

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

ALAMAR BIOSCIENCES, INC.,
Petitioner,

v.

OLINK PROTEOMICS AB,
Patent Owner.

IPR 2024-01353
Patent 7,883,848 B2

Before SUSAN L. C. MITCHELL, TAWEN CHANG, and
TIMOTHY G. MAJORS, *Administrative Patent Judges*.

CHANG, *Administrative Patent Judge*.

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

I. INTRODUCTION

Petitioner Alamar Biosciences, Inc. (“Petitioner”) filed a Petition for *inter partes* review of claims 1–20 of U.S. Patent No. 7,883,848 B2 (Ex. 1001, “the ’848 patent”). Paper 2 (“Pet.”). Patent Owner, Olink Proteomics AB (“Patent Owner”), timely filed a Preliminary Response. Paper 6 (“Prelim. Resp.”).

For the reasons provided below, we determine Petitioner has satisfied the threshold requirement set forth in 35 U.S.C. § 314(a). Because Petitioner has demonstrated a reasonable likelihood that at least one claim of the ’848 patent is unpatentable, we institute an *inter partes* review of all challenged claims on each of the Grounds raised in the Petition. *See SAS Inst., Inc. v. Iancu*, 138 S. Ct. 1348, 1359–60 (2018); *PGS Geophysical AS v. Iancu*, 891 F.3d 1354, 1360 (Fed. Cir. 2018) (interpreting the statute to require “a simple yes-or-no institution choice respecting a petition, embracing all challenges included in the petition”); 37 C.F.R. § 42.108(a).

A. Real Parties-in-Interest

Petitioner identifies itself as the real party-in-interest. Pet. 73. Patent Owner identifies itself, Olink Proteomics Inc., and Thermo Fisher Scientific Inc. as the real parties-in-interest. Paper 4, 2.

B. Related Matters

Petitioner and Patent Owner indicate the ’848 patent is the subject of litigation in *Olink Proteomics AB and Olink Proteomics Inc. v. Alamar Biosciences, Inc.*, C.A. No. 1:23-cv-01303-MN, pending in the United States District Court for the District of Delaware, which was filed on November 15, 2023. Pet. 73; Paper 4, 2.

C. The '848 Patent and Relevant Background

The '848 patent states that, “[t]o identify molecular networks, information concerning at least two molecular species must be gathered since there are at least two molecules involved in any interaction.”

Ex. 1001, 1:23–25. The '848 patent describes “[s]everal . . . approaches . . . in the art which can be utilized for interaction screening,” including protein microarrays, yeast two hybrid system, display techniques such as phage display, DNA templated synthesis (DTS), and proximity ligation. *Id.* at 1:57–5:13.

1. DNA Templated Synthesis (DTS)

The '848 patent teaches that “[i]n DTS, two molecules are forced together by using nucleic acids to allow the molecules to interact to a higher degree than if they were not brought in proximity,” for instance when “one of the molecules forced together is attached to a ‘template’ nucleic acid which specifically directs the second compound by direct hybridization of the nucleic acid attached to the second molecule.” Ex. 1001, 3:46–53.

The '848 patent states, however, that in at least one example of a DTS-based method, “the ‘template’ nucleic acid contains both tags used to identify the compounds which are forced together”; thus, “[t]o create interactions between all members of a library with n members with this approach, the number of ‘template’ oligonucleotides which have to be synthesized are in the range of $n^2/2$, since one specific oligonucleotide has to be synthesized for each individual interaction on the library.” *Id.* at 3:53–60. The '848 patent further notes that, in this DTS approach, “the link between nucleic acid identification tag and the molecules in the interaction depend on correct hybridization of one tag molecule to the template nucleic

acid. If any cross hybridization occurs then the link between the tag and the identity of the interaction is unreliable.” *Id.* at 4:5–10.

2. Proximity Ligation

The ’848 patent states that, according to the proximity ligation method,

targets are detected by utilizing two or more binders, e.g. antibodies, with known affinity to the target. The method is based upon the co-localization of the binder pair in the presence of a target. This target brings the binders into proximity, enabling ligation of nucleic acids located on the binder pair. Thus the joining of the nucleic acid becomes elevated in the presence of the target molecule. The nucleic acid can subsequently be quantified and the amount of nucleic acid corresponds to the amount of target.

Ex. 1001, 4:29–38.

The ’848 patent notes that an embodiment of the prior art proximity ligation method “aims at detection of a defined target.” Ex. 1001, 4:39–40.

The ’848 patent states that, thus,

[a]ll the affinities in the system are known and there is always at least one molecule, the target, which does not have a nucleic acid attached to it. Moreover, the [method] utilizes two or more binders which bind their unlabelled analyte pair-wise in a predefined manner. Several pairs might be used in the same reaction but they are always analyzed in a target specific pair wise fashion, not in a combinatorial fashion.

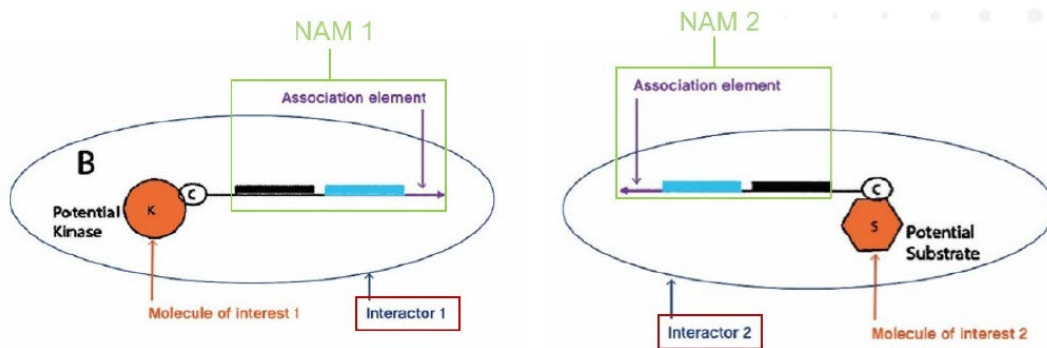
Id. at 4:40–47.

3. The Asserted Invention

The ’848 patent states that its invention is “directed to methods for discovering, as well as detecting molecular interaction networks such as

affinity interactions or functional interactions, e.g., enzymes-substrate pairs.” Ex. 1001, 5:22–25.

The ’848 patent teaches tagging “[e]ach molecule of interest (MOI) in [a] library . . . with . . . a nucleic acid moiety (NAM)” comprising “an identification sequence element and an association element,” in order to form “interactors.” Ex. 1001, 5:35–37, 6:7–11. An annotated and slightly modified version of Fig. 4(B) of the ’848 patent, which appears in Patent Owner’s Preliminary Response, is reproduced below:



Prelim. Resp. 17. The modified Fig. 4(B) provides a schematic depiction of two interactors and is annotated to show the molecules of interest, the NAMs, and the association element. *Id.* In addition, the portion of the NAMs that is color-coded blue in the annotated figure represents the “tag motif,” i.e., the identification sequence element. Ex. 1001, Fig. 4(A).

The ’848 patent teaches detecting functional interactions between molecules of interest by binding interactors in proximity to each other through the association of their NAMs, subjecting bound interactors to conditions that stimulate a desired functional interaction, selecting the interactors that interacted in the desired manner, and determining the identification sequence elements in the NAMs of the selected interactors. Ex. 1001, 6:4–23.

The '848 patent states that, in contrast to the DTS method, in its invention “nucleic acid encoding the tags to identify both members of the interaction are formed upon joining of the two molecules,” such that the number of oligonucleotides required to investigate all interactions in a library of n members is in the order of n , rather than $n^2/2$. Ex. 1001, 3:61–66. The '848 patent further states that in its invention “the link between the identification sequences in the associated nucleic acid molecule and the phenotype of the molecule is more effectively maintained.” *Id.* at 4:11–15. The '848 patent states that its invention differs from proximity ligation in that it does not rely on molecules with predefined affinities. *Id.* at 4:48–5:13.

D. Overview of Challenged Claims

Petitioner challenges claims 1–20 of the '848 patent. Claim 1, reproduced below, is the sole independent claim:

1. A method of detecting functional interactions between at least two molecules of interest, the method comprising:
 - a. forming a plurality of interactors by coupling each molecule of interest with at least one nucleic acid moiety, the nucleic acid moiety comprising an identification sequence element and an association element;
 - b. forming a plurality of cis-reactive cells wherein a cis-reactive cell comprises at least two interactors bound in proximity to one another by an associated oligonucleotide formed from the association between at least two nucleic acid moieties, wherein the associated oligonucleotide comprises at least two identification elements derived from the at least two nucleic acid moieties;
 - c. subjecting the plurality of cis-reactive cells to conditions which stimulate a desired functional interaction having a detectable trace;
 - d. selecting all cis-reactive cells exhibiting the detectable trace;and

- e. subjecting the associated oligonucleotides from the cis-reactive cells selected in step (d) to an analysis that permits detection of the at least two identification sequence elements.

Ex. 1001, 41:37–58.

E. Asserted Grounds of Unpatentability

Petitioner asserts the following grounds of unpatentability (Pet. 2–3):

Ground	Claims Challenged	35 U.S.C § ¹	Reference(s)/Basis
1	1–15, 17–20	103(a)	Kanan, ² Neri ³
2	16	103(a)	Kanan, Neri, Famulok ⁴
3	1–8, 11, 12	103(a)	Baez, ⁵ Landegren ⁶
4	14, 15	103(a)	Baez, Landegren, Freskard ⁷

Petitioner further relies, *inter alia*, on the Declaration of Norman C. Nelson, Ph.D. under 37 C.F.R. § 1.68 (Ex. 1005, “Nelson Declaration”).

¹ The Leahy-Smith America Invents Act (“AIA”), Pub. L. No. 112-29, 125 Stat. 284, 287–88 (2011), amended 35 U.S.C. § 103, effective March 16, 2013. Because the ’848 patent has an effective filing date before March 16, 2013, the pre-AIA version of § 103 applies. Our decision, however, would be the same under either version.

² Matthew W. Kanan et al., *Reaction Discovery Enabled by DNA-Templated Synthesis and In Vitro Selection*, 431 NATURE 545 (2004) (Ex. 1010, “Kanan” & Ex. 1013, “Kanan Suppl.”).

³ Neri et al., US 2004/0014090 A1, published Jan. 22, 2004 (Ex. 1011, “Neri”).

⁴ Michael Famulok, *Bringing Picomolar Protein Detection into Proximity*, 20 NATURE BIOTECHNOLOGY 448 (2002) (Ex. 1012, “Famulok”).

⁵ Baez et al., US 6,511,809 B2, issued Jan. 28, 2003 (Ex. 1003, “Baez”).

⁶ Landegren et al., WO 01/61037 A1, published Aug. 23, 2001 (Ex. 1004, “Landegren”).

⁷ Freskgard et al., WO 2005/003778 A2, published Jan. 13, 2005 (Ex. 1009, “Freskgard”).

II. ANALYSIS

A. Principles of Law

“In an [*inter partes* review], the petitioner has the burden from the onset to show with particularity why the patent it challenges is unpatentable.” *Harmonic Inc. v. Avid Tech., Inc.*, 815 F.3d 1356, 1363 (Fed. Cir. 2016) (citing 35 U.S.C. § 312(a)(3) (2012) (requiring *inter partes* review petitions to identify “with particularity . . . the evidence that supports the grounds for the challenge to each claim”)). This burden of persuasion never shifts to Patent Owner. *See Dynamic Drinkware, LLC v. Nat’l Graphics, Inc.*, 800 F.3d 1375, 1378 (Fed. Cir. 2015) (discussing the burden of proof in *inter partes* review). The Board may authorize an *inter partes* review if we determine that the information presented in the Petition and Patent Owner’s Preliminary Response shows a reasonable likelihood that Petitioner will prevail with respect to at least one of the claims challenged in the Petition. 35 U.S.C. § 314(a).

Petitioner contends that claims 1–20 would have been obvious under § 103 in view of (1) Kanan and Neri, (2) Kanan, Neri, and Famulok, (3) Baez and Landegren, and/or (4) Baez, Landegren, and Freskgard. Pet. 2–3. A claim is unpatentable under 35 U.S.C. § 103 if the differences between the subject matter sought to be patented 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. *See KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 406 (2007). The question of obviousness is resolved on the basis of underlying factual determinations 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 ordinary skill in the art; and (4) objective evidence of nonobviousness, if any. *Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966).

In analyzing the obviousness of a combination of prior art elements, it can be important to identify a reason that would have prompted one of skill in the art “to combine . . . known elements in the fashion claimed by the patent at issue.” *KSR*, 550 U.S. at 418. A precise teaching directed to the specific subject matter of a challenged claim is not necessary to establish obviousness. *Id.* Rather, “any need or problem known in the field of endeavor at the time of invention and addressed by the patent can provide a reason for combining the elements in the manner claimed.” *Id.* at 420.

Accordingly, a party that petitions the Board for a determination of unpatentability based on obviousness over a combination of references must show that “a skilled artisan would have been motivated to combine the teachings of the prior art references to achieve the claimed invention, and that the skilled artisan would have had a reasonable expectation of success in doing so.” *In re Magnum Oil Tools Int’l, Ltd.*, 829 F.3d 1364, 1381 (Fed. Cir. 2016) (internal quotations omitted).

We address Petitioner’s challenges with these standards in mind, and in view of the definition of the skilled artisan and the claim constructions discussed below.

B. Level of Ordinary Skill in the Art

Factual indicators of the level of ordinary skill in the art include “the various prior art approaches employed, the types of problems encountered in the art, the rapidity with which innovations are made, the sophistication of the technology involved, and the educational background of those actively working in the field.” *Jacobson Bros., Inc. v. U.S.*, 512 F.2d 1065, 1071 (Ct.

Cl. 1975); *see also Orthopedic Equip. Co. v. U.S.*, 702 F.2d 1005, 1011 (Fed. Cir. 1983) (quoting with approval *Jacobson Bros.*).

Relying on the Nelson Declaration, Petitioner asserts that a POSA⁸ for purposes of the '848 patent would have

- (a) an advanced degree, such as a Ph.D., in organic chemistry, molecular biology, biochemistry, or a related field; and at least two years of experience in industry and/or laboratory experience relating to small molecules and proteins and would have been familiar with nucleic acid chemistry and conventional hybridization techniques; and
- (b) access to one or more team members having an advanced degree, such as a Ph.D., in organic chemistry, molecular biology, biochemistry, or a related field; and at least two years of experience in industry and/or laboratory experience relating to high throughput screening techniques such as nucleic acid sequencing.

Pet. 11–12 (quoting Ex. 1005 ¶ 25). Petitioner further asserts “[a] person could also have qualified as a POSA with less formal education and more technical or professional experience.” *Id.*

Patent Owner states that, “[s]olely for the purposes of [the] Preliminary Response, [Patent Owner] does not contest Petitioner’s definition of a POSA.” Prelim. Resp. 15.

On the current record, for purposes of this Decision, we apply Petitioner’s proposed definition, as it appears consistent with the level of skill in the art reflected in the prior art of record and the disclosure of the '848 patent. *See Okajima v. Bourdeau*, 261 F.3d 1350, 1355 (Fed. Cir. 2001) (“the prior art itself [may] reflect[] an appropriate level” as evidence of the ordinary level of skill in the art) (quoting *Litton Indus. Prods., Inc. v. Solid State Sys. Corp.*, 755 F.2d 158, 163 (Fed. Cir. 1985)). We note,

⁸ “POSA” refers to “person of ordinary skill in the art.” Pet., cover page.

however, that the open-ended language “at least” expands the range of experience indefinitely with no upper bound. Therefore, we do not apply this aspect of Petitioner’s definition.

C. Claim Construction

We construe claims “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. Therefore, we construe the challenged claims under the framework set forth in *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312–19 (Fed. Cir. 2005) (en banc). Under this framework, claim terms are given their ordinary and customary meaning, as would be understood by a person of ordinary skill in the art, at the time of the invention, in light of the language of the claims, the specification, and the prosecution history of record. *Id.*

Petitioner states that, “[f]or Grounds 1 and 2, the claims are assumed to be given their plain and ordinary meaning based on the understanding of a POSA” and that, “[f]or Grounds 3 and 4, the claim terms are given meaning based on PO’s application of the claims in related litigation with Petitioner.” Pet. 12–13 (citing Exs. 1007, 1008, 1015). Petitioner asserts that, although “[t]here are no prior claim construction rulings on the ’848 patent . . . , [Patent Owner] filed a Complaint (Ex. 1007) and later provided an infringement chart (Ex. 1008) reflecting [Patent Owner’s] application of the claim terms.” *Id.* at 13 (footnote omitted).

Patent Owner does not address claim construction in the Preliminary Response, except to point out that the claim construction analysis in the Petition is allegedly deficient under 37 C.F.R. § 42.104(b)(3). Prelim. Resp. 11–14. We address this argument below.

We emphasize that any final written decision entered in this case may include express claim constructions, or may include discussion of claim scope that differs from that provided in our analysis below. Any final claim constructions will be based on the full trial record.

D. 37 C.F.R. § 42.104(b)(3)

Patent Owner asserts that Petitioner has not met its burden of stating “[h]ow the challenged claim is to be construed,” because the Petition “provides no guidance whatsoever regarding the constructions that Petitioner is asking the Board to apply.” Prelim. Resp. 12 (citing 37 C.F.R. § 42.104(b)(3)).

Patent Owner first argues that Petitioner applies different claim constructions in Grounds 1 and 2 as compared to Grounds 3 and 4, without “identify[ing] which claim terms it is construing” or “explain[ing] what constructions it is applying in each argument.” *Id.* at 11. In particular, Patent Owner argues that, “for Grounds 1 and 2, Petitioner provides no more than a generic assertion that ‘the claims are assumed to be given their plain and ordinary meaning based on the understanding of a [person of ordinary skill in the art]’” rather than constructions based on “[Patent Owner’s] position taken in the district court litigation with Petitioner.” *Id.* at 12–13. Patent Owner argues that, “[f]or grounds 3 and 4, Petitioner shifts what the alleged meanings of the claims are, arguing that the claims should now be ‘given meaning based on [Patent Owner’s] application of the claims in related litigation with Petitioner.’” *Id.* at 13.

As to Grounds 1 and 2, we find based on the preliminary record here that Petitioner has satisfied the requirements in 37 C.F.R. § 42.104(b)(3) by stating that the claims are to be construed as having “their plain and ordinary

meaning based on the understanding of a POSA.” Pet. 12. Although Petitioner bears the burden of stating “[h]ow the challenged claim is to be construed,” 37 C.F.R. § 42.104(b)(3), only those terms that are in controversy need be construed by the Board, and only to the extent necessary to resolve the controversy. *Vivid Techs., Inc. v. Am. Sci. & Eng’g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999); *see also Nidec Motor Corp. v. Zhongshan Broad Ocean Motor Co.*, 868 F.3d 1013, 1017 (Fed. Cir. 2017) (applying *Vivid Techs.* in the context of an AIA trial proceeding). Based on the preliminary record, we find it unnecessary to more explicitly construe any claim term to decide whether Grounds 1 and 2 satisfies the “reasonable likelihood” standard for instituting trial.⁹ If there is a dispute between the parties on whether the plain and ordinary meaning of the claims should apply (and how that, or some alternative interpretation, applies to the asserted art), Patent Owner has the opportunity to propose its own construction for our consideration during trial.

Patent Owner further argues that, for Grounds 3 and 4, Petitioner’s attempted reliance on “the ‘positions’ that Olink asserted in the litigation” is “[n]ot only . . . an improper incorporation by reference requiring Olink and the Board to sift through exhibits to determine the arguments that Petitioner

⁹ We note that the ’848 patent provides explanations for several terms, including, e.g., “nucleic acid moiety” (NAM), Ex. 1001, 7:41–52; “molecule of interest” (MOI), *id.* at 7:53–9:9; “interactor,” *id.* at 9:33–34; “CIS Reactive Cell” (CRC), *id.* at 9:35–38; “association of NAMs,” *id.* at 9:44–53; and “[f]unctional interactions,” *id.* at 14:22–27. However, we understand at this preliminary stage of the proceeding that, to the extent these are definitions, they are consistent with the plain and ordinary meaning of those terms as they would have been understood by a person of ordinary skill in the art in view of the claims, the specification, and the prosecution history of record.

is advancing,” but also fails because Petitioner does not and cannot “point to any explanation in the district court papers regarding specific claims needing construction and how those claims should be construed.” Prelim. Resp. 13.

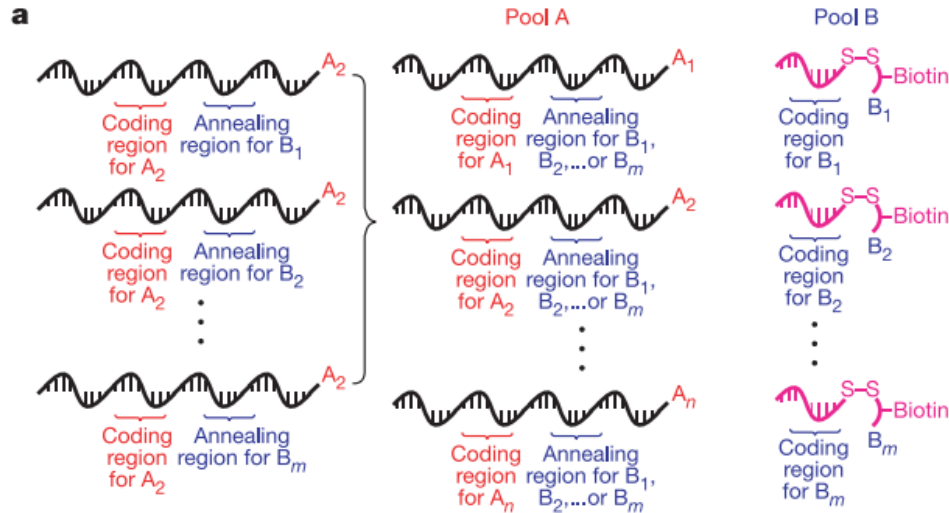
As noted above, we find that Petitioner has met its burden under 37 C.F.R. § 42.104(b)(3) for Grounds 1 and 2. Because, for the reasons set forth below, we also find Petitioner has demonstrated a reasonable likelihood that at least one claim of the ’848 patent is unpatentable based on those grounds, we need not, and thus do not, separately decide the sufficiency of Grounds 3 and 4 under 37 C.F.R. § 42.104(b)(3) for purposes of instituting *inter partes* review. *See SAS*, 138 S. Ct. at 1359–60; *PGS*, 891 F.3d at 1360; *see also* 37 C.F.R. § 42.108(a).

E. Ground 1: Alleged Obviousness over Kanan and Neri

1. Overview of Kanan (Ex. 1010)

Kanan teaches a “reaction discovery approach that uses DNA-templated organic synthesis and *in vitro* selection to simultaneously evaluate many combinations of different substrates for bond-forming reactions in a single solution.” Ex. 1010, 545 (endnotes omitted). In this approach, “two pools of DNA-linked substrates [are prepared], with n substrates in pool A

and m substrates in pool B,” as shown in Kanan’s Figure 1a reproduced below:



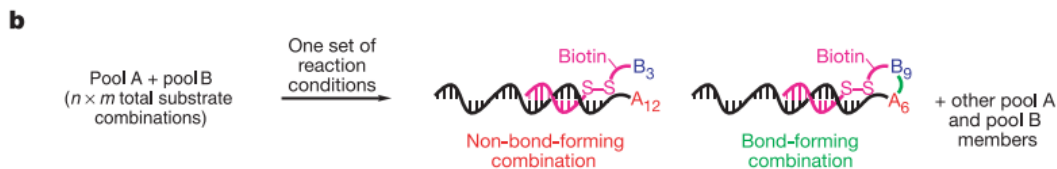
Id. at 545, 546, Fig. 1. Figure 1(a) depicts “[t]wo pools of DNA-linked organic functional groups that associate each of $n \times m$ substrate combinations with a unique DNA sequence.” *Id.* at 546, Fig. 1. More particularly,

[e]ach substrate in pool A is covalently linked to the 5’ end of a set of DNA oligonucleotides containing one ‘coding region’ (uniquely identifying that substrate) and one of m different ‘annealing regions’ (Fig. 1a). Each of the m substrates in pool B is attached to the 3’ end of an oligonucleotide containing a coding region that uniquely identifies the substrate and complements one of the m annealing regions in pool A.

Id. at 545.

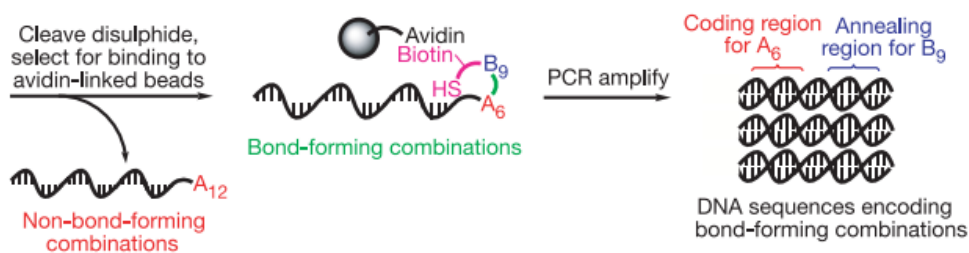
In Kanan’s approach, “[w]hen pools A and B are combined in a single aqueous solution . . . , Watson-Crick base pairings [among DNA oligonucleotides] organizes the mixture into $n \times m$ discrete pairs of substrates attached to complementary sequences,” where “substrates linked

to non-complementary oligonucleotides . . . do not react with each other at a significant rate.” Ex. 1010, 545. Kanan further teaches “covalently link[ing] each pool B substrate to its corresponding oligonucleotide by a linker containing a biotin group and a disulfide bond [S–S],” as shown in the portion of Figure 1(b) reproduced below:



Id. at 545, 546, Fig. 1. The excerpted portion of Figure 1(b) depicts two pool A substrates (A_{12} , A_6) paired with two pool B substrates (B_3 , B_9) through their linked complementary oligonucleotides, where A_{12} and B_3 do not form a bond and A_6 and B_9 do form a bond. *Id.* at 546, Fig. 1.

As Kanan explains and as shown in another portion of Figure 1(b) reproduced below, “[a]fter incubation under a set of chosen reaction conditions, followed by cleavage of the disulphide [*sic*, disulfide] bonds, only pool A sequences encoding bond formation between a pool A and pool B substrate remain covalently linked to biotin”:



Ex. 1010, 545, 546, Fig. 1. The excerpted portion of Figure 1(b) depicts the results of cleaving the disulfide bond linking pool B substrates with its oligonucleotide, wherein the only oligonucleotide that remains linked to biotin are those linked to pool A substrates that form a bond with pool B

substrates. *Id.* at 545, 546, Fig. 1. Finally, Kanan teaches that “[s]treptavidin affinity selection of the resulting solution separates the biotinylated from non-biotinylated sequences,” which allows identification of reactive substrate pairs by PCR amplification of the selected sequences followed by DNA microarray analysis. *Id.* at 545.

Kanan teaches that its “selection-based approach does not depend on any specific substrate or product property but instead can identify all substrate pairs capable of forming a covalent bond under the reaction conditions.” Ex. 1010, 545.

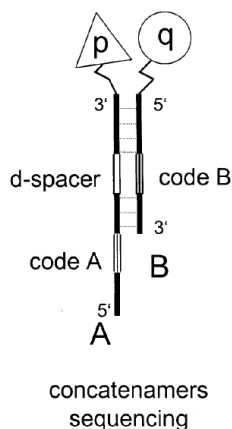
2. Overview of Neri (Ex. 1011)

Neri teaches that “[t]he isolation of specific binding molecules (e.g. organic molecules) is a central problem in chemistry, biology, and pharmaceutical sciences,” for instance because “the isolation of specific binders against a relevant biological target typically represents the starting point in the process which leads to a new drug.” Ex. 1011 ¶¶ 3, 6. Neri teaches that “[t]ypically, millions of molecules have to be screened, in order to find a suitable candidate,” but “[t]he preparation of very large libraries of organic molecules is . . . cumbersome,” and “the complexity associated with the identification of specific binding molecules from a pool of candidates grows with the size of the chemical library to be screened.” *Id.* ¶ 3.

As a solution, Neri teaches the use of “self-assembling libraries of organic molecules . . . , in which the organic molecules are linked to an oligonucleotide which mediates the self-assembly of the library and/or provide a code associated to each binding moiety” Ex. 1011 ¶ 5. Figure 5

of Neri, partially reproduced below, depicts an example of an assembly of two such organic molecules:

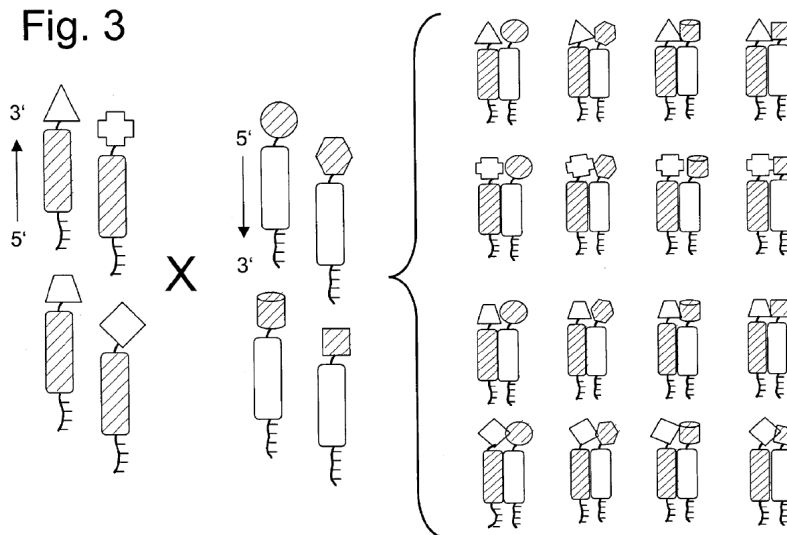
Fig. 5



Ex. 1011, Fig. 5. The reproduced portion of Figure 5 shows an oligonucleotides of sub-libraries A and B bearing chemical entity p and q, respectively, at their 3' and 5' ends. *Id.* ¶ 29. Neri explains that “[t]owards the 3' extremity, the DNA sequence [of the oligonucleotide of sub-library A] is designed to hybridize to the DNA sequences at the 5' extremity of oligonucleotides of sub-library B.” *Id.* The portions of the oligonucleotides labelled “code A” and “code B” contains a “unique sequence” for each member of sub-library A and sub-library B, respectively. *Id.*

Neri explains that its “encoded self-assembled chemical library (ESACHEL) can be very large (as it originates from the combinatorial self-assembly of two smaller libraries).” Ex. 1001 ¶ 20; *see also id.* ¶ 5. Neri’s Figure 3, reproduced below, provides a schematic depiction of an example ESACHEL:

Fig. 3



Pool A : n

Pool B : m

Library : m x n

Id. at Fig. 3. Figure 3 shows n chemical compound-oligonucleotide conjugates in pool A that “self assembles” with m chemical compound-oligonucleotide conjugates in pool B to produce a number of m x n combinations. *Id.* ¶ 27. Neri teaches that “[t]he oligonucleotides of pool A are designed to have” “one portion of the DNA sequence which can hybridize to compounds of pool B” and “a distinctive DNA sequence for each of the n members of [p]ool A.” Ex. 1011 ¶¶ 48–50. The oligonucleotides of pool B are similarly designed to have “one portion of the DNA sequence which can hybridize to compounds of pool A” and “a distinctive DNA sequence for each of the m members of [p]ool B.” *Id.* ¶¶ 53–55. Neri teaches that the identities of binders of interest can be obtained after capture using the code associated with each binding moiety. *Id.* ¶ 20; *see also id.* ¶ 5.

3. Analysis of Challenge to Claim 1

Petitioner asserts that claim 1 is unpatentable as obvious over Kanan and Neri. Pet. 2. Petitioner has provided an element-by-element analysis of

the claim, indicating where each element is allegedly disclosed in the combination of Kanan and Neri. *Id.* at 23–36. Petitioner also provides an explanation why a skilled artisan would have had reason to combine Kana and Neri to arrive at the invention of claim 1, with a reasonable expectation of success. *Id.* at 17–23.

At this stage of the proceeding, Patent Owner asserts that Petitioner “fails to establish that its asserted references disclose all elements of the claimed method” and “fails to adequately explain why a [POSA] would have been motivated to combine the asserted references.” Prelim. Resp. 15.

a. Asserted Failure by Kanan and Neri to Disclose All Elements

Step (a) of claim 1 recites a step of “forming a plurality of interactors by coupling each molecule of interest [(MOI)] with at least one nucleic acid moiety [(NAM)], the [NAM] comprising an identification sequence element and an association element.” Ex. 1001, 41:38–41. Patent Owner emphasizes that this step requires “tagging *each* MOI with at least one NAM,” where “[e]ach NAM comprises (i) a unique identification sequence for downstream detection and (ii) an association element that allows for association with any other NAM.” Prelim. Resp. 16.

Patent Owner asserts that neither Kanan nor Neri discloses this step. Prelim. Resp. 15. Patent Owner first agrees with Petitioner that Kanan does not disclose claim element 1(a) because, although Kanan teaches two groups (pool A and pool B) of molecules of interest that potentially interact with each other, “only pool A molecules have nucleic acid moieties that contain both an ‘identification sequence element’ and an ‘association element.’” *Id.* at 16–17. Patent Owner asserts that,

[c]ritically, not all nucleic acid strands in Kanan [used to label MOIs] contain an association element that allows for

association with any other nucleic acid strand. Rather, the nucleic acid strands in Kanan are designed such that one strand in a potential interacting pair (the “targeting strand”) specifically targets the nucleic acid strand of only **one** other molecule (the “receiving strand”). *Id.*

Id. at 18.

Patent Owner asserts that Neri does not cure the deficiencies of Kanan. Prelim. Resp. 18. Patent Owner asserts that “Neri discloses a method for tethering chemical moieties together by attaching each moiety to a nucleic acid containing (i) an identification sequence and (ii) a universal association element that facilitates binding of the nucleic acids.” *Id.* at 18–19. Patent Owner asserts that “[t]hese complexes are not designed to interact with each other” and that, instead, Neri teaches “screening these libraries of complexed chemical moieties for interaction with a separate binding partner lacking any nucleic acid tether or label.” *Id.* at 19. Patent Owner asserts that, “[a]s such, Neri does not disclose methods for making **a plurality of interactors.**” *Id.* at 20.

Patent Owner’s argument is unavailing on the present record. Patent Owner attacks Kanan and Neri individually. However, the Petitioner does not rely on Kanan or Neri alone to assert step (a) of claim 1 would have been obvious. Rather, Petitioner acknowledges that only pool A library members are interactors in Kanan, but argues that it would have been obvious to an ordinarily skilled artisan to modify pool A and pool B members in Kanan by coupling the molecules of interest in the two pools with the oligonucleotides disclosed in Neri, which includes both a self-assembling region (i.e., association elements) and a unique identification sequence for the chemical moiety to which it is attached. Pet. 27–31.

“Non-obviousness cannot be established by attacking references individually where the rejection is based upon the teachings of a combination of references. . . . [The reference] must be read, not in isolation, but for what it fairly teaches in combination with the prior art as a whole.” *In re Merck & Co.*, 800 F.2d 1091, 1097 (Fed. Cir. 1986). Accordingly, we find that, at this preliminary stage of the proceeding, Petitioner sufficiently establishes that the combination of Kanan and Neri teaches or suggests step (a) of claim 1 for purposes of institution.

b. Asserted Lack of Motivation to Combine with Reasonable Expectation of Success

Patent Owner asserts that “the methods of Kanan and Neri serve different purposes and are not directed at studying the same types of chemical interactions,” because Neri teaches “methods to diversify a pool of chemical moieties for use in binding interactions with a separate library of targets” rather than “a method of promoting or detecting interaction between library members.” Prelim. Resp. 22–23. Patent Owner argues that “Petitioner fails to adequately articulate why a POSA would have looked at Neri, a reference entirely unconcerned with the functional screening method disclosed in Kanan to resolve” the issues Petitioner identified for improvements to Kanan. *Id.* at 24.

As an initial matter, two criteria determine whether prior art is analogous: “(1) whether the art is from the same field of endeavor, regardless of the problem addressed, and (2) if the reference is not within the field of the inventor’s endeavor, whether the reference still is reasonably pertinent to the particular problem with which the inventor is involved.” *In re Clay*, 966 F.2d 656, 658–59 (Fed. Cir. 1992). We find that, at this stage of the proceeding, Petitioner has sufficiently shown that Kanan and Neri are

from the same field of endeavor, namely the creation of a chemical library, and/or are reasonably pertinent to the problem which the inventor is involved, in particular “encoding individual members of a library of chemicals with unique nucleotide sequences that can later be detected and analyzed to determine the identification of the members involved in the interaction.” Pet. 17.

We also find unavailing Patent Owner’s arguments that a skilled artisan would not have looked to combine Kanan with Neri because the references are ultimately directed to different purposes. Patent Owner first argues that “[p]etitioner does not explain *why* a POSA would have looked to Neri, a method that is not combinatorial, to modify Kanan, another method that is not combinatorial, to create a screening method whereby each member in the library would be coupled with a NAM and would provide for a combinatorial approach.” Prelim. Resp. 25. Contrary to Patent Owner’s argument, Neri teaches that its method is combinatorial. In particular, Neri explains that “its encoded self-assembled chemical library (ESACHEL) can be very large (as it originates from the *combinatorial* self-assembly of two smaller libraries.” Ex. 1011 ¶ 25 (emphasis added).

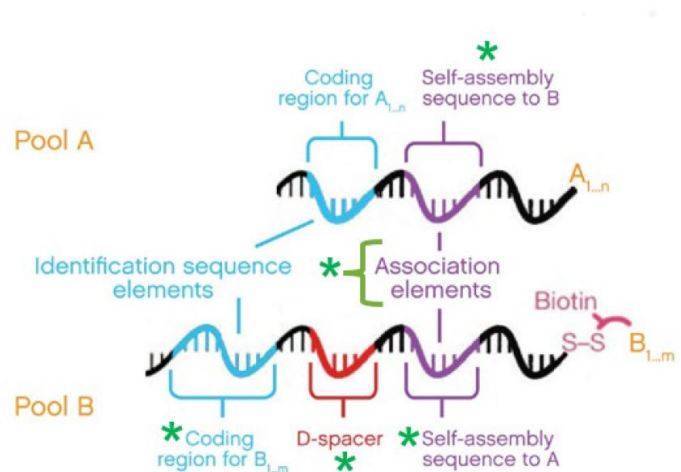
We likewise find Petitioner has provided sufficient rationale, at this preliminary stage and for purposes of institution, “as to why a POSA would have understood that Neri would address the inefficiencies in the Kanan method.” Prelim. Resp. 22.

Petitioner has explained, for instance, that “Kanan discussed a desire to search ‘large number[s] of substrate combinations for unexpected reactions’ and that “a POSA would have understood that synthesizing the library members is [a] rate limiting factor.” Pet. 17–18 (citing Ex. 1005 ¶¶ 82, 97–99; Ex. 1010, 548, 549; Ex. 1013). Petitioner explains that this is

because in Kanan's library pool A members are "created through a six-step process to [incorporate] both the coding region for [an] A substrate and the annealing region for *each* B substrate" B_{1-m}, which process "must be repeated for each different A substrate (A_{1-n})" in order to ensure that all possible interactions (n x m) are evaluated. Pet. 18 (emphasis added) (citing Ex. 1013, Fig. S1; Ex. 1005 ¶ 99, Ex. 1010, 546, Fig. 1). Petitioner further explains that a POSA would have understood Neri to address the above-identified inefficiency in Kanan's method, because Neri teaches the use of self-assembly sequences that "reduce the time to synthesize a library where all members can interact," by requiring the synthesis of only one pool A member for each A substrate. *Id.* (citing Ex. 1005 ¶¶ 97–101).

Patent Owner further asserts that "Petitioner identifies at least five changes that a POSA would have needed to make to the method of Kanan to arrive at the claimed invention and asserts various, disparate motivations that would have allegedly led a POSA to make these changes." Prelim. Resp. 23. To show these five asserted changes, Patent Owner provides an annotated

version of Petitioner’s proposed “modified library members combining Neri with Kanan,” which we reproduce below:



Prelim. Resp. 25. The graphic above represents Petitioner’s proposed “modified library members” when Neri is combined with Kanan, annotated by Patent Owner with green asterisks to show the asserted changes from Kanan. *Id.*

For similar reasons to those discussed above, we find that this argument does not undermine Petitioner’s challenge at this stage. In particular, Petitioner has explained that the modification of Kanan with Neri’s self-assembly sequence would “reduce the time to synthesize a library where all members can interact.” Pet. 18 (citing Ex. 1005 ¶¶ 97–101). Similarly, Petitioner has explained the reason for including a “coding region” for each library member, i.e., to “provide a unique nucleic acid identification sequence for each conjugate that can be identified downstream,” as for instance taught by Neri. *Id.* at 30 (citing Ex. 1005 ¶ 97). Finally, Petitioner has explained “a POSA . . . would . . . add the d-spacer taught in Neri, as this prevents the identification sequence element of pool B members from interacting with the identification sequence element of

pool A members.” Pet. 30 (citing 1005 ¶ 105). Dr. Nelson’s testimony supports Petitioner’s contentions and that testimony is, at present, substantively un rebutted.

On the record before us, and at this preliminary stage of the proceeding, we do not find Petitioner’s asserted motivations to be improperly disparate or based on hindsight. *In re McLaughlin*, 443 F.2d 1392, 1395 (CCPA 1971) (explaining that reconstruction of prior art is not improper “so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made and does not include knowledge gleaned only from applicant’s disclosure”).

To the extent Patent Owner is also arguing that Petitioner’s assertions regarding reasonable expectation of success are unsupported, Prelim. Resp. 24, the argument is similarly unavailing. Petitioner has pointed to teachings in Neri and the knowledge of an ordinarily skilled artisan to support its assertions. Pet. 21–23 (citing, e.g., Ex. 1005 ¶¶ 104–105, 149, 171, 183 and Ex. 1011 ¶¶ 10, 82 to explain why an ordinarily skilled artisan would have reasonably expected success in applying, to Kanan’s small molecules, Neri’s “method of preparing organic molecules, peptides, and oligomeric proteins linked to an oligonucleotide that results in stable self-assembled associated oligonucleotides”). In this regard, we note that “the expectation of success need only be reasonable, not absolute.” *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1364 (Fed. Cir. 2007).

Accordingly, at this preliminary stage of the proceeding, we determine that Petitioner has established a reasonable likelihood that it would prevail in showing claim 1 to be unpatentable over Kanan and Neri.

4. Analysis of Claims 2–15 and 17–20

Petitioner has provided an adequate element-by-element analysis of the additional limitations in dependent claims 2–15 and 17–20. Pet. 36–42, 43–46. As discussed above, we also find Petitioner has shown sufficiently, at this stage of the proceeding, that an ordinarily skilled artisan would have been motivated to combine Kanan and Neri with a reasonable expectation of success.

Patent Owner “does not agree with Petitioner that all other elements in the . . . dependent claims are met”; however, at this stage of the proceeding, Patent Owner does not point to any specific deficiencies in Petitioner’s analysis of these claims. Prelim. Resp. 15–16. On this record—and without the benefit of a response from Patent Owner specific to these dependent claims—we determine that Petitioner has established a reasonable likelihood that it would prevail in showing claims 2–15 and 17–20 are unpatentable over Kanan and Neri.

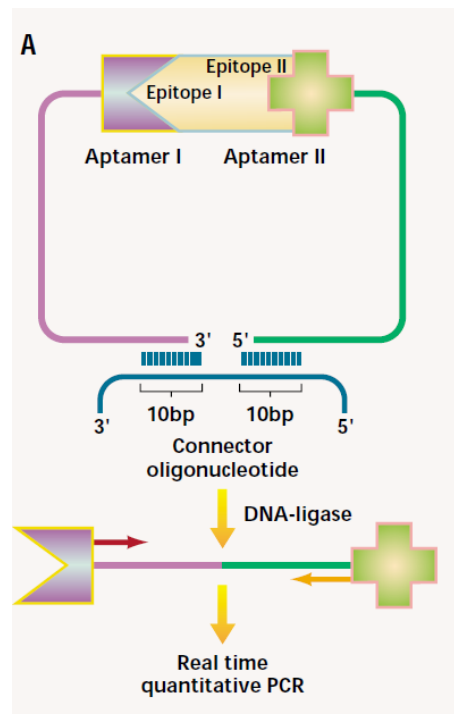
F. Ground 2: Alleged Obviousness over Kanan, Neri, and Famulok

1. Overview of Famulok (Ex. 1012)

Famulok teaches that “[t]he ability to monitor slight differences in the amounts of proteins and other biomolecules within the smallest possible detection volumes . . . is of utmost importance not only for proteomics research but also for diagnostic and technological purposes.” Ex. 1012, 448.

Famulok discusses the proximity ligation method and teaches that, by “[c]ombining target recognition by two aptamers, enzymatic ligation, and PCR, the . . . method enables the detection of minute amounts of proteins.” Ex. 1012, 448. In particular, Famulok discusses a test case wherein a pair of DNA aptamers—nucleic acid-based receptor molecules—that binds to the

homodimer of a target analyte protein each includes “a different DNA-sequence extension that does not interfere with its folding and is not required for target recognition.” *Id.* Famulok teaches that “[b]inding of the aptamer pair brings the ends of the oligonucleotide extensions into close spatial proximity . . . so that a ‘splint’ oligonucleotide can hybridize to both ends,” as illustrated in Figure 1A reproduced below:



Famulok 449, Fig. 1. Figure 1(A) is a schematic that shows a pair of aptamers binding to epitopes of a target protein such that “the free ends of their sequence extensions [are brought] into close spatial proximity,” which “allows the core sequence of the connector oligonucleotide to hybridize both ends, acting as a template for enzymatic ligation.” *Id.* (caption).

Famulok teaches that the ends of the sequence extensions are “subsequently ligated together by [a] ligase.” Ex. 1012, 448. Famulok further teaches that “[t]he ligated species can then act as a PCR template and the amplified PCR product can be monitored and quantified under real-time

PCR conditions, whereas no signal is obtained with unligated probes.” *Id.* Famulok teaches that “[t]he sensitivity that can be achieved with the method is remarkable.” *Id.* Famulok further teaches that “there is no reason that the approach should be limited to aptameric receptors” and that “[p]roximity ligation will likely work for antibody probes that are linked to a DNA sequence.” *Id.* at 449.

2. Analysis of Claim 16

Claim 16 depends from claim 1 and further recites “wherein association [between at least two nucleic acid moieties in the cis-reactive cell] is via ligation.” Ex. 1001, 41:37–57 (claim 1), 43:20–22 (claim 16).

Petitioner asserts that Famulok discloses this additional limitation because it teaches “associating the oligonucleotides of [its] aptamers by connecting the two oligonucleotides to a third ‘splint’ oligonucleotide that is incorporated into double-stranded DNA by DNA ligase.” Pet. 42. Petitioner asserts it would have been obvious to combine Kanan, Neri, and Famulok to arrive at the subject matter of claim 16 with a reasonable expectation of success, because

Neri teaches how to design interactors that contain an overhang region (*see* Ex. 1011, Fig. 7) that can be ligated together using the method taught in Famulok, and the use of a splint and DNA ligase to connect oligonucleotides was well-known at the time of the application. *E.g.*, Ex. 1013, Fig. S1; Ex. 1005, ¶178. A POSA would have also known that all the references relate to encoding a molecule with a unique nucleotide sequence, allowing the encoded molecules to interact, and then detecting and analyzing the identification of the members involved in the interaction. *Id.*; Ex. 1010, 545; Ex. 1011, [0117]–[0119]; Ex. 1012.

Pet. 23; *see also id.* at 42–43 (citing Ex. 1005 ¶¶ 177–178).

Patent Owner “does not agree with Petitioner that all other elements in the . . . dependent claims are met”; however, at this stage of the proceeding, Patent Owner does not point to any specific deficiencies in Petitioner’s analysis of claim 16, other than stating that “the arguments presented [in Ground 1] apply equally to Ground 2, which is directed to dependent claim 16.” Prelim. Resp. 15–16.

As discussed above, we determine at this preliminary stage of the proceeding that Petitioner has established a reasonable likelihood that it would prevail with respect to Ground 1. On this record—and without the benefit of a response from Patent Owner specific to Ground 2—we determine that Petitioner has established a reasonable likelihood that it would prevail in showing claim 16 is unpatentable over Kanan, Neri, and Famulok.

G. Grounds 3 and 4: Alleged Obviousness over Baez and Landegren or Baez, Landegren, and Freskard

1. Overview of Baez

Baez teaches that “nonspecific binding of the analyte to be detected and general assay noise . . . has limited the application and sensitivity” of immunoassays. Ex. 1003, 1:26–32.

Baez teaches a process for detecting an analyte wherein “[t]he binding of [at least two] reporter conjugates to the analyte facilitates the juxtaposition of [their] nucleic acid labels, forming a single nucleic acid amplicon.” Ex. 1003, Abstract. Baez teaches that, “[o]ptionally, the analyte may be immobilized on a solid support through the action of a capture reagent.” *Id.* at 10:48–49. Baez teaches that “the amplicon may be formed

by the overlap of the nucleic acid labels, or they [may] be joined enzymatically by means of ligation.” *Id.* at 4:21–23.

Figure 1 of Baez, reproduced below, illustrates Baez’s “basic method”:

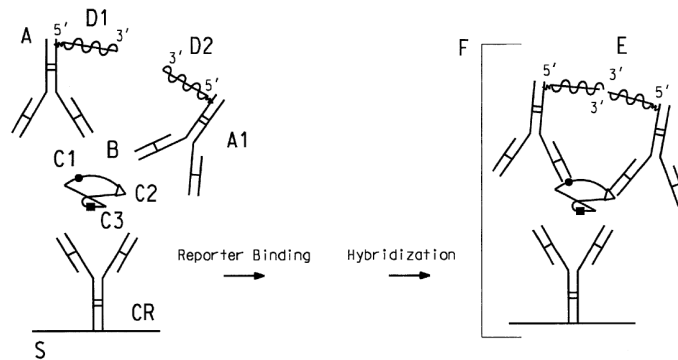


FIG. 1

Ex. 1003, Fig. 1, 11:10–12. In particular, Figure 1 depicts the “formation of [analyte specific amplicon (ASA)] by nucleic acid label overlap.” *Id.* at 11:10–12. As shown in this figure, “nucleic acid-labeled reporter conjugates (A and A1) . . . selectively bind to the analyte (B),” “forming analyte-dependent-[reporter]-complex (F).” *Id.* at 11:18–21. Baez teaches that, “[a]s a consequence, the nucleic acid-labels (D1 and D2) of the bound reporter conjugates are positioned and maintained in close molecular proximity” so as to enable the labels to be joined to form “an analyte-specific amplicon (E).” *Id.* at 11:21–28. Baez teaches that “[t]he amplicon may . . . be detected directly, or may be used as a template of the generation of amplification products.” *Id.* at Abstract.

In Baez’s method, “when the reporter conjugates . . . are not bound to the analyte,” they are “not appropriately aligned or are positioned at distances too great to enable their joining. Consequently, an analyte specific amplicon is not formed. Thus non-analyte bound reporter fraction is either

not detected or detected at greatly diminished efficiency.” Ex. 1003, 11:36–46. Furthermore, “the nucleic acid-labels can be designed to produce amplification products that can be differentiated on the basis of size of sequence.” *Id.* at 11:55–59. Baez teaches that, accordingly, “[d]etection of the analyte by this process significantly reduces assay background caused by non-specific reporter conjugate binding.” *Id.* at Abstract.

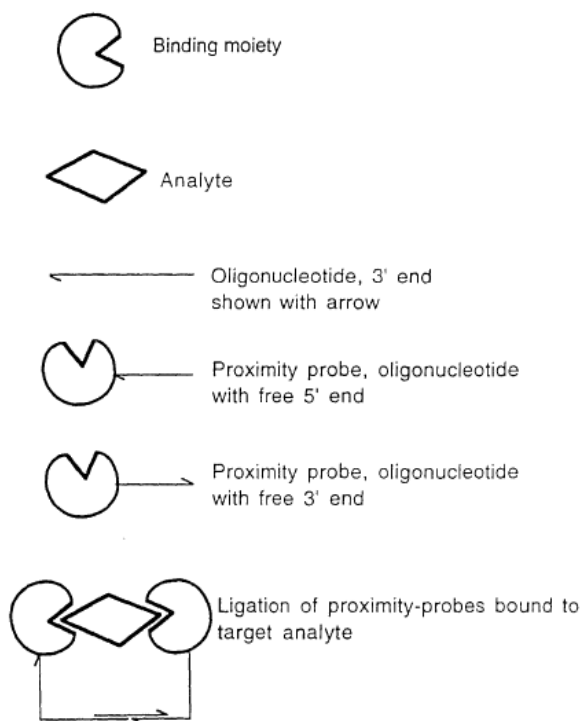
2. Overview of Landegren

Landegren teaches that “[m]ost protein detection assays rely on the efficient separation of target bound detector reagents from non-bound reagents.” Ex. 1004, 1.

Landegren teaches a method to “detect and quantify one or several analytes in solution in a homogenous one tube assay with high sensitivity and specificity,” using “proximity-probes comprising a binding moiety with affinity for the analyte and also a reactive functionality” comprising of a “nucleic acid coupled to the binding moiety.” Ex. 1004, 2, 3. In Landegren’s method, these probes are “added to the sample solution” and “permitted to interact with one another,” with interactions occurring “to a greater extent if two or more proximity-probes have bound the same

individual analyte molecule.” *Id.* Figure 1 of Landegren, which illustrates this method, is reproduced below:

Figure 1. Definition of symbols



Ex. 1004, Fig. 1. Figure 1 depicts “[l]igation of proximity-probes bound to target analyte” and explains the symbols used therein. *Id.*

Landegren teaches that,

[s]ince the proximity-probes are capable of binding the analyte at multiple sites, the analyte acts in a way analogous to a catalyst by bringing the reactive probes closer to one another and increasing their ability to interact through an increased local concentration. The interaction between the coupled functionalities results in a detectable signal in a secondary reaction.

Ex. 1004, 2. Landegren teaches that “[c]omplexes of different proteins can also be detected by the assay. In such a case, the proximity-probes bind to

two different proteins, but gain proximity if these two proteins are close to each other.” *Id.*

Landegren further teaches using proximity-probes in a multiplexed detection assay, in which “[s]everal analytes may be simultaneously detected by using several proximity-probe pairs,” which have “unique nucleic acid sequences in order to distinguish them from other pairs.” Ex. 1004, 15. Landegren teaches that, in such multiplex assay, “[a] true positive ligation must contain both sequence identification tags [from] correct pairs of oligonucleotides in order to score as a true positive.” *Id.*

Landegren teaches that “[i]n most cases the secondary detection of the amount of nucleic acid interaction will involve a specific amplification of the interaction product.” Ex. 1004, 3. However, Landegren teaches that where “a lot of ligation product is produced” it can be directly analyzed, for instance by binding “the first of the two united nucleic acid sequence . . . through hybridization to an immobilised oligonucleotide probe,” washing off unbound sequences, and detecting the ligation product through “a labelled hybridisation probe specific for the second sequence.” *Id.* at 4–5.

3. Overview of Freskgard

Freskgard teaches a method for identifying a lead compound (i.e., a molecule having an affinity towards a target) by using a library of bifunctional complexes each comprising a molecule attached to an identifier coding for the molecule. Ex. 1009, Abstract, 1:33–34. Freskgard teaches that “[t]he identifier sequence is suitably a nucleic acid which uniquely identifies the potential lead compound.” *Id.* at 2:26–27. Freskgard teaches subjecting the library to a target under binding conditions, removing the non-binding complexes, and then separate and decode the identifiers of the

remaining complexes to establish the identity of the molecule having affinity towards the target, for instance by sequencing the identifier. *Id.* at Abstract, 2:29–31.

4. Analysis

Petitioner provides an element-by-element analysis of the claims at issue in Grounds 3 and 4. Pet. 55–67. Petitioner also provides argument that a skilled artisan would have had reason to combine Baez and Landegren, or Baez, Landegren, and Freskgard to arrive at the claimed inventions, with a reasonable expectation of success. *Id.* at 52–55. As Patent Owner points out, however, Petitioner neither states that the terms were given their plain and ordinary meaning based on the understanding of a POSA at the time of the invention, nor provides an explicit construction of the claim terms. Prelim. Resp. 13–14. Instead, Petitioner states that “the claim terms are given meaning based on PO’s application of the claims in related litigation with Petitioner.” Pet. 12–13.

In its Preliminary Response, Patent Owner also asserts that “neither Baez nor Landegren discloses selecting all [cis-reactive cells] exhibiting [the] detectable trace,” as recited in step (d) of claim 1. Prelim. Resp. 27–30. Patent Owner further argues that “the Petition fails to establish a motivation to combine these references” to arrive at the challenged claims. *Id.* at 27, 30–31.

As noted above, we need not, and thus do not, separately decide the sufficiency of Grounds 3 and 4 under 37 C.F.R. § 42.104(b)(3) for purposes of instituting *inter partes* review. Moreover, having determined that Petitioner meets the threshold showing necessary to support institution of review based on Grounds 1 and 2, we need not resolve whether Grounds 3

and 4 also support institution. *See SAS*, 138 S. Ct. at 1359–60; *PGS*, 891 F.3d at 1360; *see also* 37 C.F.R. § 42.108(a). Thus, at this stage of the proceeding, we do not address in detail Patent Owner’s arguments with respect to Grounds 3 and 4. Those arguments (if preserved in trial) will be addressed on a fully-developed trial record to the extent necessary.

Notwithstanding the above, we have doubts that Petitioner is reasonably likely to prevail on Grounds 3 and 4. In particular, as we understand the Petition, Grounds 3 and 4 rest on the contention that Baez’s antibody-nucleic acid conjugates are “molecules of interest” and that ligation of the conjugates is a “functional interaction[] between at least two molecules of interest,” as recited in the preamble of claim 1. Pet. 55; *see also id.* at 59 (describing the ligation of the nucleic acid labels and linker in Baez as “the desired functional interaction”). However, the Petition also points to these antibody-nucleic acid conjugates as the “interactors” recited in step (a) of claim 1, which are described as formed by “coupling each molecule of interest with at least one nucleic acid moiety.” *Id.* at 56. To the extent the antibody-nucleic acid conjugates are asserted to be the molecules of interest, the Petition fails to clearly explain what nucleic acid moiety is then coupled to it to form the interactors.

III. CONCLUSION

For the above reasons, on this preliminary record, we determine that Petitioner demonstrates a reasonable likelihood that the subject matter of at least one challenged claim is unpatentable. Accordingly, we institute an *inter partes* review of all challenged claims based on all grounds asserted in the Petition pursuant to 35 U.S.C. § 314(a). *See PGS*, 891 F.3d at 1359–60.

We emphasize that, at this stage of the proceeding, we have not made a final determination with respect to the patentability of any of the challenged claims. In addition, any argument not raised in a timely Patent Owner Response to the Petition, or as permitted in another manner during trial, shall be deemed waived and/or forfeit even if asserted in the Preliminary Response. Furthermore, nothing in this Decision authorizes Petitioner to supplement information advanced in the Petition in a manner not permitted by the Board's Rules.

IV. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that *inter partes* review of claims 1–20 of U.S. Patent No. 7,883,848 is instituted with respect to all grounds of unpatentability set forth in the Petition; and

FURTHER ORDERED that pursuant to 35 U.S.C. § 314(a), *inter partes* review of U.S. Patent No. 7,883,848 is instituted commencing on the entry date of this Order, and pursuant to 35 U.S.C. § 314(c) and 37 C.F.R. § 42.4, notice is given of the institution of a trial.

IPR 2024-01353
Patent 7,883,848 B2

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