United States Court of Appeals for the Federal Circuit

RESTEM, LLC,
Appellant

v.

JADI CELL, LLC,
Appellee

2023-2054

Appeal from the United States Patent and Trademark Office, Patent Trial and Appeal Board in No. IPR2021-01535.

Decided: March 4, 2025

JOSEPH J. RICHETTI, Bryan Cave Leighton Paisner LLP, New York, NY, argued for appellant. Also represented by KEVIN C. HOOPER, ETHAN R. FITZPATRICK, ALEXANDER DAVID WALDEN; K. LEE MARSHALL, San Francisco, CA.

JED H. HANSEN, Thorpe North & Western, LLP, Salt Lake City, UT, argued for appellee. Also represented by MARK BETTILYON.

Before MOORE, *Chief Judge*, SCHALL and TARANTO, *Circuit Judges*.

MOORE, *Chief Judge*.

Restem, LLC (Restem) appeals from an *inter partes* review final written decision in which the Patent Trial and Appeal Board (Board) held Restem failed to prove claims 1–15 of U.S. Patent No. 9,803,176 were unpatentable. We affirm.

BACKGROUND

Jadi Cell, LLC (Jadi Cell) owns the '176 patent, which is directed to stem cells with specific cell markers (*i.e.*, the Claimed Cells) obtained from the subepithelial layer (SL) of mammalian umbilical cord tissue through a two-step process: (1) placing the SL in direct contact with a tissue culture growth substrate and (2) culturing the SL. '176 patent at 1:31–50, 2:9–28. Independent claim 1, a product-by-process claim, is representative:

> 1. *An isolated cell* prepared by a process comprising:
>
> *placing a subepithelial layer of a mammalian umbilical cord tissue in direct contact with a growth substrate*; and
>
> culturing the subepithelial layer such that the isolated cell from the subepithelial layer is capable of self-renewal and culture expansion,
>
> wherein the *isolated cell expresses* at least three cell markers selected from the group consisting of CD29, CD73, CD90, CD166, SSEA4, CD9, CD44, CD146, or CD105, and
>
> wherein the *isolated cell does not express* NANOG and at least five cell markers selected from the group consisting of CD45, CD34, CD14, CD79, CD106, CD86, CD80, CD19, CD117, Stro-1, or HLA-DR.

Id. at 19:5–19 (emphases added).

Restem challenged claims 1–15 of the '176 patent as inherently anticipated by Majore,[1] or, in the alternative, obvious in view of Majore, Phan,[2] or Kita,[3] in combination with five secondary prior art references. The Board held all challenged claims were not shown to be unpatentable. J.A. 1–77. Restem appeals. We have jurisdiction pursuant to 28 U.S.C. § 1295(a)(4)(A) and 35 U.S.C. § 141(c).[4]

DISCUSSION

I. Claim Construction

Claim construction is a question of law that may be based on underlying factual findings. *Kamstrup A/S v. Axioma Metering UAB*, 43 F.4th 1374, 1381 (Fed. Cir. 2022). We review the Board's claim construction de novo and any underlying factual findings for substantial evidence. *Id.*

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[1] Ingrida Majore et al., *Growth and Differentiation Properties of Mesenchymal Stromal Cell Populations Derived from Whole Human Umbilical Cord*, STEM CELL REV. & REP. 7:17–31 (2011). J.A. 1931–45.

[2] Toan-Thang Phan & Ivor Jiun Lim, WO 2006/019357 A1 (published Feb. 23, 2006). J.A. 2167–2280.

[3] Katsuhiro Kita et al., *Isolation and Characterization of Mesenchymal Stem Cells From the Sub-Amniotic Human Umbilical Cord Lining Membrane*, STEM CELLS & DEV. 19(4):491–501 (2009). J.A. 1919–30.

[4] Restem has Article III standing to appeal due to Restem's uncontested "concrete plans for future activity that creates a substantial risk of future infringement." *Gen. Elec. Co. v. Raytheon Techs. Corp.*, 983 F.3d 1334, 1341 (Fed. Cir. 2020); Appellant's Br. 1–2.

A. "placing" step

The Board construed "placing a subepithelial layer of a mammalian umbilical cord tissue in direct contact with a growth substrate" to mean "to intentionally place umbilical cord tissue comprising the subepithelial layer so that it touches a growth substrate to permit cell culture." J.A. 20. The Board declined to import, from the specification, the additional steps of (1) isolating the SL from other umbilical cord tissue and (2) placing the isolated SL interior side down onto the growth substrate into its construction, because the specification does not uniformly require those steps in all disclosed embodiments. J.A. 20–24. The Board found that although Majore, Phan, and Kita all disclose placing umbilical cord tissue (which includes the SL) in environments fostering cell culture and replication and therefore teach the claimed two-step process as construed, J.A. 31–33, 59, 68, the references do not disclose the Claimed Cells because the prior art processes do not necessarily produce cells with the claimed cell marker expression profile, J.A. 40–43, 62–63, 70.

Restem argues the Board legally erred by implicitly construing the claims to require steps beyond the claimed two-step process. Appellant's Br. 32–46. Restem points to the Board's statement, "Majore's process differs from at least the interior-down embodiment disclosed in the '176 patent," J.A. 39, as evidence the Board imported limitations from the specification into the claims despite construing the "placing" step to not require placing the SL interior side down onto the growth substrate, J.A. 22–24; *see also* '176 patent at 8:42–58 (describing interior-down embodiment). Restem also points to the Board's finding that cell marker expression can be influenced by various "conditions" and "factors," *see, e.g.*, J.A. 28 n.18, 41, and argues the Board read requirements into the claims that were not described in the specification.

We do not agree with Restem that the Board's analysis constituted an implicit construction of the "placing" step beyond its stated construction. Instead, the Board made factual findings that supported its anticipation analysis. The Board's analysis of differences between Majore's process and the claimed process provided support for its factual finding that Majore's process steps do not necessarily produce cells with the claimed cell marker expression profile. J.A. 40. The Board's finding that conditions and factors can influence cell marker expression similarly provided support for its holding that Majore does not inherently anticipate claim 1 of the '176 patent. J.A. 43. We see no error in the Board's construction of the "placing" step.

B. "isolated cell"

The Board declined to construe "isolated cell," J.A. 17–18, but construed "expresses/does not express" to mean "the marker is confirmed present/absent relative to a control sample," which is "consistent with [the Board's] interpretation of 'isolated cell' as indicating a cell population," J.A. 28. The Board found the intrinsic evidence unclear because it does not define with particularity how a skilled artisan would have assessed a positive or negative result, and the Board looked to extrinsic evidence to assess how a skilled artisan would determine whether an isolated cell expresses or does not express the claimed cell markers. J.A. 26. The Board found both parties' experts agreed cell marker analysis was performed at a cell population level at the time of the invention. J.A. 26–27.

Restem argues the Board legally erred by implicitly construing "isolated cell" contrary to the express definition of the '176 patent. Appellant's Br. 47–50; '176 patent at 6:32–34 ("As used herein, the term 'isolated cell' refers to a cell that has been isolated from the subepithelial layer of a mammalian umbilical cord."). We agree the Board implicitly construed "isolated cell" as "a cell population," but see

no error in the Board's construction, which is supported by intrinsic evidence.

The claims and specification support this construction. The claim language refers to "isolated cell" in the context that it "expresses/does not express" certain cell markers. '176 patent at claim 1. It is undisputed a population of cells is used when determining whether a cell marker is expressed or not. J.A. 26–27; J.A. 1717 ¶ 54 (Restem Expert Rpt.). The "expresses/does not express" claim language thus supports a conclusion that the claimed "isolated cell" is "a cell population." The specification consistently describes the claimed invention as a "cell population." *See* '176 patent at 7:23–25 ("The present disclosure presents a novel discovery of an allogenic cell or stem cell population . . . ."); 7:42–45 ("Also described are methods of producing cell and stem cell populations . . . .").

The prosecution history also supports such a construction. At the start of prosecution, the examiner issued a restriction requirement regarding claims "drawn to a cell population." J.A. 1342. During prosecution, the examiner repeatedly referred to the claimed invention as a "cell population" or a "population of cells." J.A. 1006 ("the claims only contain limitations directed to a population of cells"); J.A. 1227 ("applicant's claimed cell population"). In the Notice of Allowance, the examiner's reason for allowance makes clear the claims are directed to a cell population. J.A. 909 ("Applicant's submission of an affidavit . . . establishes that the methods for isolating the claimed population produce a markedly different cell population than that of other methodologies.").

Restem argues "an isolated cell" should be construed as "one or more cells isolated from the SL of a mammalian umbilical cord" based on express lexicography in the specification. '176 patent at 6:29–34. We do not agree. Throughout prosecution, it was clear that the examiner only allowed the patentee to claim a cell population.

J.A. 1342; J.A. 1227; J.A. 1006; J.A. 909. The examiner states, consistent with the rest of the prosecution history, that "the claimed product by process limitations produce a population of isolated cells," and "[t]he claims only contain limitations directed to a population of cells." J.A. 953.

An applicant's acquiescence to an examiner's clear statements regarding claim scope can impact claim construction. *See Phillips v. AWH Corp.*, 415 F.3d 1303, 1317 (Fed. Cir. 2005) (en banc) ("[T]he prosecution history can often inform the meaning of the claim language by demonstrating how the inventor understood the invention and whether the inventor limited the invention in the course of prosecution, making the claim scope narrower than it would otherwise be."). It is not uncommon for an applicant to narrow the scope of their claims during prosecution. *Cf. PSN Illinois, LLC v. Ivoclar Vivadent, Inc.*, 525 F.3d 1159, 1166 (Fed. Cir. 2008) ("[D]uring prosecution, an applicant may have cancelled pending claims but not amended the specification to delete disclosure relevant only to the cancelled claims.").

Although the specification states "the term 'isolated cell' refers to a cell that has been isolated from the subepithelial layer of a mammalian umbilical cord," '176 patent at 6:32–34, the claim scope was narrowed during prosecution to a "cell population," *e.g.*, J.A. 909. We see no error in the Board's construction of "an isolated cell" as "a cell population."

II. Inherent Anticipation

Anticipation is a question of fact we review for substantial evidence. *Blue Calypso, LLC v. Groupon, Inc.*, 815 F.3d 1331, 1341 (Fed. Cir. 2016). Inherent anticipation requires "the disclosure of the prior art [be] sufficient to show that the natural result flowing from the operation as taught in the prior art would result in the claimed product." *SmithKline Beecham Corp. v. Apotex Corp.*, 403 F.3d 1331, 1343–44 (Fed. Cir. 2005) (cleaned up).

The Board found the cell marker expression profile distinguishes the Claimed Cells from other stem cells and is therefore limiting. J.A. 37. In particular, the Claimed Cells do not express the NANOG cell marker and at least five other cell markers from the eleven markers listed (*i.e.*, non-expression limitations). '176 patent at claim 1. The Board found Majore does not expressly disclose the non-expression limitations and Restem did not show Majore inherently meets the non-expression limitations. J.A. 39.

Restem argues that, once the process steps are met, the product is necessarily present. Appellant's Br. 50–59. In other words, Restem argues inherency is automatic for product-by-process claims, and the Board legally erred in finding Majore did not inherently anticipate claim 1 of the '176 patent. We do not agree.

A product-by-process claim is one where the product is defined, at least in part, in terms of the process by which it is made. *SmithKline Beecham Corp. v. Apotex Corp.*, 439 F.3d 1312, 1315 (Fed. Cir. 2006). In determining validity of such a claim, "the focus is on the product and not on the process of making it," because "an old product is not patentable even if it is made by a new process." *Amgen Inc. v. F. Hoffman-La Roche Ltd*, 580 F.3d 1340, 1369–70 (Fed. Cir. 2009). In determining infringement, however, "the focus is on the process of making the product as much as it is on the product itself." *Id.* at 1370. Restem's argument conflates the anticipation and infringement analyses for product-by-process claims by improperly shifting the analysis from whether the prior art discloses the *claimed product* to whether the prior art discloses the *claimed process*.

Substantial evidence supports the Board's finding that cells produced by Majore's process would not necessarily have the claimed cell marker expression profile and thus Majore does not inherently anticipate claim 1 of the '176 patent. The '176 patent does not address whether an isolated cell with a cell marker expression profile consistent

with claim 1 would always result from following the two-step process of (1) placing umbilical cord tissue on a growth substrate and (2) culturing the tissue. J.A. 39–40. And Restem did not provide any testing evidence to show cells produced by Majore's process would inevitably, as inherency requires, have the claimed cell marker expression profile. J.A. 38–39; *see In re Montgomery*, 677 F.3d 1375, 1380 (Fed. Cir. 2012) ("The inherent result must inevitably result from the disclosed steps . . . .").

The Board found, based on both parties' expert testimony and the prior art, cell marker expression can depend on a variety of factors, such as cell-to-cell interactions. J.A. 28 n.18, 41–42. Majore's cells are produced from umbilical cord tissue and would have different cell-to-cell interactions than cells produced from the SL alone, which would result in a different cell marker expression profile. J.A. 3813 ¶ 30, J.A. 3816 ¶¶ 32–33 (Jadi Cell Expert Rpt.); *compare* J.A. 1932 (Majore teaching umbilical cord tissue is "minced" and placed in culture flasks), *with* '176 patent at 8:34–58 (teaching the isolated cell is cultured, "[i]n one aspect," from the SL by removing "Wharton's Jelly or gelatinous portion[s] of the umbilical cord"). Restem argues the evidence the Board relied on is directed to cell markers generally, not the specific cell markers recited in claim 1, but contrary evidence is insufficient to overcome substantial evidence review. We affirm the Board's finding that Majore did not inherently anticipate claim 1 of the '176 patent as supported by substantial evidence.

III. Obviousness

Claim 9 recites: "The isolated cell of claim 1, wherein culturing comprises culturing in a culture media that is free of animal components." The Board determined claim 9 would not have been obvious for two independent reasons. J.A. 74. First, the Board found claim 9 would not have been obvious for the same reasons as claim 1—Restem had not shown the cells produced using Kita's

process would have the cell marker expression profile recited in claim 1, or that Majore or three other secondary references would cure the deficiencies when combined with Kita. *Id.*; *see also* J.A. 48–54, 67–72 (Board's obviousness analysis for claim 1). Second, the Board found the record evidence showing an animal component in the culture media favored Jadi Cell. J.A. 74.

Obviousness is a legal determination we review de novo. *Adidas AG v. Nike, Inc.*, 963 F.3d 1355, 1358 (Fed. Cir. 2020). We review any underlying factual findings for substantial evidence. *Id.*

Restem only challenges the Board's alternative basis regarding the record evidence. Appellant's Br. 59–60. Because Restem did not challenge the Board's conclusion that claim 9 is not obvious for the same reasons as claim 1, we need not reach the Board's alternative basis to affirm.

CONCLUSION

For the foregoing reasons, we affirm the Board's decision holding Restem failed to prove claims 1–15 of the '176 patent are unpatentable.

AFFIRMED