United States District Court
District of Massachusetts

Oxford Immunotec Ltd.,	)	
	)	
Plaintiff,	)	
	)	
v.	)	**Civil Action No. 15-13124-NMG**
	)	
Qiagen, Inc. et al.,	)	
	)	
Defendants.	)	
	)	

MEMORANDUM & ORDER

GORTON, J.

Plaintiff Oxford Immunotec Ltd. ("plaintiff" or "Oxford") alleges defendants Qiagen, Inc., Quest Diagnostics, Inc. and Laboratory Corporation of America Holdings (collectively, "defendants") infringed six of its patents relating to a method and kit for diagnosing tuberculosis.

The Court held a Markman hearing on June 8, 2017, during which the parties presented tutorials on the subject technology and disputed the meaning of eleven groups of terms that are included in 16 claims of the patents-in-suit.

I. Overview of the Patented Technology

Oxford is owner of six different patents describing a method and kit for diagnosing tuberculosis in vitro (outside of the human body). Five of the six patents-in-suit (collectively,

"the '646 patent family") share a common specification. Those five patents, each entitled "Tuberculosis Diagnostic Test," are:

1) U.S. Patent No. 7,632,646 ("the '646 patent"), issued on December 15, 2009,

2) U.S. Patent No. 7,901,898, ("the '898 patent"), issued on March 8, 2011,

3) U.S. Patent No. 8,216,795, ("the '795 patent"), issued on July 10, 2012,

4) U.S. Patent No. 8,507,211, ("the '211 patent"), issued on August 13, 2013 and

5) U.S. Patent No. 9,005,902 ("the '922 patent"), issued on April 14, 2015.

The sixth patent-in-suit, U.S. Patent No. 8,617,821 ("the '821 patent"), entitled "Assay Method for Peptide Specific T-Cells," has a different specification. It was issued on December 31, 2013.

Oxford's amended complaint contains six counts alleging infringement of those six patents, in violation of 35 U.S.C. § 271(a)-(c).

II. Analysis

A. Principals of Claim Construction

In analyzing a patent infringement action, a court must 1) determine the meaning and scope of the patent claims asserted to be infringed and 2) compare the properly construed claims to the infringing device. Markman v. Westview Instruments, Inc., 52 F.3d 967, 976 (Fed. Cir. 1995) (en banc), aff'd, 517 U.S. 370

(1996). The first step, known as claim construction, is an issue of law for the court to decide. Id. at 979. The second step is determined by the finder of fact. Id.

The Court's responsibility in construing claims is to determine the meaning of claim terms as they would be understood by persons of ordinary skill in the relevant art. Bell Atl. Network Servs., Inc. v. Covad Commc'ns Grp., Inc., 262 F.3d 1258, 1267 (Fed. Cir. 2001). The meanings of the terms are initially discerned from three sources of intrinsic evidence: 1) the claims themselves, 2) the patent specification and 3) the prosecution history of the patent. See Vitronics Corp. v. Conceptronic, Inc., 90 F.3d 1576, 1582-83 (Fed. Cir. 1996).

The claims themselves define the scope of the patented invention. See Phillips v. AWH Corp., 415 F.3d 1303, 1312 (Fed. Cir. 2005) (en banc). Claim terms are generally given their "ordinary and customary meaning," which is the meaning that a person skilled in the art would attribute to the claim term. See id. at 1312-13. Even if a particular term has an ordinary and customary meaning, however, a court may need to examine the patent as a whole to determine if that meaning controls. Id. at 1313 ("[A] person of ordinary skill in the art is deemed to read the claim term . . . in the context of the entire patent . . . ."); see also Medrad, Inc. v. MRI Devices Corp., 401 F.3d 1313, 1319 (Fed. Cir. 2005) (noting that a court cannot

construe the ordinary meaning of a term "in a vacuum"). Ultimately, the correct construction will be one that

> stays true to the claim language and most naturally aligns with the patent's description of the invention.

Phillips, 415 F.3d at 1316 (quoting Renishaw PLC v. Marposs Societa' Per Azioni, 158 F.3d 1243, 1250 (Fed. Cir. 1998)).

The patent specification is "the single best guide to the meaning of a disputed term" because it

> may reveal a special definition given to a claim term . . . that differs from the meaning it would otherwise possess . . . [such as] an intentional disclaimer, or disavowal, of claim scope by the inventor.

Id. at 1316, 1321.

The Court should also consult the prosecution history to see how the inventor and PTO understood the patent and to ensure the patentee does not argue in favor of an interpretation it has disclaimed. Id. at 1317.

In the rare event that analysis of the intrinsic evidence does not resolve an ambiguity in a disputed claim term, the Court may turn to extrinsic evidence, such as inventor and expert testimony, treatises and technical writings. Id. at 1317. Although extrinsic evidence may be helpful in construing claims, the intrinsic evidence is afforded the greatest weight in determining what a person of ordinary skill would have

understood a claim to mean. V-Formation, Inc. v. Benetton Grp. SpA, 401 F.3d 1307, 1310-11 (Fed. Cir. 2005).

B. The '646 Patent Family

1. The Technology

When the body encounters a pathogen such as Mycobacterium tuberculosis ("M. tuberculosis"), proteins from that pathogen are broken down into pieces known as peptides comprised of strings of amino acids. When T cells, cells that mediate immune responses in the body, first encounter a harmful peptide, they become "antigen-experienced". Then, in a process known as activation, T cells that encounter that peptide again can bind to it. Once activated, the T cells release so-called cytokines, such as IFN-γ, which act as chemical messengers in order to elicit a full immune response.

The '646 patents-in-suit are drawn to a method for diagnosing tuberculosis whereby T cells are placed in contact with peptides from a protein known as ESAT-6, a product of M. tuberculosis. After that contact, someone can measure the level of cytokines released (e.g., IFN-γ) to determine whether there is a tuberculosis infection. The invention also provides a kit for carrying out the claimed method.

2. Disputed Claim Terms

a. The preambles

At the Markman hearing, the parties notified the Court that there are no longer any viable disputes as to the language of the preambles in the '646 patent family (and the '821 patent). Accordingly, the Court will not construe the meaning or scope of such terms.

b. "Peptides represented by" (claims 1, 2, 7, 10 of the '646 patent, claims 1, 2, 17, 19 of the '898 patent) and "peptide SEQ ID NO: [1-11]"/"SEQ ID NO: [1-11]" (claims 1, 2, 17, 18 of the '795 patent, claims 1, 2, 17, 18 of the '211 patent and claims 1, 19 of the '902 patent)

The parties dispute the scope of the above-listed claim terms. See O2 Micro Int'l Ltd. v. Beyond Innovation Tech Co., 521 F.3d 1351, 1362 ("When the parties present a fundamental dispute regarding the scope of a claim term, it is the court's duty to resolve it.").

In light of several references to peptides identified as SEQ ID NOs: 1 through 11 in the '646 patent family, defendants contend that the term "represented by" refers only to peptides so identified. Plaintiff disagrees, primarily relying upon the definition "represented by," which is open-ended and synonymous with the term "comprising".

The Federal Circuit Court of Appeals has "repeatedly warned" against confining claim terms to specific embodiments in

the specification. Phillips, 415 F.3d at 1323. Thus, although plaintiff makes several references to peptides in the form of SEQ ID NOs 1 to 8 in the patent specification, those references are insufficient to limit plaintiff's claim term only to peptides in those forms.

Moreover, the '646 patent specification explains that plaintiff's invention could be achieved by using "analogues" consisting of chains of 8 to 80 amino acids. Those chains differ significantly in numbers of amino acids from the peptides identified as SEQ ID NOs: 1 through 8 which contain exactly 15 amino acids each. In the context of the entire patent, therefore, the open-ended meaning of "represented by" comports with the inventor's description of the patent in the specification. Id. at 1313, 1316.

The Court thus construes "peptides represented by" SEQ ID NOs: 1 to 11 to mean "peptides comprising" SEQ ID NOs: 1 to 11.

With respect to the term "peptide SEQ ID NO: 1" or "SEQ ID NO: 1," in claims 1, 2, 17 and 18 of the '795 patent, claims 1, 2, 17 and 18 of the '211 patent and claims 1 and 19 of the '902 patent, the Court concludes that no construction is necessary. A peptide SEQ ID NO: 1, for example, is exactly what it is defined as in the '646 patent family specifications: a specific sequence of 15 amino acids identified in the ESAT-6 protein as SEQ ID NO: 1. Defendants' proposed construction thus adds

unnecessary language to the subject claim terms. See Harris Corp. v. IXYS Corp., 114 F.3d 1149, 1152 (Fed. Cir. 1997) (rejecting construction of a term that "contribute[d] nothing but meaningless verbiage").

c. "Panel of eight peptides" (claims 1, 7 of the '646 patent) and "peptide panel" (claims 1, 2, 17, 18 of the '795 patent, claims 1, 2, 17, 18 of the '211 patent and claims 1, 19 of the '902 patent)

First, the Court will construe the phrase "panel of eight peptides" in claims 1 and 7 of the '646 patent as "eight peptides". Defendants' argument that the panel must consist of eight unique peptides is unsupported by the intrinsic record. In addition to the use of open-ended language in the claim, the patent specification allows for panels that do not consist only of peptides with the SEQ ID NOs 1 through 8:

> The invention also provides one or more of the peptides or analogues selected from the peptides represented by SEQ ID NO: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or 11 and analogues thereof . . . .

'646 Patent, col. 3 ln. 42-45. The Court will not construe the claim to exclude a recited embodiment of the invention. See Funai Elec. Co. v. Daewoo Elecs. Corp., 616 F.3d 1357, 1371 (Fed. Cir. 2010) (citing Hoechst Celanese Corp. v. BP Chems. Ltd., 78 F.3d 1575, 1581 (Fed. Cir. 1996) (noting that "a claim construction that excludes a preferred embodiment is rarely, if ever, correct").

Similarly, intrinsic evidence does not support defendants' proposed construction of the phrase "peptide panel".

The use of the word "comprising" in the disputed claims indicates that the claims are open-ended.[1] CIAS, Inc. v. Alliance Gaming Corp., 504 F.3d 1356, 1359-60 (Fed. Cir. 2009). Moreover, the specifications provide that ESAT-6 peptides or their analogues may be used. Because the meaning of the phrase "peptide panel" is otherwise clear, the Court will not further construe the phrase.

d. "Determining," "detecting" and "to detect" "a recognition response" to a "peptide panel" (claims 1, 6 of the '646 patent, claims 1, 21, 22 of the '795 patent, claims 1, 17 of the '211 patent and claims 1, 19 of the '902 patent) and "determining" a "recognition response" to a "peptide" (claim 1 of the '821 patent)

The parties dispute both the meaning of "determining," "detecting" and "to detect" and the scope of "peptide" and "peptide panel" in claims 1 and 6 of the '646 patent, claim 1 of the '898 patent, claims 1, 21 and 22 of the '795 patent, claims 1 and 17 of the '211 patent and claims 1 and 19 of the '902 patent. First, defendant's proposed construction of "determining," "detecting" and "to detect" amounts to excess

[1] For example, claim 2 of the '795 patent recites:

> The method of claim **1**, wherein the peptide panel further comprises one or more epitopes contained within one or more peptides selected from the group of consisting of: [peptides SEQ ID NOs 2-11].

verbiage. Further construction of "determining" is not required because the meaning is "readily apparent". See Phillips, 415 F.3d at 1314.

Defendant's suggestion to expand the term "peptide panel" to read "the panel of eight peptides represented by SEQ ID NOs: 1 to [11]" is also unnecessary.

For example, claim 1 of the '646 patent recites, in full:

> A method of diagnosing infection in a human host by, or exposure of a human host to, a mycobacterium that expresses ESAT-6, which method comprise the steps of:
>
> (i) contacting a population of T cells from the host with a panel of eight peptides represented by SEQ ID NOS: 1 to 8, and
>
> (ii) determining in vitro whether T cells of the T cell population show a recognition response to the panel by detecting IFN-γ secretion from the T cells.

When read in context of the entire claim, "peptide panel" in the second limitation refers to "a panel of eight peptides represented by SEQ ID NOS: 1 to 8" as provided in the first limitation. Defendant's construction merely restates what is already been recited in the subject claim. U.S. Surgical Corp. v. Ethicon, Inc., 103 F.3d 1554, 1568 (Fed. Cir. 1997) (explaining that the district judge need not "repeat or restate every claim term").

That analysis also applies to claim 1 of the '898 patent which differs from the disputed claims of the '646 patent family

in ways that are irrelevant to the dispute. Thus, the Court will adopt plaintiff's constructions with respect to claim 1 of the '646 patent and claim 1 of the '898 patent.

e. "Detecting IFN-γ" "secretion" or "production" from or by the T cells (claim 1 of the '646 patent, claims 9, 16 of the '795 patent, claims 9, 16 of the '211 patent, claims 10, 18 of the '902 patent)

Here, the parties dispute the phrase "detecting IFN-γ" "secretion" or "production" from or by the T cells in claim 1 of the '646 patent, claims 9 and 16 of the '795 patent, claims 9 and 16 of the '211 patent and claims 10 and 18 of the '902 patent. Defendants add additional wording to explain the meaning of "detecting" as well as limit the term "panel" to "eight peptides represented by SEQ ID NOs: 1 to 8". Plaintiff responds that no construction of the term is necessary. The Court agrees with plaintiff.

Just as with the word "determining," defendant's proposed construction of "detecting" amounts to unnecessary language. The meaning of the word "detecting" is clear. Phillips, 415 F.3d at 1314.

Second, for the same reasons as those just explained, "panel" will not be construed as defendants proffer. Their construction adds words that are already provided in the claim.

f. "Population of T cells" (claim 1 of the '646 patent, claim 1 of the '898 patent and claims 1, 17 of the '211 patent)

Defendants' proposed construction attempts to limit the scope of the term "T cells" in claim 1 of the '646 patent, claim 1 of the '898 patent and claims 1 and 17 of the '211 patent to only those T cells that are "in the form of peripheral blood mononuclear cells or mononuclear cells isolated from a sample from the host". That construction is unsupported by the intrinsic record.

The claim language itself does not make such a limitation and the specifications in the '646 patent family provide that the T cells removed from the host can be used in several forms:

> Generally the T cells which are contacted in the method are taken from the host in a blood sample . . . . The sample may be added directly to the assay or may be processed first . . . . Peripheral blood mononuclear cells], [mononuclear cells], and T cells can be separated from the sample. . . . Preferably the T cells used in the assay are in the form of unprocessed or diluted samples or are freshly isolated T cells. . . .

'646 Patent, col. 4 ln. 34-37, 48-49, 52-53 (emphasis added).

Defendants' proposed construction is thus an optional not mandatory embodiment of the invention. Moreover, the proposed construction ignores a preferred embodiment of the invention (that the T cells are unprocessed before being placed into an assay). See Funai Elec. Co., 616 F.3d at 1371.

Accordingly, the Court will construe the term "population of T cells" as recited in claim 1 of the '646 patent, claim 1 of the '898 patent and claims 1 and 17 of the '211 patent as "T cells that have been removed from a host or subject".

g. "One or more epitopes contained within" (claims 1, 2 of the '795 patent, claims 1, 2 of the '211 patent and claims 1, 19 of the '902 patent)

Defendants aver that the term "one or more epitopes contained within" is indefinite because 1) it is unclear what kinds of epitopes the claims are referring to and 2) the epitopes will vary from person to person as a result of genetic differences.

A patent is indefinite

> if its claims, read in light of the specification delineating the patent, and the prosecution history, fail to inform, with reasonable certainty, those skilled in the art about the scope of the invention.

Nautilus, Inc. v. Biosig Instruments, Inc., 134 S. Ct. 2120, 2124 (2014).

As the plaintiff correctly explains, the inventor did not have to list the precise length or size of all the epitopes within a peptide. See All Dental Prodx, LLC. v. Advantage Dental Prods., Inc., 309 F.3d 774, 779-80 (Fed. Cir. 2002) (concluding that the term "original unidentified mass" met the definiteness requirement even though no specific size or shape of the mass was recited in the patent).

Defendants' second contention is also unpersuasive because individual genetic variations typically do not render a claim term indefinite. Young v. Lumenis, Inc., 492 F.3d 1336, 1346-47 (Fed. Cir. 2007) (rejecting an indefiniteness challenge based upon variations in anatomy).

Accordingly, the Court concludes that the term "one or more epitopes contained within," recited in claims 1 and 2 of the '795 patent, claims 1 and 2 of the '211 patent and claims 1 and 19 of the '902 patent, is sufficiently definite.

C. The '821 Patent

1. The Technology

The '821 patent is drawn to an "assay," an investigative procedure, for identifying the presence of activated peptide-specific T cells and the corresponding cytokine secretions.

2. Disputed Claim Terms

a. "Determining whether said T cells are activated" (claims 1, 6) and "activation of said T cells is determined by" (claim 3)

As with the term "determining" in the '646 patent family, the parties dispute the use of the term in claims 1, 3 and 6 of the '821 patent. For the reasons explained above, the Court concludes that defendants' proposed constructions add unnecessary language to the claims. Accordingly, the court will adopt plaintiff's construction with respect to claims 1 and 6

and concludes that no construction is needed for claim 3. See Phillips, 415 F.3d at 1314.

b. "Wherein activation of said T cells identifies the presence of Mycobacterium tuberculosis-specific immediate effector T cells" (claims 1, 6)

Defendant's construction of the language in claims 1 and 6 regarding "the presence of Mycobacterium tuberculosis-specific immediate effector T cells" adds excess language. No construction of that phrase is needed. See id.

c. "Providing a sample from said subject containing T cells" (claims 1, 6) and "T cells are peripheral mononuclear cells" (claim 2)

As for several claims in the '646 patent family, defendants attempt to limit claims 1 and 6 in the '821 patent to specific kind of isolated T cell. For similar reasons to those described above, the Court will not so limit the claims.

The specification is not, as defendants claim, drawn only to an ELISPOT assay which tests for the presence of IFN-γ and requires the kind of T cell defendants' proposed construction recites. Rather the specification provides that the ELISPOT assay is the "preferred" embodiment of the invention but that cytokines other than IFN-γ may be tested for and thus possibly necessitating the need for other assays.

Furthermore, defendant's proposed construction of the language in claims 1 and 6 would render claim 2 meaningless

because claim 2 specifically recites that the T cells are "peripheral blood mononuclear cells". See Evntl. Designs Ltd. v. Union Oil Co. of Cal., 713 F.2d 693, 699 (Fed. Cir. 1983) ("It is improper for courts to read into an independent claim a limitation explicitly set forth in another claim.").

Defendants also request that the Court construe claim 2 by adding the word "isolated" in front of "T cells" but here, too, the patent specification is not limited to only isolated T cells and, therefore, the Court declines to construe claim 2 of the '821 patent.

d. "Peptide subfragment of ESAT-6 that contains a CD8+ epitope" and "immunogenic amount" (claims 1, 6)

Defendants submit that the term "peptide subfragment of ESAT-6 that contains a CD8+ epitope" in claims 1 and 6 of the '821 patent is indefinite for two reasons: 1) the patent and prosecution history do not list the specific length and sequence of the claimed peptide fragments and 2) the peptide subfragments will react differently in people with different genetic backgrounds. The Court disagrees.

As plaintiff submits, it is not required to list all possible lengths and sequences that practice the claimed invention. All Dental Prodx, LLC., 309 F.3d at 779-80. Moreover, individual genetic variations typically do not render a claim term indefinite. Young, 492 F.3d at 1346-47.

Therefore, the Court concludes that the term "peptide subfragment of ESAT-6 that contains a CD8+ epitope" in claims 1 and 6 of the '821 patent is not indefinite and no further construction is necessary.

The term "immunogenic amount" in claims 1 and 6 of the '821 patent is also sufficiently definite.

A term is not indefinite, as defendants contend, merely because of the possibility of variations in experimental conditions. Enzo Biochem, Inc. v. Applera Corp., 599 F.3d 1325, 1335-36 (Fed. Cir. 2010) (concluding that a claim term was not indefinite even though the length and sequence of the subject DNA strand would vary depending on the experimental conditions).

Whether a particular peptide is "immunogenic" involves scientific analysis not subjective opinion that is explained and exemplified through a preferred embodiment in the '821 patent specification. See id. at 1326 ("[T]he binding strength of a DNA strand will depend on the length and sequence of the strand, not on the subjective opinion of the particular chemist performing the hybridization.").

Also, as previously noted, individual variations in human genetics is an insufficient ground to find a term indefinite. "Immunogenic amount" is not indefinite because the '821 patent specification teaches a person having ordinary skill in the art how to determine whether a peptide is immunogenic. See Young,

492 F.3d at 1346-47 (rejecting an indefiniteness challenge to the term "near" even though "the size of the appendage and the amount of skin required to be incised will vary from animal to animal" because "a person having ordinary skill in the art would know where to make the cut").

MARKMAN ORDER

In accordance with the foregoing,

1) with respect to United States Patent Nos. 7,632,646, 7,901,898, 8,216,795, 8,507,211 and 9,005,902:

   a) "peptides represented by" means:

      "**peptides comprising**";

   b) "peptide SEQ ID NO: [1-11]"/"SEQ ID NO: [1-11]" are accorded their plain and ordinary meaning;

   c) "panel of eight peptides" means:

      "**eight peptides**";

   d) "peptide panel" is accorded its plain and ordinary meaning;

   e) "determining," "detecting" and "to detect" "a recognition response" to a "peptide panel" means:

      "**determining," "detecting" or "to detect" "whether the T cells respond to the peptide panel**";

   f) "determining" a "recognition response" to a "peptide" means:

      "**determining whether the T cells respond to the peptide**";

   g) "detecting IFN-γ" "secretion" or "production" is accorded its plain and ordinary meaning;

h) "population of T cells" means:

"T cells that have been removed from a host or subject"; and

i) "one or more epitopes contained within" is accorded its plain and ordinary meaning; and

2) with respect to U.S. Patent No. 8,617,821:

a) "determining whether said T cells are activated" means:

"determining whether the T cells respond";

b) "activation of said T cells is determined by" is accorded its plain and ordinary meaning;

c) "wherein activation of said T cells identifies the presence of Mycobacterium tuberculosis-specific immediate effector T cells" is accorded its plain and ordinary meaning;

d) "providing a sample from said subject containing T cells" means:

"T cells that have been removed from the subject";

e) "T cells are peripheral mononuclear cells" is accorded its plain and ordinary meaning;

f) "peptide subfragment of ESAT-6 that contains a CD8+ epitope" is accorded its plain and ordinary meaning; and

g) "immunogenic amount" is accorded its plain and ordinary meaning.

So ordered.

/s/ Nathaniel M. Gorton
Nathaniel M. Gorton
United States District Judge

Dated June 14, 2017