

United States District Court,
C.D. California, Western Division.

UNIVERSITY OF PITTSBURGH OF the Commonwealth SYSTEM OF HIGHER EDUCATION,
Plaintiff.

v.

Marc H. HEDRICK, Prosper Benhaim, Hermann Peter Lorenz, and Min Zhu,
Defendants.

No. CV 04-9014 CBM (AJWJx)

Feb. 13, 2007.

Adam Perlman, Dane H. Butswinkas, David I. Berl, David S. Blatt, Glenn J. Pfadenhauer, Matthew J. Peed, Williams & Connolly LLP, Washington, DC, Alan A. Garfinkel, University of Pittsburgh, Pittsburgh, PA, Gary A. Clark, Sheppard Mullin Richter and Hampton, Los Angeles, CA, for Plaintiff.

Erin Dunston, Bingham McCutchen LLP, Malcolm K. McGowan, Bingham McCutchen, Washington, DC, George L. Fox, Bingham McCutchen, San Francisco, CA, James B. Lewis, Bingham McCutchen, East Palo Alto, CA, Jeffrey M. Olson, Sandra S. Fujiyama, Sidley Austin, Ryan M. Nishimoto, Bingham McCutchen, Los Angeles, CA, for Defendants.

**ORDER DENYING IN PART AND GRANTING IN PART PLAINTIFF'S AND DEFENDANTS'
MOTIONS FOR CONSTRUCTION OF THE CLAIMS**

CONSUELO B. MARSHALL, District Judge.

The matters before the Court, the Honorable Consuelo B. Marshall, presiding, are Plaintiff's and Defendants' Motion for the Court to Construe the Claims of U.S. Patent No. 6,777,231. The Court has considered both parties' briefs and oral argument made during a *Markman* hearing.

JURISDICTION

The Court has jurisdiction pursuant to 28 U.S.C. s. 1331.

INTRODUCTION

This case involves the proper inventors of Patent No. 6,777,231 ("the 231 Patent"), a patent for the invention of stem cells derived from fat tissue. There is a dispute over the correct inventors of the patent. "An inventorship analysis, like an infringement or invalidity analysis, begins as a first step with a construction of each asserted claim to determine the subject matter encompassed thereby." *Trovan, Ltd. v. Sokvmat Sa*, 299 F.3d 1292, 1302 (Fed.Cir.2002). The parties have asked the court to construe the following five terms that appear within the ten claims of the '231 Patent: (1) adipose-derived, (2) stem cell, (3) multi-potent cell, (4) isolated, and (5) substantially homogeneous population.

BACKGROUND AND PROCEDURAL HISTORY

On October 29, 2004, University of Pittsburgh ("UPitt") filed a complaint against Drs. Mark Hedrick, Prosper Behnhaim, H. Peter Lorenz and Min Zhu ("Defendants") to remove Defendants from the '231 Patent because they were not the proper inventors. On February 9, 2006, pursuant to a stipulation, Defendants filed an amended answer that contained a counterclaim, arguing that UPitt and Drs. Williams W. Futrell, Adam Katz, and Ramon Llull ("the UPitt inventors") were not the true inventors of the patent. The UPitt inventors were allowed to intervene as a result of the February 9, 2006 stipulation. On June 20, 2006, Dr. Futrell conceded that he was not an inventor of the patent at issue and the Court granted an unopposed motion to dismiss him from the case.

Now, both parties move to have the Court construe five claims within the ' 231 Patent. The Court held a *Markman* hearing on the issue of claims construction.

LEGAL STANDARD

Claims define the legal scope of the invention and claim construction is a question of law. *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 979 (Fed.Cir.1995). "[T]he definition in the specification controls the meaning of [the term], regardless of any potential conflict with the term's ordinary meaning as reflected in technical dictionaries." *3M Innovative Props. Co. v. Avery Dennison Corp.*, 350 F.3d 1365, 1374 (Fed.Cir.2003). If there is no clear definition in the specification, the words of a [patent] claim are generally given their ordinary and customary meaning, i.e. "the meaning that the term would have to a person of ordinary skill in the art in question ... as of the [patent's] effective filing date." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312-13 (Fed.Cir.2005) (en banc); *Ventana Medical Systems Inc. v. Biogenex Lab.*, 473 F.3d 1173, 1180 (Fed.Cir.2006). "In some cases, the ordinary meaning of claim language as understood by a person of skill in the art may be readily apparent even to lay judges, and claim construction in such cases involves little more than the application of the widely accepted meaning of commonly understood words." *Id.* at 1314.

The patent specification is central to a determination of "the meaning of a claim term as it is used by the inventor in the context of the entirety of his invention." *Comark Comm'ns v. Harris Corp.*, 156 F.3d 1182, 1187 (*Fed. Cir.* 1998). The patent 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." *Phillips*, 415 F.3d at 1315 (quoting *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed.Cir.1996)). "The construction that stays true to the claim language and most naturally aligns with the patent's description of the invention [in the specification] will be, in the end, the correct construction." *Id.* at 1316 (quoting *Renishaw PLC v. Marposh Societa' Per Azioni*, 158 F.3d 1243, 1250 (Fed.Cir.1998)). Although a patent claim may at times contain terms that do not appear in the specification, all "terms and phrases used in the claims must find clear support or antecedent basis in the [specification] so that the meaning of the terms in the claims may be ascertainable by reference to the [specification]." *Tandon Corp. v. U.S.I.T.C.*, 831 F.2d 1017, 1024 (Fed.Cir.1987); *see Lockwood v. Am. Airlines, Inc.*, 107 F.3d 1565, 1572 (Fed.Cir.1997).

CLAIM CONSTRUCTION

1. The Construction of "Adipose-Derived"

Plaintiffs contend that "adipose-derived stem cell" means that the cell is "derived from fat tissue."

Defendants do not dispute that "adipose-derived stem cell" means a cell that was "derived from fat tissue" but Defendants contend that the full construction of the term is a "stem cell that is obtainable from fat tissue, but is a species of stem cell distinct from the mesenchymal stem cell ("MSC") that is obtainable from bone marrow tissue." Defendants contend that by not including the additional language that an adipose-derived stem cell is a "species of stem cell distinct from the mesenchymal stem cell that is obtainable from bone marrow tissue," Plaintiffs ignore the distinction drawn in the specification and prosecution history and do not sufficiently distinguish the claimed stem cell from prior art stem cells. (Def. Motion, 15: 12-15.) The Court must address several factors to determine if the Defendant's additional language should be included in the construction of the term.

A. Whether the Prosecution History Supports the Additional Language

In construing claims, Courts consider the prosecution history to determine "whether the patentee disclaimed or disavowed subject matter, narrowing the scope of the claim terms." *Nystrom v. Trex Co.*, 374 F.3d 1105, 1113 (Fed.Cir.2004). The standard for adding a limitation to a claim based on prosecution history requires that the alleged statements disavowing the language in the specification be so clear as to show reasonable clarity and deliberateness. *Omega Eng'g, Inc. v. Raytek Corp.*, 334 F.3d 1314, 1325 (Fed.Cir.2003). For prosecution disclaimer to attach the alleged disavowing actions or statements made during prosecution must "be both clear and unmistakable." *Id.* at 1326.

Here, adding the language of "stem cell that is obtainable from fat tissue, but is a species of stem cell distinct from the mesenchymal stem cell ("MSC") that is obtainable from bone marrow tissue" to the construction of the term "adipose derived" narrows the scope of the claim term. Accordingly, the Court looks to the prosecution history for a clear disavowal that supports narrowing the scope of the term.

Defendants state that the prosecution history of the '231 patent compels the interpretation that the adipose-derived stem cell is distinct from the MSC because the patentability of the claimed invention rested on the claimed cell being distinct from prior art. Def. Motion, 15: 21-24. Furthermore, Defendant contends that the '231 claim was patentable because the actual product or cell was different than the MSC-not because of a novel process by which the cell is obtained. *See SmithKline Beecham Corp. v. Apotex Corp.*, 439 F.3d 1312, 1318 (Fed.Cir.2006) ("anticipation by an earlier product patent cannot be avoided by claiming the same product more narrowly in a product-process claim"); *Fox Decl.*, Ex. A at 64:19-65:5. In support of this contention, Defendants cite that the '231 claim was originally rejected because it was too closely related to the patent disclosing MSCs obtained from bone marrow. Def. Mot. 15:24-25-16:1. During an in-person interview, the patent applicants and the patent examiner agreed "that a submission to distinguish between the adipose derived stem cell and bone marrow derived stem cell will be submitted." *Tiu Deck*, Ex. B at 299. The patent applicant and the examiner agreed that "the adipose derived stem cells are distinct from mesenchymal stem cells derived from Pittenger et. al. (prior art)." *Id.* at 301. In response, patent applicants submitted a scientific publication describing the work, which Defendants' expert explains as confirming "the results shown in Example 2 of the '231 patent by demonstrating that the adipose-derived stem cells and bone marrow derived stem cells are phenotypically distinct." FN1 *Tiu Decl.*, Ex. F at 12. The ' 231 patent was issued. *Tiu Decl.*, Ex. N at 82:18-83:15. Defendant contends that the examiner's acceptance of the applicant's submission constitutes evidence of clear disclaimer. *See Elkay Mfg. Co. v. Ebco Mfg. Co.*, 192 F.3d 973, 979 (Fed.Cir.1999).

Plaintiffs contend that the prosecution history does not provide a basis for adding an extraneous limitation to the meaning of "adipose-derived" because there is no clear and unmistakable language disavowing the

language in the specification. *Plaint. Opp.*, 5:17-19. During patent prosecution the Examiner rejected claims anticipated by the prior art discussing stem cells derived from bone marrow. *Skinner Decl.*, Ex. P at 3-4. In response to the rejection, the applicants explained that the prior patent "does not teach the claimed multipotent stem cells derived from adipose tissue or a population of these stem cells." *Skinner Decl.*, Ex. Q at 8. The applicant's explanation pointed out how the claimed stem cells were different from the prior art, but did so without a clear disavowal to the meaning of adipose-derived as being "obtained from fat tissue" or other disavowing language that would clearly suggest a narrower scope of the claim term.

B. Whether the Patent Specification Supports the Additional Language

The patent 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." *Phillips*, 415 F.3d at 1315 (quoting *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed.Cir.1996)). The specification gives this Court guidance to the construction of adipose-derived.

The "Background of the Invention" section of the '231 patent follows the development of the identification of MSCs, chiefly obtained from bone marrow. It states the advantages of MSCs and cites the drawbacks to using cells obtained from bone marrow. Following this discussion, the Background states, "there is a need for a more readily available source for pluripotent stem cells, particularly cells that can be cultured without the requirement for costly prescreening of culture materials." The brief summary of the invention states that the "present invention provides adipose-derived stem cells and lattices." In the Patent's Detailed Description of the Invention, it states that:

One aspect of the invention pertains to a lipo-derived stem cell. Preferably the stem cell is substantially free of other cell types (e.g. adipocytes, red blood cells, other stromal cells, etc.) and extracellular matrix material; more preferably, the stem cell is completely free of such other cell types and matrix material. Preferably, the inventive cell is derived from the adipose tissue [sic] of a primate, and more preferably a higher primate (e.g., a baboon or ape). Typically, the inventive cells will be derived from human adipose tissue, using methods such as described herein.

While the inventive cell can be any type of stem cell, for use in tissue engineering, desirably the cell is of mesodermal origin ...

Skinner Decl., Ex. F at 70-71.

The specification does distinguish between the claimed cells and MSCs. The specification does not, however, state that an adipose-derived cell is a species of stem cell distinct from the mesenchymal stem cell ("MSC") that is obtainable from bone marrow tissue.

C. The Plain Meaning of "Adipose Derived"

If there is no clear definition in the specification, the words of a [patent] claim are generally given their ordinary and customary meaning, i.e. "the meaning that the term would have to a person of ordinary skill in the art in question ... as of the [patent's] effective filing date." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312-13 (Fed.Cir.2005) (en banc).

Plaintiffs dispute the addition of the latter part of Defendants' construction on the basis that Defendants' construction strays from the plain meaning of the term. The meaning of the term "adipose-derived," is

simply that-a stem cell derived from adipose tissue (fat tissue). The patent explains that "the inventive stem cell can be obtained from adipose tissue by any suitable method," including liposuction. Skinner Decl., Ex. F at 70. Even Defendants' expert concedes that the meaning of adipose-derived is "pretty obvious," it means "it comes from fat." Skinner Decl, Ex. N. 131:22-132:9. The plain meaning of adipose-derived to those skilled in the art, is "derived from adipose tissue (fat)."

D. Conclusion

Accordingly the Court construes "adipose-derived" to mean "derived from fat tissue" without the added limitation that it be distinct from the mesenchymal stem cell that is obtainable from bone marrow tissue.

2. The Construction of "Stem Cell"

Defendants' construction of "stem cell" is "a type of cell that meets the following criteria: (1) the ability to self-renew and (2) the ability of a clonal population of the cells to differentiate into at least two discrete developmental pathways." Plaintiffs contend that "stem cell" should be construed as it is defined in the '231 patent, as "a pluripotent cell that has the capacity to differentiate in accordance with at least two discrete developmental pathways," the same definition that is contained in the '231 patent. The parties agree that the cell must have the capacity to differentiate into two discrete developmental pathways. The parties' constructions differ on (1) whether the meaning of "stem cell" requires self-renewing" capability and (2) whether "stem cell" requires the ability of a clonal population to self-renew while maintaining pluripotency so as to distinguish it from progenitor cells.

A. Whether the Court Should Construe "Stem Cell" Consistent with the Definition of "Stem Cell" Provided in the '231 Patent

"[T]he definition in the specification controls the meaning of [the term], regardless of any potential conflict with the term's ordinary meaning as reflected in technical dictionaries." 3M Innovative Props. Co. v. Avery Dennison Corp., 350 F.3d 1365, 1374 (Fed.Cir.2003). "[T]erms in a patent document are construed with the meaning with which they are presented in the patent document." Phillips, 415 F.3d at 1316. "[C]ases recognize that the specification may reveal a special definition given to a claim term by the patentee that differs from the meaning it would otherwise possess. In such cases, the inventor's lexicography governs." *Id.* If there is no clear definition in the specification, however, the words of a patent claim are generally given their ordinary and customary meaning, i.e. "the meaning that the term would have to a person of ordinary skill in the art in question ... as of the [patent's] effective filing date." Phillips, 415 F.3d at 1312-13.

Defendants' would like the Court to construe the definition of stem cell "to ensure that the court's understanding of the technical aspects of the patent is consistent with that of a person of skill in the art, or to establish that a particular term in the patent or the prior art has a particular meaning in the pertinent field." Phillips, 415 F.3d at 1318. Defendants contend that those skilled in the art understand self-renewal capacity to be a fundamental requirement of a stem cell. Defendants' expert states that the '231 patent "explicitly and unequivocally recognizes that a stem cell must also have the capacity for self-renewal; that is, it must be able to produce many generations of new undifferentiated cells." Tiu Decl., Ex. F at 681.

Defendants' expert cites the patent language that the cells can be maintained in an undifferentiated state for many passages "proving that the cells are indeed stem cells and not merely committed progenitor cells." *Id.* He states that the "ordinary and customary meaning of the term "stem cell" to a person of ordinary skill in the art in March 2000 would have been an undifferentiated cell that has the capacity to self-renew and the

capacity to differentiate into multiple lineages." Id., at 682; see Tiu Decl., Ex. E at 496 (stating "all stem cells share at least two characteristics. First they can make identical copies of themselves for long periods of time; this ability to proliferate is referred to as a long-term self-renewal.")

Defendants contend that a stem cell's ability to clonally self-renew is crucial to distinguishing the stem cell from a mixture of progenitor cells. In support of this proposition, Defendants point to the '462 Prov. Appl. (to which the '231 patent claims priority), stating that cloning was needed to definitively show that a "heterogeneous cell population" contains "adipose-derived stem cells" rather than multiple progenitor cells. Tiu. Decl., Ex. D at 442. Defendants cite UPITT's experts recognition of cloning to distinguish multipotent stem cells from a mixture of progenitor cells. Tiu Decl., Ex. L at 758.

Plaintiffs contend that the Court should construe "stem cell" as it is defined in the patent. The specification of the '231 patent states "the following terms are defined as follows ... A stem cell is a pluripotent cell that has the capacity to differentiate in accordance with at least two discrete developmental pathways." Skinner Decl., Ex. F at 17:52-18:12. The definition in the patent does not include the stem cell's ability to self-renew.

Stem cell is clearly defined in the patent. Defendant's reliance on experts and scientific articles to define "stem cell" is informative as to the term's definition to those generally skilled in the art, however, the Court must rely on the definition of the term given within the patent itself. Phillips, 415 F.3d at 1317 ("while extrinsic evidence 'can shed useful light on the relevant art,' we have explained that it is "less significant than the intrinsic record in determining 'the legally operative meaning of claim language" ').

Aside from the patent's clear definition of "stem cell," the specification further supports Plaintiffs' definition of stem cell. In the Detailed Description of the Invention, the specification states "whether clonal or not, the isolated cells can be cultured to a suitable point when their developmental phenotype can be assessed." Skinner Decl., Ex. F at 71 (4:60-63). This further suggests that stem cells, as used here, are not assessed based upon the cell's ability to form a clonal population.

B. Conclusion

Accordingly, the Court construes the term "stem cell" according to Plaintiffs' construction of the term: "a pluripotent cell that has the capacity to differentiate in accordance with at least two discrete development pathways." The Court does not construe the claim to be dependant upon the stem cell's ability to self-renew.

3. The Construction of "Multipotent Cell"

The parties agree that "multipotent" and "stem cell" have the same meaning. Accordingly, the Court construes "multipotent cell" as "a pluripotent cell that has the capacity to differentiate in accordance with at least two discrete developmental pathways."

4. The Construction of "Isolated"

At oral argument, Plaintiffs conceded to use Defendants' construction of "isolated." Accordingly, "isolated" should be construed as "in an environment substantially free of other cellular or extracellular materials found in adipose tissue."

5. The Construction of "Substantially Homogeneous"

Plaintiffs and Defendants disagree on the term substantially homogeneous as used in Claim 5. The parties' constructions differ on whether or not the term should be construed to require a clonal population of cells. Defendants construe the term "substantially homogeneous" to mean a "clonal population or close to the purity of a clonal population including only minor contaminants that do not materially affect the basic and novel properties of the invention." Plaintiffs define "substantially homogeneous" as "consisting essentially of adipose-derived stem cells" but do not include a requirement that would suggest the population must be clonal.

A. Doctrine of Claim Differentiation as Support for Narrowing the Scope of Substantially Homogeneous

During the *Markman* hearing Defendants argued that the doctrine of claim differentiation supports their construction of "substantially homogeneous." "Each claim in a patent is presumptively different in scope." *Ecolab, Inc. v. Paraclipse, Inc.*, 285 F.3d 1362, 1365 (Fed.Cir.2002). "Dependant claims are generally narrower in scope than the claims from which they depend." *Glaxo Group Ltd. v. Ranbaxy Pharms., Inc.* 262 F.3d 1333, 1336 (Fed.Cir.2001). Claim 5 of the '231 patent recites "[a] substantially homogeneous population of adipose-derived stem cells, comprising a plurality of the stem cell of claim 1, 3 or 4." Defendants argue that because Claim 5 is dependent on claim 1, 3 or 4, it must be narrower in scope than claim 1, 3 or 4, thus denoting a greater purity than that found in an "isolated" population. Defendants contend that a substantially homogeneous population consisting of a greater purity of adipose-derived stem cells supports the interpretation that the population is clonal. Defendants interpret the term "plurality" as supporting this notion by contending that the claimed population is made up of "multiple identical copies (i.e., clones) of the same stem cell claimed in claim 1, 3, or 4." Def. Mot., 23: 4-5.

B. Whether the Patent Specification Supports that the Cells Must be Clonal

In the Detailed Description of the patent, it states that "the population is substantially homogeneous, consisting essentially of the inventive lipo-derived stem cells. As the inventive cells can be cloned, a substantially homogeneous population containing them can be clonal." Skinner Decl., Ex. F at 72 (6:48-49). The specification's language as used in reference to the clonality of the inventive cells appears to allow for cloning by saying that the "inventive cells can be cloned" and that the "substantially homogeneous population containing them can be clonal." It does not, however, require that the cells be a "clonal population" as the Defendants suggest. Instead, a reading of the specification suggests the opposite.

The '231 Patent's Guide to Interpretation states that "the term 'consisting essentially of' indicates that unlisted ingredients or steps that do not materially affect the basic and novel properties of the invention can be employed in addition to the specifically recited ingredients or steps." Skinner Decl., Ex. F at 78 (18:13-18). "By using the term 'consisting essentially of,' the drafter signals that the invention necessarily includes the listed ingredients and is open to unlisted ingredients that do not materially affect the basic and novel properties of the invention." *PPG Indus. v. Guardian Indus. Corp.*, 156 F.3d 1351, 1354 (Fed.Cir.1998). Here, "consisting essentially of" is referring to the inventive lipo-derived cells denoting that the invention in claim 5 must include the lipo-derived cells and may only include other non-affective materials, but it does not suggest that the substantially homogeneous cells must be clonal.

C. Conclusion

Accordingly the Court construes the term "substantially homogeneous" in Claim 5 as "consisting essentially

of adipose-derived stem cells" as suggested by Plaintiffs.

CONCLUSION

On the basis of the foregoing, the Court DENIES in part and GRANTS in part Plaintiff's Motion for Construction of the Claims and Defendants' Motion for the Court to Construe the Claims of U.S. Patent No. 6,777,231.

IT IS SO ORDERED.

FN1. As addressed in Defendants' oral argument, the article differentiates MSCs and PLA cells stating "[P]reliminary results on PLA cells indicated that sera screening is not necessary for their expansion and differentiation ..., a requirement for MSCs", "MSCs do not undergo ... myogenic differentiation under the condition used in this study" for PLA, and PLA cells exhibited unique characteristics distinct from that seen in MSCs, including differences in CD marker and gene expression profiles." Tiu Decl., Ex. T at 893 & 881.)

C.D.Cal.,2007.

University of Pittsburgh of Com. System of Higher Educ. v. Hedrick

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