United States Court of Appeals for the Federal Circuit

03-1409

MILTON D. GOLDENBERG and IMMUNOMEDICS, INC.,

Plaintiffs-Appellants,

v.

CYTOGEN, INC. and C.R. BARD, INC.,

Defendants-Appellees.

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Appealed from: United States District Court for the District of New Jersey

Senior Judge Anne E. Thompson

United States Court of Appeals for the Federal Circuit

03-1409

MILTON D. GOLDENBERG and IMMUNOMEDICS, INC.,

Plaintiffs-Appellants,

v.

CYTOGEN, INC. and C.R. BARD, INC.,

Defendants-Appellees.

DECIDED: June 23, 2004

Before SCHALL, GAJARSA, and PROST, Circuit Judges.

Opinion for the court filed by Circuit Judge GAJARSA. Opinion concurring-in-part and dissenting-in-part filed by Circuit Judge PROST.

GAJARSA, Circuit Judge.

Milton D. Goldenberg ("Goldenberg") and Immunomedics, Inc. (collectively, "Immunomedics"), appeal from the grant of a motion for summary judgment of noninfringement of United States Patent No. 4,460,559 (the "'559 patent") in favor of Cytogen, Inc., and C.R. Bard, Inc. (collectively, "Cytogen"), by the United States District Court for the District of New Jersey.

Goldenberg v. Cytogen, Inc., No. 00-763 (AET) (D.N.J. Apr. 30, 2003) ("Summary Judgment Opinion"). While we agree with the district court's claim construction, and that summary judgment of no literal infringement was appropriate, we disagree with the grant of summary judgment of noninfringement under the doctrine of equivalents. Accordingly, we affirm-in-part, reverse-in-part, and remand.

I. BACKGROUND

A. The Patents and the Prosecution History

The '559 patent is entitled "Tumor Localization and Therapy with Labeled Antibodies Specific to Intracellular Tumor-Associated Markers." The invention is a method for detecting and localizing tumors by targeting "intracellular marker substances" that are produced by or associated with tumor cells. '559 patent, col. 2, ll. 19-27. The claimed method includes injecting a subject with a radioactively highlighted antibody specific to the "marking substance," which, when scanned, reveals the location of concentrations of the "marking substance" within the body. Claim 1 of the '559 patent claims:

> A method for detecting and localizing a tumor which either produces or is associated with an intracellular marker substance, which comprises injecting a subject parenterally with an antibody specific to said marker substance and radiolabeled with a pharmacologically inert radioisotope capable of detection using a photoscanning device, and subsequently scanning with said device to detect and locate the site or sites of uptake of said labeled antibody by said tumor; with the proviso that when said antibody is an antibody specific to human chlorionic [sic] gonadotropin or its beta-subunit, said radioisotope is other than Tc-99m.

Id. at col. 15, ll. 24-35 (emphases added).

The written description of the '559 patent does not define the term "intracellular marker substance." It does, however, discuss the previous understanding in the art that tumor localization required "antibodies which were specific to antigens located on the surface of the tumor cell . . . ." Id. at col. 1, ll. 25-32. The written description further explains:

> The antibodies used in the present invention are specific to a variety of intracellular

> tumor-associated antigens as marker substances. These markers may be substances produced by the tumor or may be substances which accumulate within tumor cells, whether in the cytoplasm, the nucleus or in various organelles or subcellular structures.

Id. at col. 2, ll. 36-40 (emphasis added).

The '559 patent issued on July 17, 1984 from an application, Ser. No. 374,662 (the "'662 application"), filed by Goldenberg on May 4, 1982. The '662 application is a continuation of another application, Ser. No. 126,261 (the "'261 application"). Goldenberg also filed a second application, Ser. No. 126,262 (the "'262 application"), simultaneously with the '261 application. The '262 application led to a continuation-in-part application, Ser. No. 414,729 (the "'729 application"), which resulted in United States Patent No. 4,444,744 (the "'744 patent"). In the first office action after the filing of the '261 and '262 applications, the Examiner rejected the claims of the '261 application in their entirety. Claims 15-22 and 28-29 of the '261 application were specifically rejected on double patenting grounds over the '262 application.

Attempting to overcome the examiner's rejection, Goldenberg explained:

> [t]he method and compositions claimed in the ['261 application] relate to intracellular tumor associated antigens. Before the work of the present inventor, the art did not know that antibodies to such intracellular antigens, e.g., human chorionic gonadotrophin (HCG) and alpha-fetoprotein (AFP) could be successfully used for tumor localization and therapy. Accordingly, the claims of the present application do not overlap claims in [the '262 application], since the latter application claims methods and compositions for tumor localization and therapy to CEA alone.

Response to Office Action Dated March 24, 1981, at 2-3. In the same response, Immunomedics explained "[a]s noted above, the[] claims [of the '261 application] do not overlap with claims to methods and compositions for tumor localization and therapy using radiolabeled antibodies to CEA, a cell surface antigen." Id. at 3-4 (emphasis in original).

Throughout the response, Goldenberg distinguished the methods of the '261 application, which focused on intracellular antigens, from the subject matter of the '262 application, which involved cell surface antigens. See, e.g., id. at 4 ("The present specification . . . explains that the prior art considered that tumor localization in man using injected radiolabeled tumor-associated antigens required antibodies

which were specific to antigens located on the surface of the tumor cell." (emphasis added)); id. at 6 ("Reid relates to a surface glycoprotein useful in identifying the presence of tumors . . . ."); id. at 7 ("Furthermore, it was not known prior to applicant's work in this field that antibodies to non-surface antigens would preferentially localize in human tumors." (emphasis added)); id. at 10 ("The reference discloses that CEA is a surface antigen whereas alpha-fetoprotein (AFP) is a cytoplasmic or intracellular antigen."). Despite the frequency with which the distinction appears in the prosecution history, the '261 application did not define "intracellular marker substance."

The Examiner allowed claims 25-30 of the '261 application, which issued as United States Patent No. 4,361,544 on November 30, 1982. Goldenberg also continued the prosecution of the remaining claims in the '261 application with the '662 application, which resulted in the '559 patent. On September 3, 1982, Immunomedics filed the '729 application, a continuation-in-part of the '262 application. The '729 application defined the term "cell surface antigen" and incorporated by reference a 1972 article by S.J. Singer and Garth Nicholson (the "Singer article"),[1] which contained a further discussion of various antigens associated with a cell membrane. The '729 application matured into the '744 patent on April 24, 1984.

B. The Accused Product

Cytogen manufactures and sells ProstaScint. ProstaScint contains the antibody 7E11-C5.3, which is specific to prostate specific membrane antigen (PSMA). PSMA is a transmembrane antigen, extending through the cell membrane and having both intracellular and extracellular domains. 7E11-C5.3 is covered by United States Patent No. 5,162,504, which is assigned to Cytogen. The binding site, or "epitope," for 7E11-C5.3 is located on the "N-terminal" of PSMA, which is on the cytoplasmic side (i.e., interior) of the cell wall. To use ProstaScint, the radiolabeled antibody is injected into a patient, who is then photographed with a camera designed to detect radiation. Because the 7E11-C5.3 antibody targets and binds to PSMA, images from the radiation-detecting camera reveal concentrations of the antibody/antigen combination and, by association, the location of the PSMA-producing tumor.

C. The District Court Proceedings

Immunomedics filed suit against Cytogen in the District of New Jersey on February 17, 2000, alleging infringement of method claims 1, 6, 10, 15, and 17 of the '559 patent both literally and under the doctrine of equivalents. Claim 1 is the only independent claim. The district court held a Markman hearing and provided the parties with its claim construction on November 30, 2001. Goldenberg v. Cytogen, Inc., No. 00-763 (AET) (D.N.J. Nov. 30, 2001) ("Claim Construction Opinion"). The only disputed term was "intracellular marker substance" in claim 1, which had "no commonly accepted meaning outside the context of [the '559] patent." Id. at 3-4. The parties agree that the term has no commonly accepted meaning.

Turning to the written description of the '559 patent, the district court noted the discussion in the patent of the need for a method of tumor localization not confined to cell surface antigens. Id. at 4-5. The district court also noted the prosecution history of the '559 patent and the repeated distinction drawn between intracellular and cell surface antigens. Id. at 7-8. Upon concluding its review of the intrinsic evidence, the district court also considered the extrinsic evidence of two expert witness depositions. Id. at 8. The district court explained that the intrinsic evidence "provide[d] only an amorphous interpretation of the disputed term" and finally accepted the deposition testimony of Dr. Goldenberg, the inventor, which defined "intracellular marker substance" as "an antigen existing within a body cell." Id. at 10 (emphasis added).

Both parties filed motions for summary judgment based on the claim construction. Summary Judgment Opinion at 3. On July 3, 2002, the court denied both parties' motions, explaining that there remained a genuine factual dispute as to whether ProstaScint infringed under the doctrine of equivalents. Id. at 4. Specifically, the district court was uncertain of the relationship between PSMA and the cell interior, and also whether the binding location of 7E11-C5.3 to PSMA was intracellular. Following its denial of the motions, the district court conducted an evidentiary hearing "to allow both sides an opportunity to present additional information through expert testimony." Id. After the hearing, both parties renewed their summary judgment motions.

At this time, the district court granted Cytogen's motions for summary judgment of no literal

infringement and of no infringement under the doctrine of equivalents. In doing so, the court first addressed whether PSMA was a cell surface antigen. Id. at 5. The district court rejected Immunomedics' argument that, because PSMA was a transmembrane antigen, it could be both a cell surface and an intracellular marker substance, depending on where the targeted binding site was located. Instead, the court explained, "ProstaScint's targeting of a portion of PSMA at the [interior] N-terminal domain would not change the character of the antigen as being integral to the plasma membrane and being termed a cell surface antigen." Id. at 6. The district court found Cytogen's expert "not only helpful in clarifying the subject matter but also very persuasive." Id.

Next, the district court rejected Immunomedics' argument that referencing the '744 patent was improper. Id. at 7. Although the '744 patent was not related to the '559 patent, the court explained, Goldenberg distinguished the parent application of the '744 patent (the '262 application) to overcome the examiner's double-patenting rejection during prosecution. The court consequently relied on both the definition and the reference to the Singer article in the '744 patent. Based on the testimony and the statements from the '744 patent, the district court concluded that PSMA was a cell surface antigen and was therefore outside of the literal scope of claim 1. Id. at 8. Regarding infringement under the doctrine of equivalents, however, the district court found it improper to rely on the prosecution history of the '744 patent for estoppel purposes. Id. at 10. Relying on Abbott Laboratories v. Dey, L.P., 287 F.3d 1097 (Fed. Cir. 2003), the court found that there was an insufficient connection between the '559 and '744 patents to permit statements made during the prosecution of the '744 patent to create an estoppel for equivalents under the '559 patent. Despite the insufficiency, the district court found that Immunomedics' argument for insubstantial differences between ProstaScint and the claims of the '559 patent entirely ignored the intracellular/cell surface distinction that Goldenberg had drawn in the '559 patent, and Immunomedics' argument therefore failed as a matter of law. Because Immunomedics' equivalents argument did not address the intracellular/cell surface distinction, the district court concluded that Immunomedics had "not met the requirements of the 'function-way-result' test" and granted Cytogen's motion for summary judgment. Summary Judgment Opinion at 11.

II. DISCUSSION

A. Standard of Review

Claim construction is a question of law subject to de novo review on appeal. Cybor Corp. v. FAS Techs., Inc., 138 F.3d 1448, 1456 (Fed. Cir. 1998) (en banc). We review a district court's grant of summary judgment de novo, drawing all factual inferences in favor of the nonmoving party. Anderson v. Liberty Lobby, Inc., 477 U.S. 242, 255 (1986); Moore U.S.A., Inc. v. Standard Register Co., 229 F.3d 1091, 1105 (Fed. Cir. 2000). Summary judgment on the issue of literal infringement is proper "when no genuine issue of material fact exists, in particular, when no reasonable jury could find that every limitation recited in the properly construed claim either is or is not found in the accused device." Bai v. L & L Wings, 160 F.3d 1350, 1353 (Fed. Cir. 1998). Summary judgment of noninfringement under the doctrine of equivalents is appropriate if "no reasonable jury could determine two elements to be equivalent." Leggett & Platt, Inc. v. Hickory Springs Mfg. Co., 285 F.3d 1353, 1360 (Fed. Cir. 2002) (quoting Warner-Jenkinson Co. v. Hilton Davis Chem. Co., 520 U.S. 17, 39 n.8 (1997)).

B. Analysis

1. Claim Construction

Claim construction begins with the intrinsic evidence of record. Vitronics Corp. v. Conceptronic, Inc., 90 F.3d 1576, 1582 (Fed. Cir. 1996). In construing patent claims, there is a heavy presumption that the terms carry their ordinary and customary meanings as would be understood by one of ordinary skill in the art. Markman v. Westview Instruments, Inc., 52 F.3d 967, 986 (Fed. Cir. 1995) (en banc), aff'd, 517 U.S. 370 (1996); CCS Fitness, Inc. v. Brunswick Corp., 288 F.3d 1359, 1366 (Fed. Cir. 2002). Where a claim term has no ordinary and customary meaning, a court must resort to the remaining intrinsic evidence—the written description and the prosecution history—to obtain the meaning of that term. See Lear Siegler, Inc. v. Aeroquip Corp., 733 F.2d 881, 888-89 (Fed. Cir. 1984). Extrinsic evidence, although not part of the intrinsic evidence, may be used to aid a court in construing claim terms as they would be understood in the relevant art, but may not be used to vary the meaning disclosed by the patent itself. Markman, 52 F.3d at 980-81.

The district court construed "intracellular marker substance" to mean "an antigen existing within

a body cell."[2] Claim Construction Opinion at 10. Immunomedics challenges this construction by arguing that, in the absence of an ordinary meaning, the written description must be controlling. Immunomedics explains that neither claim 1 nor the written description require a marker substance to be an entire antigen or that the marker substance be wholly within a cell. To the contrary, Immunomedics continues, the intrinsic evidence actually precludes that interpretation by permitting sub-units of antigens to qualify as marker substances. Immunomedics urges us to construe "intracellular marker substance" to mean "an antigen or a portion thereof that is located inside a cell." Appellants' Br. at 27 (emphasis added). Under this interpretation, if the epitope for the specific antibody is located within the cell, the claim limitation is satisfied.

We disagree with the construction urged by Immunomedics. The parties agree that the term "marker substance" has no accepted meaning to one of ordinary skill in the art, and we find no reason to disagree with their conclusion. Accordingly, we construe it only as broadly as is provided for by the patent itself. See Johnson Worldwide Assocs. v. Zebco Corp., 175 F.3d 985, 990 (Fed. Cir. 1999); J.T. Eaton & Co., Inc. v. Atl. Paste & Glue Co., 106 F.3d 1563, 1570 (Fed. Cir. 1997) ("In this case, the dispositive claim limitation is a term unknown to those of ordinary skill in the art at the time the patent application was filed. It thus fell to the applicants, as a duty, to provide a precise definition for the . . . limitation."); Lear Siegler, 733 F.2d at 888-89 (Fed. Cir. 1984). The '559 patent discloses twenty-six different antigens that are described as "suitable . . . marker substances." '559 patent, col. 2, l. 57 to col. 3, l. 8. At a minimum, therefore, the '559 patent clearly regards "antigens" as falling within the scope of "marker substances." In addition to antigens, both claim 1 and the written description refer specifically to the "beta sub-unit" of human chorionic gonadotropin (HCG) antigen.

Immunomedics broadly construes "sub-units" as encompassing any portion of an antigen, including epitopes. As Cytogen points out, however, HCG is a dimeric antigen, which means that it is composed of two individual protein sub-units held loosely together by ionic and hydrophobic forces. Each sub-unit is itself a whole protein molecule. The alpha sub-unit is common to several hormones, but the beta sub-unit is unique to HCG. See Dorland's Illustrated Medical Dictionary 763 (29th ed. 2000). Due to its uniqueness, antibodies targeting the beta sub-unit will only localize concentrations of

HCG, while those antibodies targeting the alpha sub-unit may errantly identify concentrations of an entirely different hormone. Thus, contrary to Immunomedics' argument, the reference to the beta sub-unit of HCG is not a reference to "portions" of antigens generally, but is instead a reference to a very specific and well-known molecule in the field of immunology: the beta sub-unit in the dimeric antigen HCG. The inclusion of the sub-unit in the claims and the written description, therefore, does not support a reading of the claims as broadly as Immunomedics requests. J.T. Eaton & Co., 106 F.3d at 1570.

The prosecution history further reveals the inventor's understanding of the term "marker substance" as synonymous with "antigen." For example, Goldenberg explained: "The method and compositions claimed in the present application relate to antibodies to intracellular tumor-associated antigens." Response to Office Action Dated March 24, 1981, at 2 (emphasis omitted).[3] Nowhere does the prosecution history suggest that a "marker substance" includes epitopes as Immunomedics would now have us construe the term. Accordingly, we will not read the claim scope that broadly. See J.T. Eaton & Co., 106 F.3d at 1568. Nor does Immunomedics argue that PSMA is characteristically similar to the dimeric HCG antigen. Because neither the patent specification nor the prosecution history supports the breadth of construction that Immunomedics desires, we affirm the district court's claim construction of "marker substance" as an antigen, but clarify that molecular sub-units, such as those present in the HCG antigen, qualify as antigens under this construction.

We also agree with the district court that the marker substance must be wholly internal to the cell. Cytogen argues, and Immunomedics does not dispute, that none of the twenty-six example antigens provided in the '559 patent associates in any way with the membrane of the cells in which they are found. The written description further describes intracellular marker substances as those which are produced by tumor cells or accumulate "in the cytoplasm, the nucleus or in various organelles or sub-cellular structures" of tumor cells. '559 patent, col. 2, ll. 36-40. Each of the listed structures is completely internal to the cell. The prosecution history further supports this understanding, specifically explaining that HCG is a "cytoplasmic antigen." Response to Office Action Dated October 29, 1981, at 5 (emphasis added). Finally, the ordinary meaning of "intracellular," as reflected by its dictionary

definition, lends additional support to the interpretation adopted by the district court. See Dorland's Illustrated Medical Dictionary 912 (defining "intracellular" as "within a cell"). Combining the terms, an "intracellular marker substance" must be an antigen existing within a cell. This is the construction adopted by the district court, which we now affirm.

In addition to the intrinsic evidence, the district court permitted expert testimony at the summary judgment hearing. Immunomedics criticizes the district court's use of expert testimony as impermissible, citing this court's prohibition on using extrinsic evidence to vary the meaning of claim terms from that apparent in the intrinsic evidence. Immunomedics is correct that "[a]lthough expert testimony and declarations are useful to confirm that the construed meaning is consistent with the denotation ascribed by those in the field of the art, such extrinsic evidence cannot be used to vary the plain language of the patent document." Omega Eng'g, Inc. v. Raytek Corp., 334 F.3d 1314, 1332 (Fed. Cir. 2003) (citations omitted). However, the interpretation of the claims reached by the district court was consistent with that required by the intrinsic evidence, and the district court's use of expert testimony therefore falls within the permissible first clause of the above-quoted language rather than the impermissible second clause. Contrary to Immunomedics' apparent belief, there is no prohibition on a district court's ability to hear expert testimony. Key Pharms. v. Hercon Lab. Corp., 161 F.3d 709, 716 (Fed. Cir. 1998).

2. Summary Judgment of No Literal Infringement

As we have affirmed the district court's interpretation of "intracellular marker substance," we likewise affirm its summary judgment of no literal infringement. PSMA, as a transmembrane antigen, extends both inside and outside of the cell membrane. See Summary Judgment Opinion at 2. Despite this intracellular portion, however, the claims do not provide generally for "portions" of antigens to qualify as marker substances. We note that in affirming the district court's summary judgment, we rest not on the fact that PSMA is a cell surface antigen as did the district court, but rather on the fact that, as a transmembrane antigen, PSMA is not an intracellular marker substance. See id. at 8 ("For the reasons stated above, this Court determines that PSMA is a cell surface antigen."). Although the basis of our decision varies from that relied on by the district court, the result we reach does not.

3. The District Court's Reliance on the '744 Patent and Prosecution History

Immunomedics also argues that it was improper for the district court to reference the '744 patent and its prosecution history when construing the claims of the '559 patent. We analyze the propriety of the district court's reliance on the content and prosecution history of the '744 patent in segments. The first segment is the district court's examination of the '262 application at the point it was distinguished from the '261 application following the March 24, 1981, double-patenting rejection. The second segment is the district court's reliance on the statements contained in the '744 patent defining the cell surface and incorporating the Singer article, all of which is new matter added to a continuation-in-part of the '262 application. The district court appears to have relied primarily on the latter.

As for the first piece, the district court made no error to the extent that it referenced the contents of the '262 application as it existed when Goldenberg distinguished the '262 application from the '261 application in the office action response dated March 24, 1981. This response constitutes part of the prosecution history of the '261 application, which is a parent application to the '559 patent, and therefore part of the '559 patent's prosecution history. In an analogous situation, this court has explained that "prior art cited in a patent or cited in the prosecution history of the patent constitutes intrinsic evidence." Kumar v. Ovonic Battery Co., Inc., 351 F.3d 1364, 1368 (Fed. Cir. 2003). While the '262 application was not prior art of the sort discussed in Kumar, it did form the basis of the examiner's rejection of the '261 patent on double-patenting grounds. The reasoning underlying the court's statement in Kumar, therefore, applies equally here, and the district court was entitled to treat the '262 application as part of the intrinsic evidence of the '559 patent when construing the claim terms.

The district court did err in the second segment of its analysis, however, when it relied on the specification of the '744 patent to construe the claims. Summary Judgment Opinion at 7. The relevant passages from the '744 patent (e.g., the reference to the Singer article and the definition of cell surface antigen) were added during a continuation-in-part of the '262 application. These passages are therefore new matter added to the content of the '262 application subsequent to when it was distinguished in the March 24 office action response. While the content of the '262 application at the time it was

distinguished from the ’261 application constitutes part of the prosecution history of the ’559 patent, subsequently added new matter is not similarly incorporated.

In the absence of an incorporation into the intrinsic evidence, this court’s precedent takes a narrow view on when a related patent or its prosecution history is available to construe the claims of a patent at issue and draws a distinct line between patents that have a familial relationship and those that do not. See, e.g., Tex. Digital Sys. v. Telegenix, Inc., 308 F.3d 1193, 1211 (Fed. Cir. 2002) (explaining that an unrelated patent “sheds no light” on the claims in the patent at issue); Abbott Labs, 287 F.3d at 1105 (finding an insufficient relationship between patents to rely on statements from the prosecution history of one patent for prosecution history estoppel regarding the other where the “applications [had] no formal relationship and were presented to the patent office as patentably distinct inventions”); Jonsson v. Stanley Works, 903 F.2d 812, 818 (Fed. Cir. 1990) (using statements from one patent’s prosecution history to construe the claims of another patent where the two patents shared a parent application). This dividing line was left undisturbed by our most recent decision on the issue, Microsoft Corp. v. Multi-Tech Systems, Inc., which permitted reliance on statements made subsequent to the issuance of a patent when construing its claims where the statements were made in connection with continued prosecution of sibling applications. 357 F.3d 1340, 1350 (Fed. Cir. 2004).

The district court’s reliance on the ’744 patent when construing the claims of the ’559 patent in the second segment of its analysis does not fit the mold of the cases discussed above. The ’261 and ’262 applications were filed separately and therefore lack the formal relationship necessary for free license to use the contents of the ’744 patent and prosecution history when construing the claims of the ’559 patent. See Tex. Digital, 308 F.3d at 1211. While the ’262 application was distinguished from the scope of the ’261 application’s claims, incorporating its contents at that point into the intrinsic evidence of the ’559 patent, the relevant passages from the ’744 patent relied on by the district court are new matter added by the ’729 continuation-in-part application. Consequently, the passages are not part of the intrinsic evidence of the ’559 patent. Cf. Kumar, 351 F.3d at 1368. Absent a formal relationship or incorporation during prosecution, the new-matter content of the ’744 patent is not available to construe the claims of the ’559 patent, and the district court erred in relying on them. Given that the district

court's errant reliance on the '744 patent did not cause it to reach an incorrect claim construction, however, and we have reached the same construction based on the intrinsic evidence of the '559 patent, the district court's error was harmless. See Superguide Corp. v. DirecTV Enters., 358 F.3d 870, 888 n.14 (Fed. Cir. 2004).

4. Summary Judgment of Noninfringement Under the Doctrine of Equivalents

We turn finally to the district court's grant of summary judgment of noninfringement under the doctrine of equivalents. The district court explained that, under Dey, statements from the '744 patent could not create prosecution history estoppel for the '559 patent. Summary Judgment Opinion at 10-11. For the same reasons stated above, we agree with the district court's conclusion on this point.

Despite the lack of estoppel, however, the district court still found that Immunomedics "had not met the requirements of the 'function-way-result' test." Id. at 11. The whole of the district court's doctrine of equivalents analysis consists of the following:

> Defendants argue that ProstaScint does not bind to an antigen located within a tumor cell. Instead, ProstaScint targets PSMA. The Court has determined that PSMA is a cell surface antigen, not an intracellular marker substance. Furthermore, plaintiff's discussion of "function" and "way" ignores the distinction Dr. Goldenberg made in the '559 patent between antibodies that bind to intracellular antigens and those that bind to cell surface ones. In sum, plaintiffs have not met the requirements of the "function-way-result" test.

Id.

The district court's conclusion is based on a faulty premise to the extent that it relied on its previous classification of PSMA as a cell surface antigen. As we explained, while we agree with the district court that PSMA is not an intracellular marker substance, this does not mean that it must be a cell surface antigen. The district court appears to have viewed the world of antigens as consisting of two distinct categories—those that are intracellular and those that are on the cell surface—and concluded that antigens falling in different halves could not be equivalents as a matter of law. See id. ("The Court has determined that PSMA is a cell surface antigen, not an intracellular marker substance."). Transmembrane antigens, however, appear to be a category of their own, and are not susceptible to the black and white categorization made by the district court. As a "grey" category, transmembrane

antigens are not addressed by the '559 patent or its prosecution history and might be equivalents to either of the categories identified by the district court if such a finding was made. See generally Warner-Jenkinson, 520 U.S. at 40.

Regarding the second point in the district court's doctrine of equivalents analysis, a review of Immunomedics' Memorandum Opposing Cytogen's Motion for Summary Judgment shows that it did acknowledge the distinction between intracellular and cell surface antigens in its doctrine of equivalents argument. Immunomedics identified and the district court agreed that the relevant limitation in claim 1 was "injecting a subject parenterally with an antibody specific to said marker substance and radiolabeled with a pharmacologically inert radioisotope capable of detection using a photoscanning device." Goldenberg's Memorandum Opposing Cytogen's Motion for Summary Judgment, Goldenberg v. Cytogen, Inc., No. 00-763 (AET) (Jan. 25, 2002). The "function" of this limitation, according to Immunomedics, was "to deliver a radioisotope to a tumor cell"—a function it claimed was identical to the function of ProstaScint. Id. The "way" this was accomplished was by "binding the radiolabelled antibody to an antigen located within a tumor cell." Id. This was equivalent to ProstaScint, Immunomedics explained, because the binding of PSMA in ProstaScint occurred inside the cell membrane. The expert report of Dr. Primus, cited by the Memorandum, further explains that the processes are substantially the same because both antibodies must cross the cell membrane to bind with the antigen.

Immunomedics has accordingly presented a sufficient factual dispute to avoid summary judgment. See Fed. R. Civ. P. 56(e) ("[T]he adverse party's response, by affidavits or as otherwise provided in this rule, must set forth specific facts showing that there is a genuine issue for trial."); Arthur A. Collins, Inc. v. N. Telecom Ltd., 216 F.3d 1042, 1047 (Fed. Cir. 2000). Immunomedics' comparison of the membrane-crossing ability of the 7E11-C5.3 antibody in ProstaScint to the membrane-crossing ability required by the '559 patent presents a "lingering issue of fact preclud[ing] summary judgment . . . ." Leggett & Platt, 285 F.3d at 1360. The district court's grant of summary judgment was therefore in error.

III. CONCLUSION

Because we find that the district court correctly construed the claims and, under that construction, Cytogen's ProstaScint product was not an "intracellular marker substance," we affirm the district court's grant of summary judgment of no literal infringement. Regarding infringement under the doctrine of equivalents, however, we disagree with the district court's conclusion that there is no issue of material fact regarding ProstaScint and reverse the district court's grant of summary judgment on this point and remand for further proceedings on the issue.

AFFIRMED-IN-PART, REVERSED-IN-PART, AND REMANDED

IV. COSTS

No costs.

United States Court of Appeals for the Federal Circuit

03-1409

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PROST, Circuit Judge, concurring-in-part, dissenting-in-part.

While I concur with the majority's decision to remand this case to the district court to evaluate infringement under the doctrine of equivalents, I respectfully dissent with regard to the affirmance of the claim construction and grant of summary judgment of no literal infringement.

With respect to claim construction, I remain unpersuaded by the majority's view that "intracellular marker substance" does not encompass portions of an antigen located inside a cell. The majority concludes that "marker substance" is an equivalent term for "antigen," when in view of the intrinsic record, I believe "marker substance" bears a broader meaning. First, the claims expressly recognize that the "marker substance" may correspond to only a fragment, i.e., sub-unit, of an antigen. See '559 patent, claim 1 ("when said antibody is an antibody specific to human chlorionic [sic] gonadotropin or its beta-subunit, said radioisotope is other than Tc-99m"); claim 17 (narrowing the scope of "marker substance," recited in claim 1, to exclude a specific sub-unit of an antigen). Further, the specification expressly acknowledges that a "sub-

unit of a tumor-associated marker" may be "advantageously used to raise antibodies having higher tumor specificity." Id., col. 2, ll. 51-53. Moreover, the specification states that "such marker substances" that are "useful in the present invention include, but are not limited to, alphafetoprotein (AFP), human chorionic gonadotropin (HCG) and/or its beta-subunit (HCG-beta)." Id., col. 2, ll. 57-61 (emphases added). The specification and the claims clearly signal that part of an antigen, i.e., the epitope, may correspond to the "marker substance." My understanding of "marker substance," as derived from the intrinsic record is consistent with testimony by Goldenberg's expert, Dr. Primus, who testified that "any substance that has in this case an epitope, a marker, which an antibody sees that occurs within the cytoplasm of the cell, is an intracellular marker substance."

The appellees submit and the majority agrees that the beta sub-unit of HCG does not correspond to a portion of an antigen, but rather is an antigen itself. The specification acknowledges that HCG is an antigen made up of smaller constituents, namely, an alpha and beta sub-unit. Id. The majority rejects, in my opinion, the seemingly inescapable conclusion that the beta sub-unit, identified by the specification to be a "marker substance," composes a portion of the HCG antigen. The majority cites no intrinsic evidence, much less the extrinsic evidence of any expert, to support its position that the beta

sub-unit, which undeniably forms only a part of the HCG antigen, is recognized by those skilled in the relevant art to qualify as an antigen.

The prosecution history, which the majority discusses, ante at 11, is of little help to its proposed claim construction. The patentee had attempted to overcome a double patenting rejection by arguing that the method and compositions claimed by the '261 application (the predecessor to the application that became the '559 patent) are distinguishable from the '262 application (the predecessor to the '744 patent application) on the basis that the '261 application relates to "antibodies to intracellular tumor associated antigens" whereas the '262 application relates to "cell surface antigen[s]" that are "located on the surface of the tumor cell." (Emphases in original). In other words, the pertinent novelty and difference between the '261 application and the '262 application and prior art lay in the site of tumor localization. As explained by the patent applicant, "[b]efore the work of the present inventor, the art did not know that antibodies to . . . intracellular [tumor associated] antigens, e.g., human chorionic gonadotropic (HCG) and alpha-fetoprotein (AFP) could be used successfully for tumor localization and therapy." The specification further informs us that in addition to HCG and AFP, other "marker substances to which specific antibodies may be raised which are useful in the present invention include, but are not limited to . . . [the beta-subunit of HCG]." '559 patent, col. 2, ll. 57-61. "Occasionally, a sub-unit of a tumor associated marker is advantageously used to raise antibodies having higher tumor-specificity." Id., col. 2, ll. 51-54 (emphasis added). The distinguishing statement relied on by the majority in the prosecution history can hardly be characterized as definitional of the term "marker substance," and cannot be used, in my view, as a basis to conclude that "marker substance" corresponds to an antigen, and not portions thereof.

"Where, as here, the written description and prosecution history fail to express a manifest exclusion or restriction limiting the claim term, and where the written description otherwise supports the broader interpretation, we are constrained to follow the language of the claims, and to give the claim term its full breadth of ordinary meaning as understood by persons skilled in the relevant art." Brookhill-Wilk 1, LLC. v. Intuitive Surgical, Inc., 334 F.3d 1294, 1301-02 (Fed. Cir. 2003) (internal quotations and citation omitted); see also ACTV, Inc. v. Walt Disney Co., 346 F.3d 1082, 1091 (Fed.

Cir. 2003); Teleflex, Inc. v. Ficosa N. Am. Corp., 299 F.3d 1313, 1328 (Fed. Cir. 2002). From my review of the intrinsic evidence, the "marker substance," as described by the specification and set forth in the claims, plainly embraces portions of an antigen, provided that they are inside the cell. Because transmembrane antigens generally have an element that extends into the intracellular region, I would submit that the intracellular portion of such an antigen plainly falls within the scope of "intracellular marker substance."

Notably, the patentee clearly knew of and knew how to use the word "antigen," as shown by its use of the term throughout the applications that led to the '559 and '744 patents. Evidently, however, the patentee chose not to use that term in the claims, instead choosing "marker substance." Although the majority correctly observes that the patentee indicated that an antigen may be a marker substance, it cites to nothing in the intrinsic record that negates the indication by the specification and claims that "marker substance" may also correspond to only a portion of an antigen.

Appellees contend that even if appellants' claim construction is correct, they do not literally infringe because no portion of the antigen to which their antibody responds, is located inside the cell. This question of infringement, either literal or under the doctrine of equivalents, is a disputed factual matter that should be left to the district court to resolve in the first instance. Given my view of the term "intracellular marker substance," I would reverse the claim construction, vacate the summary judgment entirely, and remand for further findings as to infringement literally and, if necessary, under the doctrine of equivalents. Accordingly, I respectfully dissent-in-part and concur-in-part with the majority's opinion.

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[1] S.J. Singer & Garth L. Nicolson, The Fluid Mosaic Model of the Structure of Cell

Membranes, Science, Feb. 18, 1972, at 720.

[2] We note that, although "intracellular marker substance" appears in the preamble of claim 1, it provides an antecedent basis for "said marker substance" appearing in the body of the claim, thus "indicat[ing] a reliance on both the preamble and claim body to define the claimed invention." Catalina Mktg. Int'l, Inc. v. Coolsavings.com, Inc., 289 F.3d 801, 808 (Fed. Cir. 2002).

[3] While this is only one example, the applicant used the terms interchangeably throughout the prosecution history. See, e.g., Response to Office Action Dated March 24, 1981, at 3 ("The present invention is directed to methods and compositions useful for tumor localization and/or therapy using radiolabeled antibodies to intracellular tumor-associated antigens." (emphasis omitted)); id. at 5 ("There is no suggestion that antigens which are not located on the surface of the tumor cell may be used in a similar manner."); Response to Office Action Dated October 29, 1981, at 5 ("Applicant was the first to envision the use of antibodies to intracellular antigens . . . .").