

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

BERKELEY LIGHTS, INC.,
Petitioner,

v.

THE UNIVERSITY OF BRITISH COLUMBIA,
Patent Owner.

IPR2021-01250
Patent 10,421,936 B2

Before KRISTINA M. KALAN, CHRISTOPHER M. KAISER, and
CHRISTOPHER L. OGDEN, *Administrative Patent Judges*.

OGDEN, *Administrative Patent Judge*.

DECISION
Denying Institution of *Inter Partes* Review
35 U.S.C. § 314

I. INTRODUCTION

Petitioner Berkeley Lights, Inc. (“Petitioner”)¹ filed a Petition (Paper 1, “Pet.”) under 35 U.S.C. §§ 311–319 requesting *inter partes* review of claims 1, 2, 4–6, 9, 10, 16, 18, 20, 21, 24, 28, and 29 of U.S. Patent No. 10,421,936 B2 (Ex. 1001, “the ’936 patent”). Patent Owner The University of British Columbia (“Patent Owner”)² filed a Preliminary Response (Paper 6, “Prelim. Resp.”).

Under the authority delegated to us by the Director under 37 C.F.R. § 42.4(a), we may only institute an *inter partes* review when “the information presented in the petition . . . and any response . . . shows that there is a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition.” 35 U.S.C. § 314(a); *see also* 37 C.F.R. § 42.108(c) (2020). Applying that standard, we do not institute an *inter partes* review, for the reasons explained below.

II. BACKGROUND

A. RELATED PROCEEDINGS

As related matters, the parties identify the following three pending U.S. district court cases: *AbCellera Biologics, Inc. v. Berkeley Lights, Inc.*, No. 5:20-cv-08627 (N.D. Cal. filed July 9, 2020); *AbCellera Biologics, Inc. v. Berkeley Lights, Inc.*, No. 5:20-cv-08626 (N.D. Cal. filed Aug. 25, 2020); *AbCellera Biologics, Inc. v. Berkeley Lights, Inc.*, No. 5:20-cv-08624 (N.D.

¹ Petitioner identifies itself as the real party in interest. Pet. 5.

² Patent Owner identifies itself and AbCellera Biologics Inc. as the real parties in interest. Paper 5, 1.

Cal. filed Sept. 16, 2020) (collectively, “parallel district court proceedings”). Pet. 5–6; Paper 5, 1. The District Court has stayed these proceedings pending the outcome of this and two other *inter partes* review proceedings. See Ex. 1035.

We also note that *inter partes* reviews IPR2021-01249 and IPR2021-01386 also involve the same parties and related technology.

B. THE '936 PATENT (EX. 1001)

The '936 patent describes methods, in the context of microfluidic devices, “for perfusing a cell with perfusion fluid,” so that “the gravitational forces acting on the cell to keep the cell at or near . . . a retaining position exceed the hydrodynamic forces acting on the cell to move it toward an outlet.” Ex. 1001, code (57).

Figure 4 of the '936 patent, reproduced below, is a cross-sectional view of a chamber and a channel of a microfluidic device while the chamber is being perfused with a fluid. Ex. 1001, 8:33–37.

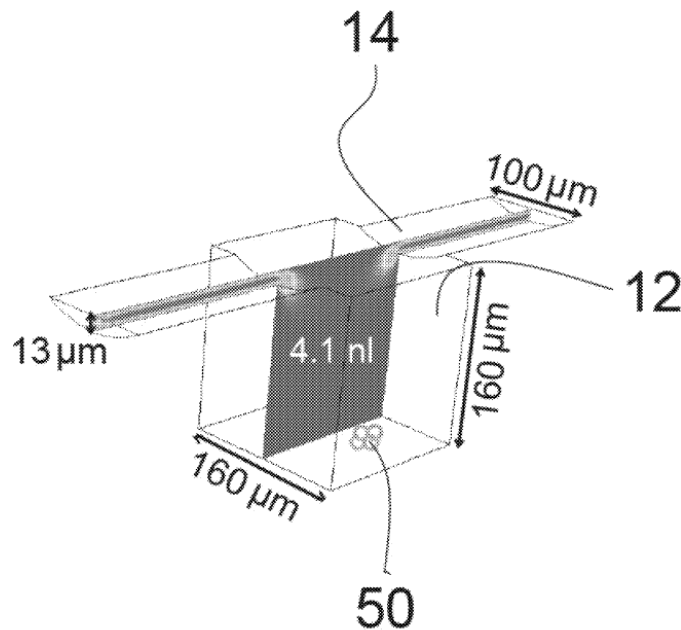


FIGURE 4

Figure 4, above, depicts culture chamber 12 (a cube of 160 μm on each side, forming a volume of about 4.1 nl) and flow channel 14 (100 μm wide and 13 μm deep at its deepest point). Ex. 1001, 34:19–21, 34:45–46, 35:66–36:1. Chamber 12 includes trapped cells 50. *Id.* at 34:17–18. The inventors discuss a numerical simulation that predicts a “sudden expansion when the fluid moves from the flow channel [14] to the chamber [12 that] creates a velocity drop,” and “minimal flow rates at the bottom 5/6 of the chamber.” *Id.* at 35:58–60, 36:1–3. “[T]he gravitational forces on the cells [are] greater than hydrodynamic forces and cells remain in the cell retaining region while the perfusion fluid exits the chamber through the flow channel outlet.” *Id.* at 26:3–7.

The '936 patent also discloses various means of measuring products secreted by cells 50 while they are within culture chamber 12, including “lineage staining; cell-surface protein staining; antibody staining; enzymatic

assay; RT-PCR analysis; PCR analysis; sequencing; functional assay; and bead capture assay to characterize the cells.” Ex. 1001, 6:47–51.

C. CHALLENGED CLAIMS AND ASSERTED GROUNDS OF
UNPATENTABILITY

Claim 1, representative of the challenged claims, reads as follows:

1. A method for selecting a cell, or a clone thereof, from a population of cells, comprising:

- [A] introducing the population of cells into 1,600 to 20,000 microfluidic chambers of a microfluidic device via a single introduction port, wherein each microfluidic chamber comprises an inlet, the single introduction port is in fluid communication with a flow channel that is in fluid communication with the inlets of the microfluidic chambers, and wherein individual cells of the population are retained in unique microfluidic chambers of the microfluidic device, and the cells are transported via the introduction port and flow channel into the unique microfluidic chambers;
- [B] providing a cell culture medium to the plurality of microfluidic chambers via the flow channel and the inlets of the chambers;
- [C] exchanging the cell culture medium in the individual microfluidic chambers via the flow channel and the inlets of the chambers, to create a plurality of individual clonal cell populations, wherein the individual clonal cell populations are retained in the same microfluidic chamber as their respective parental cells;
- [D] measuring a cell product secreted by the individual clonal cell populations, or subset thereof, within one or more of the microfluidic chambers; and
- [E] selecting one or more individual clonal cell populations from the plurality to provide one or more selected individual clonal cell populations.

Ex. 1001, 47:14–41 (Petitioner’s reference letters added).

Petitioner argues three grounds for *inter partes* review, as summarized in the following table:

Ground	Claims Challenged	35 U.S.C. §	Reference(s)/Basis
1	1, 2, 4–6, 9, 10, 16, 18, 20, 21, 24, 28, 29	103(a) ³	Lecault, ⁴ Diercks ⁵
2	1, 2, 4–6, 9, 10, 16, 28, 29	103(a)	Park, ⁶ Di Carlo ⁷
3	28, 29	103(a)	Lecault, Diercks, Di Carlo

Pet. 9.

D. DECLARATORY TESTIMONY

Petitioner relies on the declaration of Dr. Carl Meinhart. Ex. 1002. Patent Owner does not challenge Dr. Meinhart’s qualifications to provide

³ 35 U.S.C. §§ 103(a) (2006), *amended by* Leahy–Smith America Invents Act, Pub. L. No. 112-29 § 103, sec. (n)(1), 125 Stat. 284, 287, 293 (2011) (effective Mar. 16, 2013). This version of § 103 applies because the effective priority date of the ’936 patent (no later than Sept. 28, 2012) is before the effective date of the AIA amendments. *See* Ex. 1001, code (63); *infra* part III.C.4.

⁴ Véronique Lecault et al., *High-Throughput Analysis of Single Hematopoietic Stem Cell Proliferation in Microfluidic Cell Culture Arrays*, 8 Nature Methods 581 (2011) (“Lecault,” Ex. 1011).

⁵ Diercks et al., US 2007/0183934 A1 (published Aug. 9, 2007) (“Diercks,” Ex. 1008).

⁶ Joong Yull Park et al., *Single Cell Trapping in Larger Microwells Capable of Supporting Cell Spreading and Proliferation*, 8 Microfluidics & Nanofluidics 263 (2010) (“Park,” Ex. 1006).

⁷ Dino Di Carlo & Luke P. Lee, *Dynamic Single-Cell Analysis for Quantitative Biology*, Anal. Chem. 7918 (Dec. 1, 2006) (“Di Carlo,” Ex. 1010).

expert testimony on the subject matter of his declaration, but submits rebuttal testimony in the form of a declaration by Dr. Roberta Pelanda on the issue of whether Lecault is prior art to the '936 patent. Ex. 2008.

Petitioner also relies on the declaratory testimony of Dr. Ingrid Hsieh-Yee to establish the date of public availability for certain references. Ex. 1020. Patent Owner does not contest Dr. Hsieh-Yee's testimony at this preliminary stage.

III. GROUNDS OF THE PETITION

For the reasons below, we determine that Petitioner has not established that there is a reasonable likelihood that it would prevail in showing that at least one of the challenged claims is unpatentable under the grounds raised in the Petition. Before analyzing those grounds in detail, we first address the level of ordinary skill in the art, and whether we need to construe any claim terms explicitly for our analysis.

A. LEVEL OF ORDINARY SKILL IN THE ART

The level of ordinary skill in the pertinent art at the time of the invention is relevant to how we construe the patent claims. *See Phillips v. AWH Corp.*, 415 F.3d 1303, 1312–13 (Fed. Cir. 2005) (en banc). It is also one of the factual considerations relevant to obviousness. *See Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966).

To assess the level of ordinary skill, we construct a hypothetical “person of ordinary skill in the art,” from whose vantage point we assess obviousness and claim interpretation. *See In re Rouffet*, 149 F.3d 1350, 1357 (Fed. Cir. 1998). This legal construct “presumes that all prior art references

in the field of the invention are available to this hypothetical skilled artisan.” *Id.* (citing *In re Carlson*, 983 F.2d 1032, 1038 (Fed. Cir. 1993)).

Relying on Dr. Meinhart’s testimony, Petitioner argues that a person of ordinary skill in the art “would have had a bachelor’s degree in mechanical engineering, chemical engineering, biomedical engineering, molecular biology, (bio)chemistry, or an equivalent degree relevant to microfluidic biological cell analysis, and three to five years of experience with the construction of and application of microfluidic devices to cell culture and analysis.” Pet. 9 (citing Ex. 1002 ¶ 38).

Patent Owner does not dispute this proposed level of ordinary skill in its Preliminary Response. *See* Prelim. Resp. 5–6. Because it is supported by testimonial evidence and appears reasonable at this stage in light of the subject matter of the ’936 patent, we adopt Petitioner’s proposed level of ordinary skill in the art for this decision.

B. CLAIM CONSTRUCTION

In an *inter partes* review, we construe a patent claim “using the same claim construction standard that would be used to construe the claim in a civil action under 35 U.S.C. 282(b).” 37 C.F.R. § 42.100(b). This includes “construing the claim in accordance with the ordinary and customary meaning of such claim as understood by one of ordinary skill in the art and the prosecution history pertaining to the patent.” *Id.* The ordinary and customary meaning of a claim term “is its meaning to the ordinary artisan after reading the entire patent,” and “as of the effective filing date of the patent application.” *Phillips*, 415 F.3d at 1313, 1321. We also consider “[a]ny prior claim construction determination concerning a term of the claim

in a civil action . . . that is timely made of record” in this proceeding.
37 C.F.R. § 42.100(b).

Petitioner contends that “no terms require express construction for purposes of resolving the challenges in this proceeding.” Pet. 9; *accord* Pet. 12. But Petitioner notes that in the parallel district court proceedings, Patent Owner proposed a construction for the term “chamber” that differs from Petitioner’s proposed construction, and the parties disagree on whether the term “cell trap” in claim 6 invokes 35 U.S.C. § 112 para. 6. Pet. 10–11 (citing Ex. 1013, 6, 11–12 (Patent Owner’s proposed constructions); Ex. 1021, 9 (Petitioner’s proposed constructions); Ex. 1002 ¶ 44). Although Petitioner does not contend that its arguments rely on the choice of construction for these terms, Petitioner adopts Patent Owner’s constructions for its Petition. Pet. 11. In the parallel district court litigations, Patent Owner’s proposed construction for “chamber” is “an enclosed space within a microfluidic device.” Ex. 1013, 6.

In its Preliminary Response, Patent Owner contends that, because Petitioner relies on proposed explicit constructions Petitioner does not agree with, Petitioner does not satisfy the requirement of 37 C.F.R. § 42.104(b)(3) requiring a petitioner to identify “[h]ow the challenged claim is to be construed.” Prelim. Resp. 6–12.

Regardless of whether Patent Owner is correct that the Petition is deficient under § 42.104(b)(3), our decision not to institute does not depend on the construction of “chamber” or whether claim 6 invokes § 112 para. 6. Thus, we do not need to construe either term explicitly for our decision. *See Nidec Motor Corp. v. Zhongshan Broad Ocean Motor Co.*, 868 F.3d 1013, 1017 (Fed. Cir. 2017) (“[W]e need only construe terms ‘that are in

controversy, and only to the extent necessary to resolve the controversy.”
(quoting *Vivid Techs., Inc. v. Am. Sci & Eng’g, Inc.*, 200 F.3d 795, 803 (Fed.
Cir. 1999))).

C. GROUND S BASED ON LECAULT AND DIERCKS, WITH OR WITHOUT
DI CARLO (GROUND S 1 AND 3)

In its first ground, Petitioner contends that claims 1, 2, 4–6, 9, 10, 16, 18, 20, 21, 24, 28, and 29 would have been obvious over Lecault and Diercks. *See* Pet. 17–46. For its third ground, Petitioner alternatively contends that claims 28 and 29 would have been obvious over Lecault, Diercks, and DiCarlo. *See* Pet. 70–72. Thus, both of these grounds rely in part on Lecault. Petitioner argues that Lecault is prior art under 35 U.S.C. § 102(b) because, although the ’936 patent claims priority to applications that precede Lecault, one of these applications fails to provide written description support. Pet. 7, 12–17.

As we discuss below, we do not find persuasive, on the preliminary record, Petitioner’s arguments that Lecault is prior art to the ’936 patent. Thus, we determine that Petitioner is not reasonably likely to prevail on these grounds.

1. *Overview of Lecault*

Lecault is a journal article describing “a microfluidic platform containing thousands of nanoliter-scale chambers suitable for live-cell imaging studies of clonal cultures of nonadherent cells with precise control of conditions, capabilities for *in situ* immunostaining and recovery of viable cells.” Ex. 1011, 581. Two of the article’s authors are also named as inventors in the ’936 patent. *Compare id.*, with Ex. 1001, code (72).

Lecault indicates on its face that it was published online on May 22, 2011 and was corrected June 3, 2011, while the printed version is dated July 2011. *See* Ex. 1011, 581 (footer stating, “RECEIVED 13 DECEMBER 2010; ACCEPTED 15 APRIL 2011; PUBLISHED ONLINE 22 MAY 2011; CORRECTED ONLINE 3 JUNE 2011 (DETAILS ONLINE)”).

2. *Overview of Diercks*

Diercks describes “microfluidic devices and methods, useful for simultaneously analyzing multiple analytes in each of a plurality of distinct nanoliter-volume samples.” Ex. 1008, code (57); *accord id.* ¶¶ 2, 17. It has one named inventor in common with the ’936 patent. *Compare id.*, code (75), *with* Ex. 1001, code (72). In particular, Diercks discloses analyzing “antigen concentration, antibody concentration, analytes such as cytokines, chemokines, inflammatory mediators, and their receptors that are present in biological fluids” . . . , functionalized microsphere, eTags, labeled moieties, and the like.” *Id.* ¶ 3.

3. *Overview of Di Carlo*

Di Carlo describes microfluidic or array-based techniques for quantitatively analyzing single cells. *See* Ex. 1010. This includes, for example, “optical interrogation of individual cells integrated with fast exchange of reagents,” or “isolate[ing] individual cells along with a small volume of the surrounding environment” so that “biomolecules secreted by individual cells can be concentrated and analyzed.” *Id.* at 7922.

4. *Whether the '936 Patent Is Entitled to the Priority of the '213 Provisional Application*

For the first and last grounds of the Petition, Petitioner relies primarily on Lecault. According to Petitioner, Lecault is prior art because the '936 patent is not entitled to the priority date of any of its parent applications that precede Lecault's date of publication. *See* Pet. 12–17. Petitioner presents a visual timeline of the publication events, reproduced below:



Pet. 2. Petitioner's timeline posits that the Lecault publication date of no later than July 2011 is more than one year before the September 28, 2012 date of the '629 CIP application from which the '936 patent claims priority. Ex. 1001, code (63) ("Continuation of application No. 13/631,629, filed on Sep. 28, 2012, now abandoned, which is a continuation-in-part of application No. 13/178,395, filed on Jul. 7, 2011, now Pat. No. 10,087,408.").

Petitioner argues that Lecault discloses every step in the method of independent claim 1 except for limitation 1D, which is directed to measuring a secreted cell product. Pet. 2. For that limitation, Petitioner relies on

Diercks, arguing that Diercks “discloses measuring secreted factors, such as cyto[k]ines, in individual chambers of a microfluidic cell culture device.”

Pet. 26. Petitioner also compares dependent claims 2, 4–6, 9, 10, 16, 18, 20, 21, 24, 28, and 29 with the combination of Lecault and Diercks, and alternatively compares dependent claims 28 and 29 with the combination of Lecault, Diercks, and DiCarlo. *See* Pet. 35–46, 70–72.

Having considered Petitioner’s arguments, we are not persuaded that Petitioner has shown sufficiently that Lecault is prior art to the ’936 patent. Thus, for the reasons below, we determine that Petitioner has not shown a reasonable likelihood of prevailing on the first and third grounds of the Petition.

The ’936 patent claims priority (via the ’629 continuation-in-part application) to U.S. Application No 13/178,395, filed July 7, 2011 (“the ’395 application,” Ex. 1015) and U.S. Provisional Application No. 61/362,213, filed on July 7, 2010 (“the ’213 application,” Ex. 2003). Ex. 1001, codes (60), (63). The ’395 application and the ’213 application applications precede Lecault, which appears to have been published in mid-2011. *See* Ex. 1011, 581 (stating that the article was published online May 22, 2011).

However, Petitioner contends that the ’936 patent is not entitled to the priority date of at least the ’395 application because the ’395 application fails to disclose limitation 1D (“measuring a cell product secreted by the individual clonal cell populations, or subset thereof, within one or more of the microfluidic chambers; and”). *See* Pet. 13. According to Petitioner, when the applicant was asserting written description support, during prosecution, for what became claim 1 of the ’936 patent, the applicant only cited a later continuation-in-part application and not the earlier ’395 application. Pet. 13–

14. Petitioner also argues that, in every case where the '395 application mentions “measuring, quantifying, or counting,” it is referring to “measuring, quantifying, or counting cells themselves” or something else, but not secreted cell products. Pet. 14–15 (citing Ex. 1015, 3, 14, 31–32, 36, 47, 49).

Petitioner acknowledges that the '395 application includes a passage mentioning factors secreted from cells. Pet. 15 (citing Ex. 1015, 49 (“Co-culture of different cell types at limiting dilution could further be used to investigate the effect of cell–cell influences through secreted factors.”)). Petitioner contends, however, that “[t]hat one mention of secretion contains no reference to an individual clonal cell population, or a subset thereof, or to measuring anything, let alone a cell product secreted by an individual clonal cell population or subset thereof.” *Id.* According to Petitioner, “Factors secreted from a cell need not be measured in order to investigate how they affect other cells in a co-culture.” Pet. 15–16 (citing Ex. 1002 ¶ 42).

In its Preliminary Response, Patent Owner focuses primarily on whether the '213 provisional application—rather than the later '395 application—provides a written description sufficient to support limitation 1D. *See* Prelim. Resp. 12–13.⁸ Although Patent Owner focuses on an earlier application than the one Petitioner addresses in the Petition, we consider Patent Owner’s arguments responsive to Petitioner’s arguments because, as

⁸ Patent Owner argues that the Petition is deficient because it focuses only on the written description in the '395 application and does not address the earlier '213 provisional application. Prelim. Resp. 15, 18 & n.7. We do not need to address that argument because we do not consider Petitioner’s arguments directed to the '395 application sufficiently persuasive for us to institute an *inter partes* review.

Patent Owner notes, the “’395 application[] expressly incorporate[s] the ’213 provisional by reference.” Prelim. Resp. 12 (citing Ex. 1015, 3). Thus, to the extent that there is any material difference between the two applications, any disclosure in the ’213 provisional application is also a disclosure in the ’395 application. *See, e.g., Harari v. Lee*, 656 F.3d 1331, 1335 (Fed. Cir. 2011) (holding that asserting in an application that “[t]he disclosures of [two earlier] patent applications are hereby incorporate[d] by reference” was “broad and unequivocal” language sufficient to incorporate the entire earlier disclosures into the later application).

As an example of what it deems to be written-description support in the ’213 provisional application for limitation 1D, Patent Owner points to the disclosure of using the described microfluidic system for “‘functional analysis of single cells and their clonal progeny’ . . . , which a [person of ordinary skill in the art] would have understood to include measuring secreted products from single cells based on the full disclosure of the provisional application.” Prelim. Resp. 15 (quoting Ex. 2003, 2) (citing Ex. 2008 ¶¶ 21–32).

Patent Owner also points to a passage in the ’213 provisional application describing “the use of the invention for ‘the investigation of autocrine signaling by isolated cells’ and the ‘investigat[ion of] the effect of cell–cell influences through secreted factors.’” Prelim. Resp. 15–16 (alteration in original) (quoting Ex. 2003, 16). According to Patent Owner, “[t]his type of investigation of autocrine signaling and cell–cell influences routinely includes the same measuring of secreted cell products set forth in the challenged claims.” *Id.* at 16 (citing Ex. 2008 ¶¶ 22–24; Ex. 2010, 835).

Next, Patent Owner points to the '213 application's disclosure of an embodiment that uses "a bead-containing medium" or "bead capture" to characterize cells. Prelim. Resp. 16 (citing Ex. 2003, 5, 14). According to Patent Owner, a person of ordinary skill in the art "would have understood that such bead-containing media and bead-capture technology, including protein A or protein G beads, were commonly used to measure secreted cell products like antibodies, which can be used to characterize the cells." *Id.* (citing Ex. 2008 ¶¶ 26–27).

Finally, Patent Owner points to a passage in the '213 application teaching that the microfluidic device is "highly suitable for adaptation to other applications like recombinant protein production and cell characterization." Prelim. Resp. 17 (quoting Ex. 2003, 16). According to Patent Owner, a person of ordinary skill in the art "would have understood the mention of 'recombinant protein production' in the context of the '213 provisional as a disclosure of an application wherein proteins are the cell products secreted from the cells cultured in the chambers of the described device." *Id.* (citing Ex. 2008 ¶ 30).

Petitioner has the ultimate burden of persuasion on the question of whether a claim is entitled to the priority date of an earlier application. *See Dynamic Drinkware, LLC v. National Graphics, Inc.*, 800 F.3d 1375, 1379 (Fed. Cir. 2015). "[A] patent application is entitled to the benefit of the filing date of an earlier filed application only if the disclosure of the earlier application provides support for the claims of the later application, as required by 35 U.S.C. § 112." *In re Chu*, 66 F.3d 292, 297 (Fed. Cir. 1995). In particular, "[t]o be entitled to a parent's effective filing date, a continuation must comply with the written description requirement of 35

U.S.C. § 112, ¶ 1.” *In re Owens*, 710 F.3d 1362, 1366 (Fed. Cir. 2013) (citations omitted).

The test for the written description requirement “is whether the disclosure of the application relied upon reasonably conveys to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date.” *Ariad Pharm., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc). A prior application need not contain precisely the same words as are found in the asserted claims. *See Eiselstein v. Frank*, 52 F.3d 1035, 1038 (Fed. Cir. 1995); *Purdue Pharma LP v. Faulding Inc.*, 230 F.3d 1320, 1323 (Fed. Cir. 2000) (“In order to satisfy the written description requirement, the disclosure as originally filed does not have to provide *in haec verba* support for the claimed subject matter at issue.”). On the other hand, “[e]ntitlement to a filing date does not extend to subject matter which is not disclosed, but would be obvious over what is expressly disclosed.” *Lockwood v. Am. Airlines, Inc.*, 107 F.3d 1565, 1571–72 (Fed. Cir. 1997).

A key factor in this written description analysis, which Petitioner did not clearly address in its Petition, is the meaning of “measuring a cell product” in limitation 1D. The ’936 patent discloses that “[t]he measuring the cell product [step] may be selected from one or more of: lineage staining; cell-surface protein staining; antibody staining; enzymatic assay; RT-PCR analysis; PCR analysis; sequencing; functional assay; and bead capture assay to characterize the cells.” Ex. 1001, 6:47–51. This appears to be definitional, such that the meaning of “measuring a cell product secreted by the individual clonal cell populations, or subset thereof,” as in limitation 1D, would include using any one of these listed techniques to analyze cell secretion products. This passage is also consistent with the other claims in

the '936 patent, such as claim 18, which depends from claim 1 and further states that the “measuring the cell product” step “comprises flowing a fluid comprising an immunostaining agent, an enzymatic reagent, a dye or a functionalized bead into the individual chambers.” *Id.* at 48:29–32; *see also id.* at 48:33–48 (similar limitations in claims 19–23).

As Patent Owner persuasively shows on the present record, the '213 application discloses many of these analytical techniques, including staining, functional assay, and bead capture. *See* Prelim. Resp. 15–17. We also find persuasive Dr. Pelanda’s testimony that a person of ordinary skill in the art would have understood that the references in the '213 application to these analytical techniques relate to analysis of secreted cell products, and that a particular focus of the '213 application was to use the microfluidic device for analyzing autocrine signaling, which involves detecting or analyzing cell secretions. *See* Ex. 2008 ¶¶ 22–32.

For the above reasons, on the present record, Petitioner has not shown sufficiently that the '213 application lacks disclosure such that Lecault is prior art to the challenged patent. Accordingly, we determine that Petitioner has not shown that there is a reasonable likelihood that it would prevail on its first and third grounds with respect to any of the challenged claims.

D. GROUND BASED ON PARK AND DI CARLO (GROUND 2)

For its second ground, Petitioner alleges that claims 1, 2, 4–6, 9, 10, 16, 28, and 29 are unpatentable under § 103(a) as obvious over Park in view of Di Carlo. Pet. 46–70.⁹

⁹ Petitioner erroneously omits claim 4 in its heading for Ground 2, but explicitly addresses claim 4 in its discussion. Pet. 46, 65.

A claim is unpatentable under § 103 if the differences between the claimed subject matter and the prior art are “such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains.” *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 406 (2007). For a combination of known elements that are not explicitly found together in the prior art, we consider “whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue.” *Id.* at 418 (citing *In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006)).

We base our obviousness inquiry on factual considerations including (1) the scope and content of the prior art, (2) any differences between the claimed subject matter and the prior art, (3) the level of skill in the art, and (4) any objective indicia of obviousness or non-obviousness that may be in evidence.¹⁰ *See Graham*, 383 U.S. at 17–18.

After considering the preliminary evidence in light of the *Graham* factors, we determine, for the reasons discussed below, that Petitioner has not shown sufficiently that the challenged claims would have been obvious over the combination of Park and Di Carlo.

1. Overview of Park

Park is a journal article describing “a flow method that enables single cell trapping in microwells with dimensions of 50 μm , a size sufficient to allow attachment and division of captured cells.” Ex. 1006, 263. According

¹⁰ At this stage, the parties do not identify any objective indicia of obviousness or non-obviousness, so this does not factor into our decision not to institute an *inter partes* review.

to Park, prior studies described methods for trapping multiple cells in each well, but “[s]ingle cell trapping is necessary to allow identification of differing cell phenotypes within a population of cells” and “enables observation of the direct descendants of single cells cultured under controlled biological conditions . . . , the analysis of intracellular compounds . . . , and the measurement of electrical functionality of cells.” *Id.* Thus, Park designed a triangular microwell array configured so that, “[o]nce a cell is captured, the cell presence in the microwell changes the flow pattern, thereby preventing trapping of other cells.” *Id.*

Figures 1a–c of Park are reproduced below:

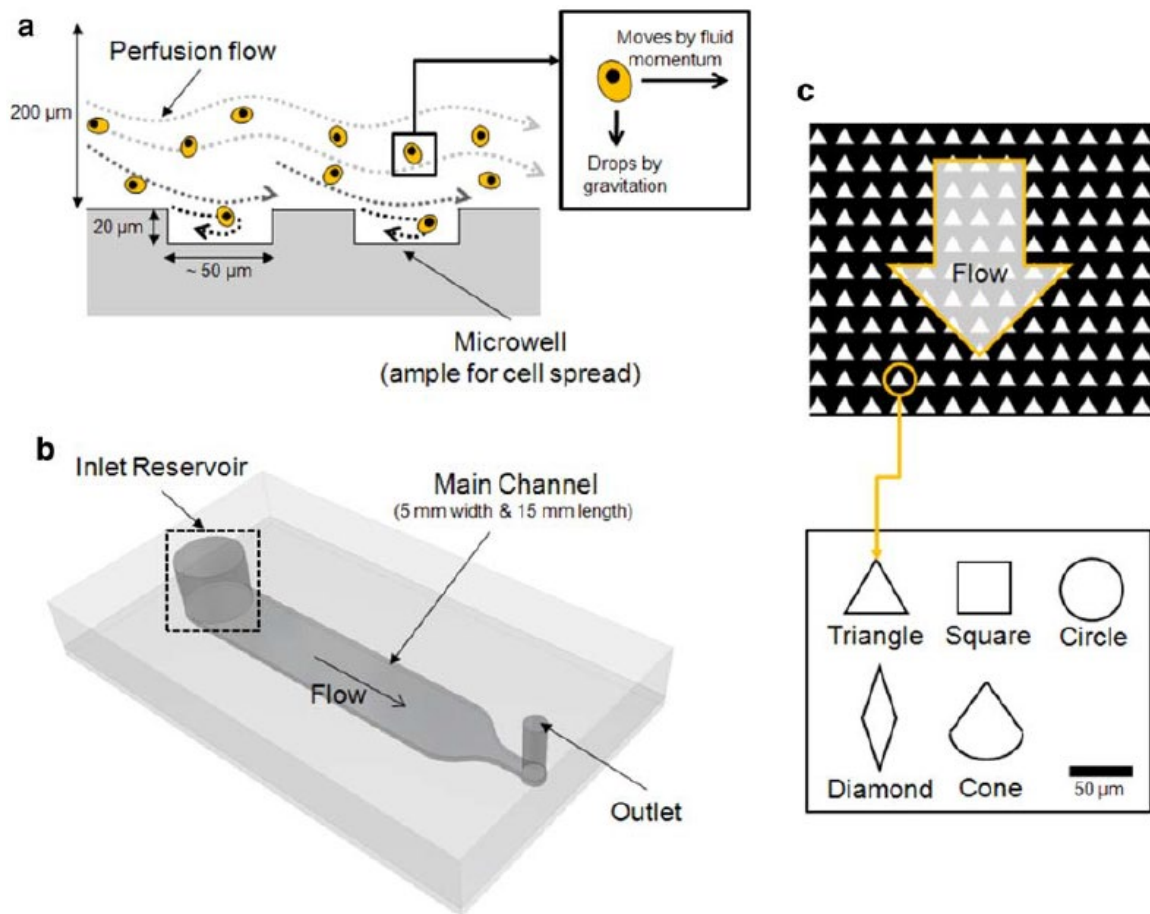


Figure 1b, above, shows the overall system, which includes an “inlet reservoir where the cell suspension is introduced, [a] main channel, microwells (not shown in the figure) patterned on the bottom surface of the main channel, and the outlet which is connected to a pulling syringe pump.”

Ex. 1006, 264. Figure 1a, above, is a cross-sectional view of the microwells (20 μm deep and 50 μm wide) and the main channel (200 μm deep). *Id.*

“During the perfusion of cell suspension in the channel, the cells sink gradually due to gravity, and some cells are caught in microwells while others pass and are carried away by flow.” *Id.* Figure 1c, above, shows various microwell shapes that the authors tested in simulation, and shows the orientation of triangular microwells compared to the flow direction. *Id.*

2. *Limitation 1C*

We focus our inquiry on Limitation 1C, which recites the step of “exchanging the cell culture medium in the individual microfluidic chambers via the flow channel and the inlets of the chambers, to create a plurality of individual clonal cell populations” Ex. 1001, 47:29–34. Petitioner argues that Park discloses this limitation “by loading the microwells of its device with a cell in culture medium and then flushing the system with more culture medium after loading.” Pet. 55; *see also* Pet. 55 (citing Ex. 1006, 268; Ex. 1002 ¶ 134) (arguing, in the context of limitation 1B, that the fact that the post-perfusion “flushing” step can use culture medium suggests that this step is “not just to remove excess cells, but also for purposes of delivering nutrients, for example, and as a necessary byproduct, removing waste, from the triangular microwells”).

In response, Patent Owner contends that Petitioner has failed to show that Park’s flushing step “involve[s] an exchange of culture medium to

create clonal cell populations, as required by the claimed inventions.”

Prelim. Resp. 23. Patent Owner argues, to the contrary, that “Park’s washout step occurs during the *loading procedure* of the cells, rather than a later culturing step.” *Id.* at 24. According to Patent Owner, “Park is focused on *preventing* flow into the wells during the washout step—the opposite of ‘exchanging the cell culture medium . . . to create a plurality of individual clonal cell populations.’” *Id.* (quoting Ex. 1001, 47:29–32).

Patent Owner also contends that “Park’s washout step takes place at a 0.18 mL/h rate for only 5 minutes.” Prelim. Resp. 25 (citing Ex. 1006, 267). By multiplying these numbers and converting units, Patent Owner calculates that “the wash step allows flushing of only 15 μ L of the fluid from Park’s device that has a ‘total volume of about 100 μ L.” *Id.* (quoting Ex. 1006, 265) (citing Ex. 1006, 267). Thus, according to Patent Owner, “[t]o exchange cell culture medium as described by the claimed invention with Park’s 5-minute washout step, Park’s rate of flow would need to be increased exponentially, which is specifically discouraged by Park to avoid ‘dislodg[ing] trapped cells.’” *Id.* (citing Ex. 1006, 268).

On the present record, we agree with Patent Owner that Petitioner has not sufficiently shown that Park’s flushing step introduces a sufficient volume of fluid into the individual microfluidic chambers to “exchange the cell culture medium” are recited in limitation 1C. Even if the flushing step did result in exchanging the culture medium, Petitioner has not adequately

explained if, or how, this brief exchange would suffice “to create a plurality of individual clonal cell populations.”¹¹

For the above reasons, we determine that Petitioner fails to “articulate specific reasoning, based on evidence of record, to support the legal conclusion of obviousness” as to independent claim 1. *In re Magnum Oil Tools Int’l, Ltd.*, 829 F.3d 1364, 1380 (Fed. Cir. 2016) (citing *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 418 (2007)). Because claims 2, 4–6, 9, 10, 16, 28, and 29 depend directly or indirectly on claim 1, the Petition is similarly lacking with respect to these claims. *See* Ex. 1001, 47:42–48, 47:51–57, 48:1–8, 48:25–26, 48:29–32, 48:37–42, 48:49–51, 48:58–61.

Thus, we determine that Petitioner has not shown that there is a reasonable likelihood that it would prevail on its second ground with respect to any of the challenged claims.

IV. CONCLUSION

After considering the evidence and arguments on the preliminary record, we determine that Petitioner has not demonstrated a reasonable likelihood of showing that at least one challenged claim of the ’936 patent is unpatentable. Therefore, we deny the Petition.

¹¹ We make no determination as to whether this phrase is limiting, and Petitioner does not clearly indicate its position on this question in the Petition. *See* Pet. 55–57.

V. ORDER

In consideration of the foregoing, it is
ORDERED that the Petition is *denied*, and no trial is instituted.

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