim 24 describes a "population of recombinant vectors" containing oligonucleotides that encode a population of peptides. It reads as follows:

24. A population of recombinant vectors comprising:

substantially identical autonomously replicating nucleic acid sequences comprising a recombinant structural gene, each structural gene having inserted therein a member of an oligonucleotide population, wherein each member of said oligonucleotide population has a coding region having a length from about 4 to about 12 nucleotide triplets that encodes a corresponding peptide sequence of from about 4 to about 12 L-amino acid residues, and wherein the sum of correspondingpeptide sequences encoded by said oligonucleotide population represents at least about 10% of all possible peptide sequences of said length,

and wherein each member of said oligonucleotide population is contained in said recombinant vector population; and

wherein the recombinant structural genes are expressed upon transfer of said recombinant vectors into *Escherichia coli* host cells, and wherein expression of said recombinant structural genes yields polypeptides, each polypeptide comprising said corresponding peptide sequence.

Claim 34 describes a method of producing the population of peptides described in claim 24. It reads as follows:

34. A method of producing a population of epitopic peptide sequences, comprising of the steps of:

providing a population of recombinant *E. coli* cells, each of said cells containing at least one member of a recombinant vector population, each member of said vector population comprising substantially identical autonomously replicating nucleic acid sequences, said nucleic acid sequences comprising a recombinant structural gene, each structural gene having inserted therein one member of an oligonucleotide population wherein each member of said oligonucleotide population has a length from about 4 to about 12 nucleotide triplets that encodes a corresponding epitopic peptide sequence of from about 4 to about 12 L-amino acid residues, and wherein each member of said oligonucleotide population is contained in said recombinant vector population and wherein the sum of said corresponding epitopic peptide sequences represents at least about 10% of all possible peptide sequences of said length; and

culturing said recombinant *E. coli* cells to allow expression of said recombinant structural genes such that said epitopic peptide sequences are accessible to antibody recognition.

The *Markman* dispute focuses on the proper construction of the following language in claim 24:

wherein each member of said oligonucleotide population has a coding region having a length from about 4 to about 12 nucleotide triplets that encodes a corresponding peptide sequence of from about 4 to about 12 L-amino acid residues, and wherein the sum of corresponding peptide sequences encoded by said oligonucleotide population represents at least about 10% of all possible peptide sequences of said length[.]

The parties also dispute the meaning of nearly identical language in claim 34:

wherein each member of said oligonucleotide population has a length from about 4 to about 12 nucleotide triplets that encodes a corresponding epitopic peptide sequence of from about 4 to about 12 L-amino acid residues, and wherein each member of said oligonucleotide population is contained in said recombinant vector population and wherein the sum of said corresponding epitopic peptide sequences represents at least about 10% of all possible peptide sequences of said length[.]

Finally, the parties disagree over the proper definition of the term "oligonucleotide," as it is used in the claims of the '363 patent (and in two prior related patents).

Legal Principles

[1] [2] "[C]onstruction of a patent claim is a matter of law exclusively for the court." Markman v. Westview Instruments, Inc., 52 F.3d 967, 977 (Fed.Cir.1995) (citations omitted). "[A]n inventor is not [ordinarily]

competent to construe patent claims" because "it is not unusual for there to be a significant difference between what the inventor thinks his patented invention is and what the ultimate scope of the claims is after allowance by the PTO." Solomon v. Kimberly-Clark Corp., 216 F.3d 1372, 1380 (Fed.Cir.2000). Thus, in construing the claims of the patent, the court must adopt the perspective of a hypothetical practitioner of ordinary skill in the patent art as of the date of the original application. Wiener v. NEC Electronics, Inc., 102 F.3d 534, 539 (Fed.Cir.1996), overruled on other grounds by Cybor Corp. v. FAS Technologies, Inc., 138 F.3d 1448 (Fed.Cir.1998).

[3] The hierarchy of accepted analytical tools requires a court to begin its analysis with the intrinsic evidence of record. A court should first "look to the words of the claims themselves, both asserted and nonasserted, to define the scope of the patented invention." Vitronics Corp. v. Conceptronic, Inc., 90 F.3d 1576, 1582 (Fed.Cir.1996), citing Bell Communications Research, Inc. v. Vitalink Communications Corp., 55 F.3d 615, 620 (Fed.Cir.1995). The court should next look to the patent specification. "The specification contains a written description of the invention which must be clear and complete enough to enable those of ordinary skill in the art to make it and use it. Thus, the specification is always highly relevant to the claim construction analysis. Usually, it is dispositive; it is the single best guide to the meaning of a disputed term." Vitronics, 90 F.3d at 1582. Finally, the prosecution history of the patent may be consulted. "[T]he record before the Patent and Trademark Office is often of critical significance in determining the meaning of the claims," Vitronics, 90 F.3d at 1582, but "it too cannot 'enlarge, diminish, or vary' the limitations in the claims." Markman, 52 F.3d at 980.

The claims, specifications and file history constitute the patent's "public record ... on which the public is entitled to rely." Vitronics, 90 F.3d at 1583. Thus, it is inappropriate for a court to consider extrinsic evidence, such as expert testimony, unless the testimony is necessary to understand the meaning or scope of a technical term in the claims. *Id.,* citing Pall Corp. v. Micron Separations, Inc., 66 F.3d 1211, 1216 (Fed.Cir.1995); Markman, 52 F.3d at 980-981 (same). Expert testimony "may not be used to vary or contradict the claim language...." Nor may it contradict the import of other parts of the specification. Vitronics, 90 F.3d at 1584 (citation omitted). "[W]here the public record unambiguously describes the scope of the patented invention, reliance on any extrinsic evidence is improper." Id., at 1583.

Discussion

The Competing Constructions

(a) "from about 4 to about 12 [nucleotide triplets] [L-amino acid residues]"

Plaintiffs construe this limitation, which is common to both claims, as encompassing lengths of from 3 to 13 *random* triplets. FN3 Plaintiffs' argument focuses on the word "about" and its "clear warning" that exactitude is not being claimed. Plaintiffs' Response, at 5. Dyax's counter-construction centers on the consistent use by the patentee of the definite integers 4 and 12. "Nowhere in the specification did the patentee say that any integer within the range should be afforded anything other than its ordinary accustomed meaning. Indeed, in the specification, when the patentee wished to refer to an amino acid sequence of length 12, he used the number 12; when he wished to refer to a length of 7 amino acids he used the number 7; and when he wished to refer to a 5 amino acid sequence, he used the number 5." Dyax Brief, at 19. Thus, according to Dyax, "from about 4 to about 12" means from 4 to 12. FN4

FN3. Dyax disputes any requirement that the triplets be random. The limitation that the oligonucleotide sequences (or the corresponding peptide sequences) be "random" appears nowhere in the language of the disputed claims, although it does appear in a number of other claims of the patent. As plaintiffs acknowledge, courts should normally not introduce into a claim by interpretation "limitations that are explicitly contained in other claims." Caterpillar Tractor Co. v. Berco, S.p.A., 714 F.2d 1110, 1116 (Fed.Cir.1983).

FN4. Dyax does not address the significance of the term "about" because of what I believe is a mistaken premise that the meaning of words of qualification has no relevance to a "literal" *Markman* construction, but "is more properly an issue relating to the availability or nonavailability of the doctrine of equivalents." Dyax Brief, at 25-26 n.* *. On this point, plaintiffs are correct that "[a]ll the limitations of a claim must be considered meaningful," Unique Concepts, Inc. v. Brown, 939 F.2d 1558, 1562 (Fed.Cir.1991), a principle of claims construction that Dyax elsewhere acknowledges in its brief.

(b) "and wherein the sum of [corresponding peptide sequences] [claim 24] [said corresponding epitopic peptide sequences] [claim 34] [encoded by said oligonucleotide population] [claim 24] represents at least about 10% of all possible peptide sequences of said length"

While written slightly differently in the two claims, this limitation refers to the size of the peptide library needed to make the invention work. Plaintiffs offer no consistent construction of what is meant by "about 10% of all possible peptide sequences," but suggest that "10%" can consist of: (1) 300,000 (or perhaps 30,000) distinct members for any coded library of random peptides with a length in the range of 5 to 13 amino acid residues; (2) 16,000 (or perhaps 1,600) distinct members for any coded library of random peptides with a length of 4 amino acid residues; and (3) 80 (or perhaps 800) distinct members for any coded library of random peptides with a length of 3 amino acid residues.FN5 Plaintiffs' Brief, at 11, 16. The limitation "all possible peptide sequences of said length" plaintiffs construe to mean "the complete range of possible epitopic peptide sequences ... within the range of 3 to 13 L-amino acid residues consistent with the means by which the 'oligonucleotide population' was generated." *Id.,* at 11.

FN5. The suggested population figure of 80 tripeptides may be a mathematical error. It is possible that plaintiffs meant 800 rather than 80 as $20^{3}/10 = 800$. Plaintiffs' calculations for populations of tetrapeptides and pentapeptides are largely faithful to the formula $0.10 \times L = 20^{L}/10$, reporting the accurate result of $20^{4}/10 = 16{,}000$ for tetrapeptides, and the approximately accurate result of $20^{5}/10 = 300{,}000$ for pentapeptides. Nonetheless, the parentheticals following the two calculations (suggesting the figures of 1,600 and 30,000 respectively) are consistent with the assertion that 10% in fact means 1%.

According to Dyax, the 10% limitation requires that the total of the peptide sequences encoded by the oligonucleotide population encompass at least 10% of the possible peptide sequences of a single given length within the range of from 4 to 12 L-amino acids. "All possible peptide sequences of said length," Dyax construes to mean the number of sequences derived by the formula $L = 20^{L}$ where ^{L} represents the given length within the specified range of L-amino acid residues and 20 signifies the number of genetically encodeable amino acids. Thus, if L is 12, the possible number of sequences is 20^{12} or 4.096×10^{15}, which when divided by 10 yields a library of 4.096×10^{14} members. Dyax Brief, at 13-14.

Analysis

The parties' dispute boils down to a basic difference in interpretation that plaintiffs accurately summarize as follows: "Dyax argues that [infringement] should be determined from the perspective of the size of the peptide library made, whereas plaintiffs' position is that infringement is determined by the size of the peptide library necessary to bind the desired target." Plaintiffs' Response, at 2. Plaintiffs, in other words, maintain that as Dr. Pieczenik refined his invention, he realized that "five amino acids [the pentapeptide] is a *representative length* of peptide sequences which can bind with differential specificity to an antibody." Plaintiffs' Brief, at 14 (emphasis in original). Moreover, "antibodies are *now known* to have specificities which can be competed by peptides in the range of 5-7 amino acids, with a mean in the range of around 5 amino acids." Plaintiffs' Response, at 10 (emphasis added). Thus, "the entire universe of antibodies is equivalent to the entire universe of epitopic peptides that are 5 amino acids long on average or 3.2×10^{6} possible antibodies." Plaintiffs' Brief, at 15. Because "many of the encoded peptides will present sufficiently similar binding surfaces that a single antibody will react with any of them .... it is not necessary to have all, or even most, of the possible coding sequences represented." *Id.,* at 15 (quoting from File History, at 202). In fact, "all possible antibodies will be found to bind specifically with one of the mixture of random peptides provided a) the peptides are 5-7 amino acid residues in length, and b) the mixture contains at least about 10% of all possible peptide sequences." *Id*. (quoting File History, at 200). Therefore a library of "about" 300,000 members is all that is required to identify the "universe" of possible antibody binding sites. *Id*.

This assertion is the crux of the dispute about the necessary size of the specified library because, as a matter of undisputed scientific fact, there are 20 naturally occurring amino acids. Thus, where the peptide length consists of 5 amino acid residues, the possible number of peptides is 20^{5}, or more conventionally stated, 3.2×10^{6}. Where, however, the length is 12 amino acid residues, the possible number of peptides is 20^{12} or 4.096×10^{15}. It follows that a library containing 10% of all *possible* peptide sequences where the length is 12 would contain 4.096×10^{14} members, as Dr. Pieczenik himself pointed out to the PTO in correcting the examiner's assumption that the correct formula for calculating the possible number of peptide sequences where L is 12 is the inverse of 20^{12}, or 12^{20}. In traversing the examiner's rejection, Dr. Pieczenik gave the following example. "For a peptide having a sequence length of 12 (L = 12), each position having an equal probability of being one of the 20 natural amino acids (N = 20), the number of possible sequences is $N^{L} = 20^{12}$, which can be converted to 4.1×10^{15}." Dyax Brief, at 21 (quoting File History, at 734). He went on to point out that the examiner's method resulted in a million-fold error on the high side. *Id*. (quoting File History, at 735).FN6 The point is crucial because, as Dyax points out, "the peptides in [its] libraries are longer than 12 amino acids-indeed, some are longer than 60 amino acids. And, Dyax's phage display libraries include far fewer than 10% of the possible peptide sequences for a selected peptide length." Dyax Brief, at 9. A library of 300,000 members would represent but 0.0000000073% of the *possible* number of sequences where L is 12, when the formula advocated by Dyax and used by Dr. Pieczenik in his illustration to the PTO is applied. *See* Table, Dyax Reply, at 5. None of the corresponding percentages for lengths 6 to 13, which range from 0.47% (6) to 0.00000000037% (13), could ever reasonably thought to be "about 10%," no matter how flexibly the limitation is to be read. It is therefore critical to an understanding of plaintiffs' position to trace the elements of the argument that the "said" in the phrase "all possible peptide sequences of said length," refers to pentapeptides.

FN6. Plaintiffs maintain that Dr. Pieczenik was taken out of context and was referring to the correct method

of calculating the number of theoretically possible sequences and not the number of sequences that are biochemically possible. Plaintiffs' Response, at 13-14. This distinction, however, appears nowhere in the exchange with the examiner.

To the extent that plaintiffs' argument is based on the actual language of claims 24 and 34, it rests on the supposed difference between the meaning of "selected length" (the term used in the antecedent application) and the term "said length" (the term ultimately chosen). "Whereas *selected* refers to the random length selected *a priori, said* refers to the length of the random peptide sequence that, for example, ***binds*** to an antibody." FN7 Plaintiffs' Response, at 8 (emphasis in original). This semantic change, plaintiffs argue, would have alerted an attentive reader of ordinary skill in the art, familiar with the "scientific presumption" that "antibodies are now known to have specificities which can be competed by peptides in the range of 5-7 amino acids, with a mean in the range of around 5 amino acids," to the fact that a pentapeptide library is sufficient to define all peptide sequences with lengths from 6 to 13 amino acid residues. *Id.,* at 10. In other words, a library of 300,000 distinct figures (roughly 10% of 3.2×10^6) would completely satisfy the 10% limitation in the claims. "Said" is a term used by patent drafters who (like many lawyers) are unexplainably uncomfortable with using the more colloquial "the" when referring back to previously recited claim elements. *See Landis on Mechanics of Patent Claim Drafting* (2001) s. 23. Neither claim 24 nor claim 34 makes any antecedent reference to pentapeptides as the sequence defining the "said" length. The element referenced is rather " *a* length from about 4 to about 12 nucleotide triplets," that is, one of 9 (or 10) designated lengths with its corresponding peptide sequence. Pentapeptides are certainly one of these lengths, but not the only length referenced. The claims language, in other words, simply will not support the load bearing weight plaintiffs attempt to assign to the word "said."

FN7. As Dyax points out, this assertion contradicts the specification of the patent, which teaches that "the invention features a discrete recombinant vector population of substantially identical autonomously replicating nucleic acid sequences including a structural gene and a population of oligonucleotide inserts therein, each insert containing a uniform length *selected* from between about 4 to about 12 nucleic acid coding triplets, preferably between 4 and 7, and most preferably five. '393 patent, Col. 4, Ins. 19-27 (emphasis added)".

Plaintiffs' prosecution file history and prior art arguments fare no better. Much emphasis is placed on the qualified disclosure in the original 1985 application that

the size of the antibody recognition site corresponds to a peptide sequence in the range of between about 4 and about 12 amino acid residues ... [and that] there are about three million (20^5) different possible sequences of the twenty amino acid residues taken five at a time and about sixty million if the amino acid residues are taken six at a time. This finite number of peptide sequences may represent the full range of possible antibody recognition sites. Production and maintenance of a representative sample of the peptide sequences of the appropriate length provides the means (1) to screen any antibody of interest in order to determine the precise peptide sequence it binds to ....

Plaintiffs' Brief, at 12 (quoting File History, at 14-15).FN8 From this, plaintiffs deduce that it would have been "clear" to one skilled in the art that the inventor had "recognized that random pentapeptides can adequately represent any random 12 amino acid sequence in terms of competitive binding to antibodies." *Id.,* at 12-13. Why this is so is not explained in any meaningful way, other than by random citations to the

discussion of the prior art in the original 1985 patent application, which when read in context, offer no support for plaintiffs' late blooming theory that the '363 patent teaches a universe of antibody binding sites bounded by pentapeptides. The citation to Geyson, *et al.,* in the file history is a good example. It is clear in context that Geyson was cited to explain to the PTO why degeneracy (the phenomenon by which an antibody may recognize more than one peptide sequence) made it possible to construct a working population consisting of only 10% of the peptides of a given length rather than, as the examiner thought would be necessary, the entire peptide population associated with that length. It does not follow from the discussion of Geyson (or Dame, *et al.,* the other principal prior art source cited) that the "prosecution file history make[s] clear to one skilled in the art that any coded library of random peptides with [a] length in the range of 5-13 amino acid residues and containing at least about 300,000 (e.g. 30,000 = 1%) distinct members is understood to mean an oligonucleotides population that *represents at least about 10% of all possible peptide sequences of said length*." Plaintiffs' Brief, at 15-16 (emphasis in original).

FN8. As Dyax argues, the assertion that the range of 3 to 60 million peptides represents the universe of possible antibody recognition sites ignores antibodies that bind conformationally dependent epitopes "for which pentapeptides and hexapeptides cannot successfully compete in many circumstances." Dyax Brief, at 25 n*. According to Dyax, when these are considered the number of possible antibody recognition sites "far exceeds" the 3 to million figure posited by Dr. Pieczenik. Even if the 3 to 60 million figure is correct, plaintiffs do not explain why the absolute bottom of that range represents the operative number of desired peptides.

Conclusion

[4] [5] The limitation establishing a library of peptide sequences representing "at least about 10% of all possible peptide sequences" of "from about 4 to about 12 L-amino acid residues" has one definite term-"all possible"-and two indefinite terms-"at least about 10%" and "from about 4 to about 12." There is no indication in the patent specification that Dr. Pieczenik intended these phrases to convey any meaning other than their ordinary English connotation. Thus, "all possible" can only be understood to mean the universe of peptide sequences associated with L-amino acid lengths of "from about 4 to about 12." While I agree with plaintiffs that the term "about" is a term of deliberate imprecision that might fairly capture the integers 3 and 13 at the boundaries of "from about 4 to about 12," the term "all possible" can only mean in context the entire universe of what could occur, that is, the total number of naturally occurring sequences that can possibly be associated with the selected length, whether 20^{3} or 20^{13} or some other specified length within the asserted range of 3 to 13 amino acid residues. In similar fashion, in the interest of lexicographic consistency, "at least about 10%" can be understood to perhaps capture 9%, or given the qualification of "at least about 10%," perhaps a number substantially above 10%, but certainly not 1%, as plaintiffs' expert, Dr. Makowski, maintains. FN9

FN9. That the phrase "at least about 10%" means "more than at least 1%" was the position taken by Dr. Makowski in his deposition. It is not clear from the briefs whether plaintiffs continue to support Dr. Makowski on this point, or whether even Dr. Makowski believes that the 1% figure is supported by the patent. *See* Dyax Brief, at 29; Plaintiffs' Response, at 14.

As Dyax points out, plaintiffs' redefinition of the universe of antibody binding diversity as corresponding with a population of pentapeptide sequences "reads out" of the claims the range of peptides of from 6 to 12

amino acids in length "by making them synonymous with the 5 amino acid member of the range." Dyax Brief, at 27. Like Dyax, I am puzzled why, if the point of the invention was to provide a population of peptide sequences representing the "universe of possible antibody binding sites," the claims would have been written "to specify lengths of peptides that admittedly cannot do so," or why it is not simply made clear that pentapeptide sequences define the intended universe. Dyax Response, at 8. Indeed, there is nothing said at all in the claims (or the specification) about this universe, nor is any meaningful suggestion made that longer peptides can be expressed as representative lengths of pentapeptides. Like Dyax, I can only conclude that plaintiffs' "pentapeptide universe" theory is an attempt to expand on the claims of the patent to broaden their coverage for purposes of this litigation.FN10

FN10. While it is true that the '393 patent identifies populations of 5 amino acid length sequences as a preferred embodiment of the invention, it is only one of four such preferred embodiments (the others being populations of sequences 4, 6, and 7 amino acids long). Moreover, as plaintiffs acknowledge, "[r]eferences to a preferred embodiment, such as those often present in a specification, are not claim limitations." Laitram Corp. v. Cambridge Wire Cloth Co., 863 F.2d 855, 865 (Fed.Cir.1988).

Oligonucleotide

[6] With respect to the '535 and '266 patents, plaintiffs indicate agreement with the construction advanced by Dyax with the exception of the meaning of the limitation "oligonucleotide." Plaintiffs' Response, at 12-13. Plaintiffs maintain that "oligonucleotide" as used in these two patents would be understood by a person of ordinary skill in the art "to mean a polymor [sic] of nucleotides comprising at least a few nucleotides in length and not usually more than about 100," although they insist that the term is given a "broader" meaning in the '363 patent. Plaintiffs' Brief, at 18, 19. According to plaintiffs, the file history of the '363 patent "makes clear" that the term "oligonucleotide" as used in that patent signifies an oligonucleotide with "an upper limit at about 600 to about 750 nucleotides triplets in length." Id., at 8. This assertion is apparently based on a reference by Dr. Pieczenik in the prosecution file history to an oligonucleotide containing 50 tandem sequences of from about 4 to about 12 nucleic acid triplets (hence 50 x 12 = 600). Id.FN11

FN11. The source of the 750 figure is not revealed.

I find no support in the patent for plaintiffs' narrow or broad definition of oligonucleotide. An oligonucleotide is defined in scientific and medical texts as a compound created by the condensation of a small number of nucleotides with 20 specified as the upper limit. *See, e.g., Stedman's Medical Dictionary* (26th ed.1995) 1244. As for the idea that the upper limit might be as high as 600 or 750 triplets based on Dr. Pieczenik's stray remark, neither claim 24 nor claim 34 makes any reference to an oligonucleotide made up of tandem sequences. *See* Markman, 52 F.3d at 980 ("Although the prosecution history can and should be used to understand the language used in the claims, it too cannot 'enlarge, diminish, or vary' the limitations in the claims").

ORDER

For the foregoing reasons, the court for *Markman* purposes will construe the disputed terms as follows. The limitation "from about 4 to about 12 nucleotide triplets," as used in claims 24 and 34 of the '363 patent, is sufficiently indefinite to include a range whose boundaries are delimited by 3 and 13. Similarly, the limitation "from about 4 to about 12 L-amino acid residues" means a range of from 3 to 13 of such residues.

The limitation "represents at least about 10% of all possible peptide sequences" means approximately 10% or more of the possible peptide sequences of a given length within the range of 3 to 13 L-amino acids where the number of possible peptide sequences is equal to 20^{L}. "Oligonucleotide" means a compound created by the condensation of typically fewer than 20 nucleotides.

SO ORDERED.

D.Mass.,2002.
Pieczenik v. Dyax Corp.

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