UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

INTEGRATED DNA TECHNOLOGIES, INC.,
Petitioner,

v.

TECAN GENOMICS, INC.,
Patent Owner.

IPR2025-00016
U.S. Patent 10,876,108

PETITIONER'S NOTICE OF APPEAL

Pursuant to 35 U.S.C. § 142 and 37 C.F.R. § 90.2(a), Petitioner Integrated DNA Technologies, Inc., provides notice that it appeals to the United States Court of Appeals for the Federal Circuit from the Final Written Decision, entered April 6, 2026 (Paper 57) and attached as Exhibit A, and from all underlying orders, decisions, rulings, and opinions regarding U.S. Patent No. 10,876,108 ("the '108 Patent") entered in the above-captioned proceeding (IPR2025-00016) before the Patent Trial and Appeal Board ("Board"). This Notice of Appeal is timely because it is filed within sixty-three (63) days of the Final Written Decision.

In accordance with 37 C.F.R. § 90.2(a)(3)(ii), Petitioner submits that the appeal will address the Board's decision concluding that claims 1-3 and 5-12, and 14-19 of the '108 Patent have not been shown by a preponderance of the evidence to be unpatentable based on the grounds in the above-captioned proceeding, and any other issues decided against Petitioner in any order, decision, ruling, or opinion in the above-captioned proceeding.

Pursuant to 35 U.S.C. § 142 and 37 C.F.R. § 90.2(a), this Notice is being filed with the Director of the United States Patent and Trademark Office, and a copy of this Notice is being concurrently filed with the Patent Trial and Appeal Board. In addition, a copy of this Notice is being filed with the Clerk of the United States Court of Appeals for the Federal Circuit, along with an electronic copy of the Notice and

the required docketing fees, which are being served electronically on the Court by CM/ECF and pay.gov.

Dated: June 3, 2026

Respectfully submitted,

/Thomas S. Fletcher/

Thomas S. Fletcher (Reg. No. 72,383)
WILLIAMS & CONNOLLY LLP
680 Maine Avenue SW
Washington, DC 20024
Phone: 202-434-5497
Fax: 202-434-5029
tfletcher@wc.com

Lead Counsel for Petitioner
Integrated DNA Technologies, Inc.

CERTIFICATE OF SERVICE AND FILING

I hereby certify that on June 3, 2026, in addition to being filed and served electronically through the Patent Trial and Appeal Board's P-TACTS System, the foregoing Notice of Appeal is being filed with the Director of the United States Patent and Trademark Office by electronic mail at efileSO@uspto.gov.

I also hereby certify that on June 3, 2026, this Notice of Appeal and the requisite docketing fees are being filed with the Clerk's Office of the United States Court of Appeals for the Federal Circuit via CM/ECF.

I also hereby certify that on June 3, 2026, this Notice of Appeal is being served via electronic mail to Linnea P. Cipriano, Scott T. Weingaertner, John P. Padro, and Timothy J. Beavers, at DG-GoodwinTecan@goodwinlaw.com, counsel of record for Patent Owner.

Dated: June 3, 2026

/Thomas S. Fletcher/
Thomas S. Fletcher (Reg. No. 72,383)
WILLIAMS & CONNOLLY LLP
680 Maine Avenue SW
Washington, DC 20024
Phone: 202-434-5497
Fax: 202-434-5029
tfletcher@wc.com

Lead Counsel for Petitioner
Integrated DNA Technologies, Inc.

EXHIBIT A

Trials@uspto.gov
571-272-7822

Paper 57
Date: April 6, 2026

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

INTEGRATED DNA TECHNOLOGIES, INC.,
Petitioner,

v.

TECAN GENOMICS, INC.,
Patent Owner.

IPR2025-00016
Patent 10,876,108 B2

Before GEORGIANNA W. BRADEN, ZHENYU YANG, and TIMOTHY G. MAJORS, *Administrative Patent Judges.*

YANG, *Administrative Patent Judge*.

JUDGMENT
Final Written Decision
Determining No Challenged Claims Unpatentable
35 U.S.C. § 318(a)

Granting Patent Owner's Motion to Seal (Paper 42)
37 C.F.R. §§ 42.14, 42.54

I. INTRODUCTION

Integrated DNA Technologies, Inc. ("Petitioner") filed a Petition (Paper 1, "Pet."), seeking *inter partes* review of claims 1–3, 5–12, and 14–19 of U.S. Patent No. 10,876,108 B2 (Ex. 1002, "the '108 patent"). Tecan Genomics, Inc. ("Patent Owner") filed a Preliminary Response. Paper 6 ("Prelim. Resp."). We instituted trial to review the challenged claims (Paper 7, "DI").

Thereafter, Patent Owner filed a Response to the Petition (Paper 39,[1] "PO Resp."), Petitioner filed a Reply to Patent Owner's Response (Paper 45, "Reply"), and Patent Owner filed a Sur-reply to Petitioner's Reply (Paper 51, "Sur-reply"). An oral hearing for this proceeding was held on January 22, 2026, and the transcript of that hearing is of record. *See* Paper 56 ("Tr.").

The Board has jurisdiction under 35 U.S.C. § 6 and issues this Final Written Decision pursuant to 35 U.S.C. § 318 and 37 C.F.R. § 42.73. For the reasons provided below, we find Petitioner has not shown, by a preponderance of the evidence, the unpatentability of claims 1–3, 5–12, and 14–19 of the '108 patent.

---

[1] Patent Owner originally filed Paper 21 as its Response, relying on the declaration of Dr. Mikhail V. Matz (Ex. 2039). Because we found that Dr. Matz was conflicted from providing expert testimony on behalf of Patent Owner, we prohibited Dr. Matz from further serving as a witness for Patent Owner in this proceeding and indicated that Dr. Matz's declaration was excluded. Paper 31. We, however, granted Patent Owner's request to substitute a declaration from Dr. Eli Meyer that would take the place of Dr. Matz's declaration. Paper 37. As a result, Patent Owner filed an amended Response (Paper 39), relying on the substitute declaration of Dr. Meyer (Ex. 2287).

A. Real Parties in Interest

Petitioner identifies itself and Danaher Corporation as the real parties in interest for Petitioner. Pet. 72. Patent Owner identifies itself and Tecan Group AG (also known as Tecan Group Ltd.) as the real parties in interest for Patent Owner. Paper 3, 1.

B. Related Matters

The parties inform us that Patent Owner has asserted the '108 patent in *Tecan Genomics, Inc. v. Invitae Corp.*, Case No. 1:23-cv-01114 (D. Del.) and *Tecan Genomics, Inc. v. QIAGEN Sciences, LLC*, Case No. 1:23-cv-01115-GBW (D. Del.). Pet. 72; Paper 3, 1.

Petitioner concurrently filed IPR2025-00015 against U.S. Patent No. 10,036,012 ("the '012 patent"), which claims priority to the same provisional patent application as the '108 patent. Pet. 73; Paper 3, 1.

Patent Owner further represents that QIAGEN Sciences, LLC filed IPR2025-00028 and IPR2025-00029, challenging the '012 patent and the '108 patent, respectively. Paper 3, 1.

C. The '108 Patent

The '108 patent "provides methods, compositions and kits for targeted nucleic acid sequence enrichment in a nucleic acid sample and for high efficiency nucleic acid library generation for next generation sequencing (NGS)." Ex. 1002, code (57); *see also id.* at 2:36–38 (disclosing "methods for enriching for target nucleic acid sequences of interest in a sample comprising nucleic acids").

The '108 patent states that, with the rapid development of NGS technologies and platforms, whole genome sequencing became more feasible and less expensive. Ex. 1002, 1:18–20. It was nonetheless "often

more practical and cost-effective to select genomic regions of interest for sequencing and analysis." *Id.* at 1:27–29.

Target enrichment was commonly used in genomic DNA sequencing to selectively capture genomic regions of interest from a DNA sample before sequencing. *Id.* at 1:29–32. At the time of the '108 patent invention, there were three major categories of target enrichment methods, including PCR-based methods, capture-by-hybridization, i.e., on-array or in-solution hybrid capture methods, and capture-by-circularization, i.e., molecular inversion probe-based methods. *Id.* at 1:44–49. According to the '108 patent, each of these methods has its distinct advantages and disadvantages. *Id.* at 1:44–46.

The '108 patent explains that "[t]here is a need for improved methods for selective target enrichment that allow for low-cost, high-throughput capture of genomic regions of interest without specialized instrumentation. Additionally, there is also a need for high efficiency nucleic acid library generation." *Id.* at 2:27–31. The '108 patent purports to address both of these needs. *Id.* at 2:31–32.

D. Illustrative Claim

Independent claim 1 is illustrative of the claimed subject matter and is reproduced below.

> 1. A method for sequencing an enriched nucleic acid sequence of interest, the method comprising:
>
> a) annealing one or more oligonucleotides in solution in a reaction mixture to the nucleic acid sequence of interest in a nucleic acid fragment, wherein the reaction mixture comprises a plurality of nucleic acid fragments, wherein the nucleic acid fragment comprising the nucleic acid sequence of interest comprises a first adaptor sequence, wherein the one or more oligonucleotides comprise a 3′

portion with at least 10 bases designed to be complementary to the nucleic acid sequence of interest and a 5′ tail portion comprising a second adaptor sequence that is non-complementary to the nucleic acid sequence of interest;

b) extending the one or more oligonucleotides annealed to the nucleic acid sequence of interest in the nucleic acid fragment comprising the first adaptor sequence with a polymerase, in the reaction mixture, thereby generating one or more oligonucleotide extension products comprising sequence complementary to the first adaptor sequence at a first end, sequence complementary to the nucleic acid sequence of interest, and the second adaptor sequence at a second end;

c) amplifying the one or more oligonucleotide extension products, in the reaction mixture, using a first primer that anneals to the complement of the first adaptor sequence and a second primer that anneals at its 3′ end to a complement of the second adaptor sequence, thereby enriching the nucleic acid sequence of interest, by generating amplified products comprising the enriched nucleic acid sequence of interest; and

d) sequencing the amplified products comprising the enriched nucleic acid sequence of interest on a massively parallel sequencing platform.

Ex. 1002, 35:18–51.

E. Asserted Challenges to Patentability

Petitioner asserts the following challenges to patentability:

Claims Challenged	35 U.S.C. §[2]	Reference
1, 3, 5–10, 14–18	102	Meyer[3]
8, 17, 18	103(a)	Meyer
2	103(a)	Meyer, Siebert[4]
11, 12, 19	103(a)	Meyer, Caruccio[5], Bronner[6]

In support of their respective positions, Petitioner relies on the Declaration of Peter A. Sims, Ph.D. (Ex. 1085), and Patent Owner relies on the Declarations of Carlos D. Bustamante, Ph.D. (Ex. 2038) and Eli Meyer, Ph.D. (Ex. 2287).

---

[2] The Leahy-Smith America Invents Act ("AIA"), Pub. L. No. 112-29, 125 Stat. 284, 287–88 (2011), amended 35 U.S.C. §§ 102 and 103, effective March 16, 2013. AIA §§ 3(b), 3(c), and 3(n). The '108 patent claims priority to a provisional application filed on January 26, 2012. Ex. 1002, code (60). Petitioner's challenge assumes this earliest potential priority date (Pet. 26) and Patent Owner provides no argument to the contrary. Accordingly, we apply the pre-AIA version of §§ 102 and 103.

[3] Meyer et al., *Sequencing and* de novo *analysis of a coral larval transcriptome using 454 GSFlx*, 10:219 BMC GENOMICS (2009) (Ex. 1006, "Meyer").

[4] Siebert et al., *An improved PCR method for walking in uncloned genomic DNA*, 23(6) NUCLEIC ACIDS RESEARCH 1087–88 (1995) (Ex. 1007, "Siebert").

[5] Caruccio, *Preparation of next-generation sequencing libraries using Nextera™ technology: simultaneous DNA fragmentation and adaptor tagging by in vitro transposition*, *in* HIGH-THROUGHPUT NEXT GENERATION SEQUENCING: METHODS AND APPLICATIONS, 733 METHODS IN MOLECULAR BIOLOGY Ch. 17 (2011) (Ex. 1008, "Caruccio").

[6] Bronner et al., *Improved Protocols for Illumina Sequencing*, 18 CURR. PROTOC. HUM. GENET. (2009) (Ex. 1009, "Bronner").

II. ANALYSIS

A. Principles of Law

To prevail in this *inter partes* review, Petitioner "shall have the burden of proving a proposition of unpatentability by a preponderance of the evidence." 35 U.S.C. § 316(e); 37 C.F.R. § 42.1(d).

Anticipation is a question of fact. *In re Gleave*, 560 F.3d 1331, 1334–35 (Fed. Cir. 2009). Whether a reference anticipates a claim is assessed from the perspective of an ordinarily skilled artisan. *See Dayco Prods., Inc. v. Total Containment, Inc.*, 329 F.3d 1358, 1368 (Fed. Cir. 2003). To show anticipation, each and every claim element, arranged as in the claim, must be disclosed in a single piece of prior art. *Net MoneyIN, Inc. v. VeriSign, Inc.*, 545 F.3d 1359, 1369 (Fed. Cir. 2008).

A claim is unpatentable for obviousness 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." 35 U.S.C. § 103 (pre-AIA); *see also 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) when in evidence, objective evidence of nonobviousness. *Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966).

We analyze the challenges to patentability in accordance with these principles.

B. Level of Ordinary Skill in the Art

In determining the level of ordinary skill in the art, various factors may be considered, including the "type of problems encountered in the art; prior art solutions to those problems; rapidity with which innovations are made; sophistication of the technology; and educational level of active workers in the field." *In re GPAC, Inc.*, 57 F.3d 1573, 1579 (Fed. Cir. 1995). Furthermore, the prior art itself can reflect the appropriate level of ordinary skill in the art. *Okajima v. Bourdeau*, 261 F.3d 1350, 1355 (Fed. Cir. 2001).

Petitioner asserts that:

> [b]ecause the '108 patent is directed to library preparation and data interpretation methods for NGS, the POSA [person of ordinary skill in the art] could have had academic training in any of a variety of fields that used NGS, including chemistry, molecular biology, biochemistry, or medicine. The POSA would have a PhD or equivalent training in one of those fields and several years of work experience (or commensurately less education and more work experience). The POSA further would have had specific experience with implementing and designing library preparation methods for 454 and Illumina, the leading NGS platforms in 2012. This would have included specific experience with, and understanding of, the sequences contained in adaptors for 454 and Illumina sequencing at the priority date, and the chemistry used to attach those adaptors to DNA fragments prior to sequencing.

Pet. 23–24 (citing Ex. 1085 ¶¶ 121–123).

In the DI, we addressed Patent Owner's arguments disputing Petitioner's proposed definition. DI 10–12 (citing Prelim. Resp. 15–17). We stated that

> for purposes of this Decision, we find a POSA would have had a Ph.D. in the field of chemistry, molecular biology, or biochemistry. Alternatively, a POSA would have had a B.S. or M.S. degree with three to five years of experience working in any of those fields. Additionally, the POSA would have had

> experience with NGS sequencing methods and a working knowledge of how those methods functioned.

Id. at 12.

After institution, Patent Owner states that, for purposes of this proceeding, it adopts the Board's definition of a POSA. PO Resp. 16.

After reviewing the record developed during trial, we see no reason to change our finding on this issue. As we stated in the DI, our "definition of a POSA is consistent with the skill level reflected in the disclosures of the '108 patent and prior art." DI 12.

We find the parties' declarants, Drs. Sims, Bustamante, and Meyer are qualified to opine from the perspective of a POSA, because each has at least ordinary skill in the art. *See* Ex. 1085 ¶¶ 4–16; Ex. 2038 ¶¶ 11–25; Ex. 2287 ¶¶ 5–14.

C. Claim Construction

In an *inter partes* review, we construe a claim term "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) (2020). Under that standard, the words of a claim "are generally given their ordinary and customary meaning," which is "the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention, i.e., as of the effective filing date of the patent application." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312–13 (Fed. Cir. 2005) (en banc).

1. <u>"Sequence of Interest"</u>

Petitioner proposes that we construe the terms "sequence of interest" and "barcode." Pet. 24–25. According to Petitioner, the '108 patent defines "sequence of interest," which is used interchangeably with terms "target nucleic acid sequence" and "target sequence," as "a polynucleotide sequence

of interest, for which enrichment is desired." *Id.* at 24 (citing Ex. 1002, 21:3–5, 21:8–11). In the DI, we adopted Petitioner's proposed construction of the term "sequence of interest." DI 13. Patent Owner does not dispute, and we see no reason to change, this construction. *See* PO Resp. 16. We maintain the construction for our analysis here.

2. "Enrich"

Claim 1 is directed to a method "for sequencing an enriched nucleic acid sequence of interest." It recites in step (c) "amplifying the one or more oligonucleotide extension products . . . thereby enriching the nucleic acid sequence of interest, by generating amplified products comprising the enriched nucleic acid sequence of interest" and in step (d) "sequencing the amplified products comprising the enriched nucleic acid sequence of interest."

In the DI, we stated that

> [n]either party proposes any special meaning for the term "enrich." We see no reason to do so either. To the extent express construction of "enrich" is necessary, we adopt the plain and ordinary meaning of the term. *See* Ex. 3001 (entry e defining "enrich" to mean "to process so as to add or increase the proportion of a desirable ingredient").

DI 13.

Petitioner does not dispute the plain and ordinary meaning of "enrich" that we set forth in the DI. Reply 3. Patent Owner also "does not dispute the Board's preliminary definition of the term 'enrich' in the abstract." PO Resp. 17. Despite the purported agreement with our claim construction, the parties debate the meaning of the term "enrich" in step (c) of claim 1. We address those arguments below.

a. Relative to Other Fragments

As an initial matter, we acknowledge that the definition "to process so as to add or increase the proportion of a desirable ingredient" has two possible interpretations. In the first interpretation, "add or increase" shares the same object "the proportion of a desirable ingredient." When the proportion of one ingredient goes higher, the proportion of at least another ingredient would necessarily go lower. Thus, the enrichment process under this interpretation results in a higher proportion of the desirable ingredient relative to other ingredients.

Patent Owner adopts this interpretation. *See* PO Resp. 17 ("In the context of preparing a sequencing library, [Patent Owner] Tecan proposes that a nucleic acid sequence of interest is 'enriched' when the proportion of nucleic acid fragments containing the sequence of interest is increased relative to other nucleic acid fragments in the sample."). According to Patent Owner, "amplifying the one or more oligonucleotide extension products . . . thereby enriching the nucleic acid sequence of interest, by generating amplified products comprising the enriched nucleic acid sequence of interest" in step (c) means "increas[ing] the proportion of the nucleic acid sequence of interest relative to the nucleic acid fragments in the solution not containing the sequence of interest by amplifying the oligonucleotide extension product and its complement." *Id.* at 19–20.

Under the second interpretation, the object for "add" is "a desirable ingredient," whereas the object for "increase" is "the proportion of a desirable ingredient." This interpretation is broader than the first one in that the result of the enrichment process not only encompasses a higher proportion of the desirable ingredient relative to other ingredients, but also more desirable ingredient in raw number.

In its Reply, Petitioner argues that the enrichment process only needs to result in more sequence of interest in raw number. *See* Reply 1 ("[T]he claims simply require that more fragments containing the sequence of interest are created."); *see also id.* at 7 (arguing that Patent Owner's expert "Dr. Bustamante conceded the proper 'baseline' is not a comparison to other fragments but rather the number of fragments with the sequence of interest expected if the method were not performed") (citing Ex. 1125, 283:9–14, 286:2–287:6); *id.* (arguing that Patent Owner's "other expert, Dr. Meyer, confirmed that amplification of the sequence of interest necessarily results in 'enrichment'") (citing Ex. 1126, 170:18–171:1). According to Petitioner, we should reject Patent Owner's contention that "the amplification step must amplify fragments with the sequence of interest relative to other unrecited fragments (instead of relative to the sequence of interest absent the claimed amplification)." *Id.* at 5.

Elsewhere, however, Petitioner argues differently. *See* Pet. 40 (arguing that Meyer discloses step (c) because Meyer's amplification "was to enrich for the 3′ end fragments *compared to other cDNA fragments* present in the sample that lacked the requisite adaptors") (emphasis added); 42 ("[T]he library preparation and sequencing method disclosed in Meyer is specifically designed to enrich for nucleic acid fragments (i.e., specifically amplify *relative to other fragments*) containing a particular 'nucleic acid sequence of interest.'") (emphasis added); 50 ("[T]he Meyer authors confirmed that these fragments were found at a greater prevalence than fragments at other portions of the strand, thus confirming that they were enriched *compared to other mRNA fragments*.") (emphasis added). Putting aside whether Meyer discloses as Petitioner alleges, these arguments suggest

that, in the Petition, Petitioner interprets "enrich" as being "relative to other fragments."

Thus, Petitioner's interpretation of "enrich" has changed from "relative to other fragments" in the Petition to "not a comparison to other fragments" in the Reply. *Compare* Pet. 40, 42, 50, *with* Reply 5, 7.

Nonetheless, during oral hearing, counsel for Petitioner clarified that to "enrich" means to "increase[] relative to the rest of the fragments." Tr. 12:25–26. The panel asked: "In the starting material, there are three components, A, B, C, that say it's 30 percent, 50 percent and 20 percent. You do PCR and it -- they all get amplified and the end result is still 30 percent, 50 percent, and 20 percent. Anything got enriched?" *Id.* at 12:18–21. Petitioner responded that "petitioner's position is that in that situation, there is no enrichment." *Id.* at 12:22–23. In other words, Petitioner does not disagree with Patent Owner that mere increase in the raw number is not enrichment. *See also id.* at 13:7–9 ("[W]e would agree that if it is truly unbiased amplification, that does not result in an increase in the proportion, and so that does not meet the plain meaning of enrich.").

We find the record, including the testimony from all three declarants, supports Patent Owner's argument. *See* Sur-reply 1–5 (citing Ex. 1125, 283:1–6, 286:22–287:14; Ex. 1126, 170:18–171:1; Ex. 2037, 150:18–22, 173:15–17; Ex. 2038 ¶ 95), 8 (citing Ex. 1125, 271:10–15; Ex. 2037, 188:22–189:1). Thus, we adopt Patent Owner's proposal that "a nucleic acid sequence of interest is 'enriched' when the proportion of nucleic acid

fragments containing the sequence of interest is increased relative to other nucleic acid fragments in the sample."[7] *See* PO Resp. 17–18.

b. Result of Amplification

Step (c) recites that "amplifying the one or more oligonucleotide extension products . . . thereby enriching the nucleic acid sequence of interest, by generating amplified products comprising the enriched nucleic acid sequence of interest." Petitioner argues that the "thereby enriching" clause "merely states the result of the limitations in the claim." Reply 6 (citing *Texas Instruments Inc. v. Int'l Trade Comm'n*, 988 F.2d 1165, 1172 (Fed. Cir. 1993)). According to Petitioner, "[s]uch a clause 'in a method claim is not given weight when it simply expresses the intended result of a process step positively recited.'" *Id.* (quoting *Minton v. Nat'l Ass'n of Securities Dealers, Inc.*, 336 F.3d 1373, 1381 (Fed. Cir. 2003)). We are not persuaded by Petitioner's argument for two reasons.

First, the language in the "thereby enriching" clause serves as the antecedent basis for step 1(d), which recites "sequencing the amplified products comprising the enriched nucleic acid sequence of interest."

---

[7] Patent Owner asserts that "the claims require that the sample include fragments in the solution that do not contain the sequence of interest and that those fragments are not amplified." PO Resp. 15. During oral hearing, counsel for Patent Owner clarified that "it is not Tecan's position . . . that there can only be one thing that's amplified in a solution." Tr. 45:16–21. In any event, to the extent Patent Owner argues that fragments without the sequence of interest cannot be amplified in any step of claim 1, including any unrecited step, we disagree. Fragments with the sequence of interest are enriched as long as their proportion is increased relative to other fragments in the sample, regardless of whether the other fragments are amplified or not.

Second, when construing a claim term, a POSA "is deemed to read the claim term not only in the context of the particular claim in which the disputed term appears, but in the context of the entire patent, including the specification." *Phillips*, 415 F.3d at 1313. The Specification of the '108 patent demonstrates that the claimed invention is ultimately a method for enriching for target nucleic acid sequences of interest. *See, e.g.*, Ex. 1002, code (54) (patent title "Compositions and Methods for Targeted Nucleic Acid Sequence Enrichment and High Efficiency Library Generation"); code (57) ("The present invention provides methods, compositions and kits for targeted nucleic acid sequence enrichment in a nucleic acid sample . . . "); 2:27–28 ("There is a need for improved methods for selective target enrichment . . ."); 2:36–38 ("In one aspect, disclosed herein are methods for enriching for target nucleic acid sequences of interest in a sample comprising nucleic acids . . ."); 3:15–17 ("In another aspect, disclosed herein are methods for enriching for target nucleic acid sequences of interest in a sample comprising nucleic acids . . ."); 4:57–59 ("In further aspect, disclosed herein are methods for enriching for target nucleic acid sequences of interest from a library . . ."); 6:27–29 ("Altogether, the methods of the present invention create a simple, low cost, high throughput system for target enrichment and library preparation.").

In view of the claim language and the Specification, we agree with Patent Owner that "[e]nrichment of the target sequence resulting from the amplification step is critical to the invention." *See* Sur-reply 6. Because the "thereby enriching" clause "states a condition that is material to patentability, it cannot be ignored in order to change the substance of the invention." *See Hoffer v. Microsoft Corp.*, 405 F.3d 1326, 1329 (Fed. Cir. 2005).

Patent Owner argues that "the plain language of the claim and this limitation [of step (c)] confirms that the amplification step must cause enrichment of the fragment defined in this limitation." PO Resp. 20. Petitioner does not dispute that "at least ***some*** of the enrichment must result from the recited steps." Reply 12. Petitioner, however, argues that we should reject Patent Owner's contention that "the amplification step must be solely responsible for enrichment." *Id.* at 5.

We agree with Petitioner that "enrichment need not be solely the result of amplification." *See* Reply 11 (heading normalized). As we understand it, however, Patent Owner does not argue otherwise.

Indeed, claim 1 employs the open-ended transitional phrase "comprising." As such, the claimed method may encompass other, unrecited steps, which may result in enrichment of the nucleic acid sequence of interest. During the oral hearing, counsel for Patent Owner acknowledged such a scenario but argued that, under the claimed method, the amplification step must independently enrich for the nucleic acid sequence of interest. Tr. 50:24–51:19 (denying that "amplification has to be the sole reason" for enrichment and agreeing that "enrichment could be because of other [steps], but amplification itself has to enrich"); *see also* Sur-reply 8 ("Step 1(c) requires that amplification enrich the sequence of interest. That other steps in the method may further enrich genetic material is irrelevant.").

c. Summary

In sum, the parties agree that a nucleic acid sequence of interest is enriched not when the raw number is increased, but when the proportion of fragments containing the sequence of interest is increased relative to other fragments in the sample. The parties also agree that the amplification step

must result in at least some enrichment of the sequence of interest, even though it does not have to be the only cause. As explained above, we agree with the parties on both issues.

Claim terms need only be construed to the extent necessary to resolve the controversy. *Wellman, Inc. v. Eastman Chem. Co.*, 642 F.3d 1355, 1361 (Fed. Cir. 2011). On this record and for purposes of this Decision, we see no need to construe any other claim term expressly.

D. Alleged Anticipation by Meyer

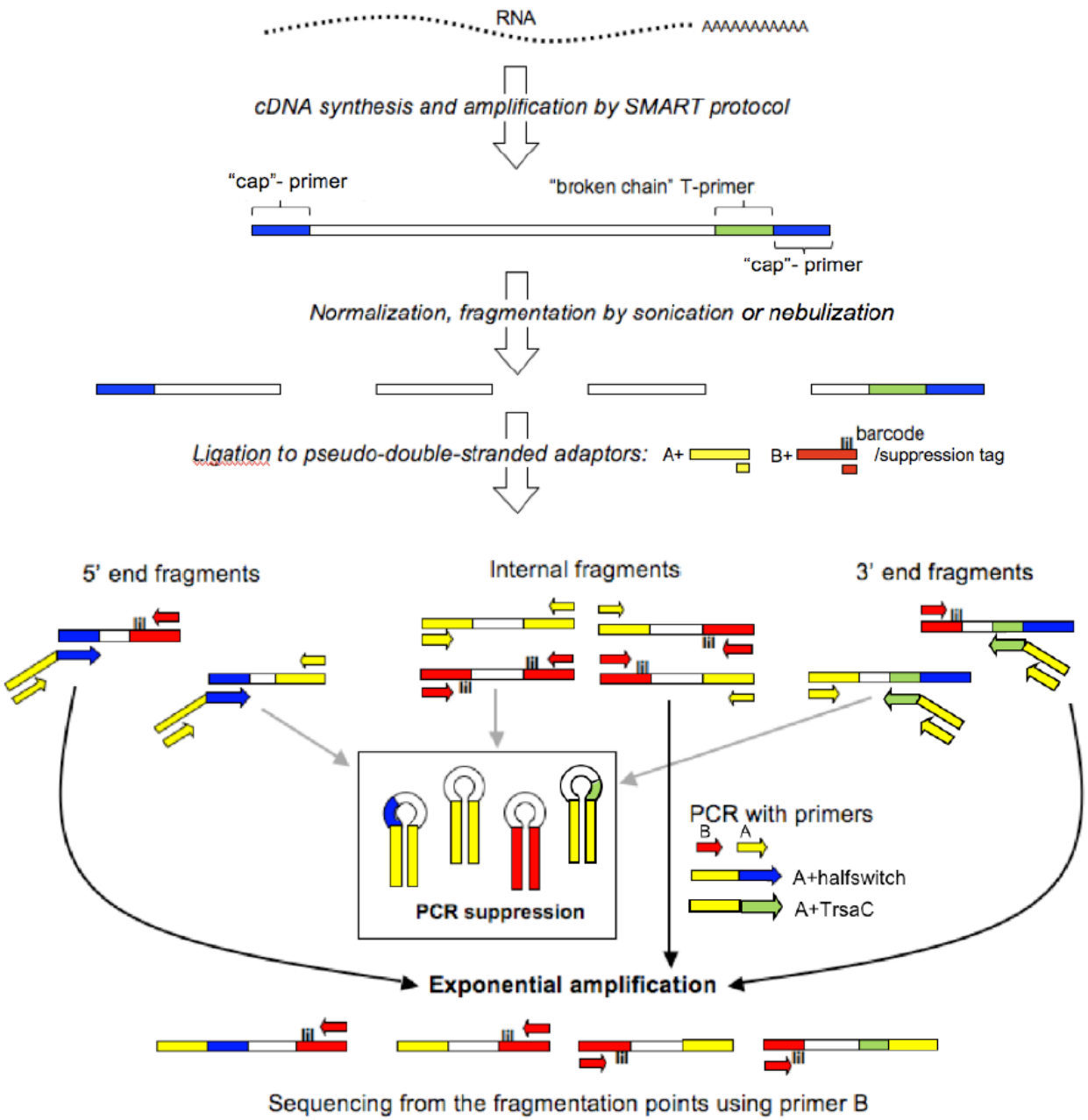
Petitioner asserts that Meyer anticipates claims 1, 3, 5–10, and 14–18. Pet. 28–60. After reviewing the entire record developed at trial, and as explained below, we determine Petitioner has not shown by a preponderance of the evidence that Meyer anticipates the challenged claims.

1. Disclosure of Meyer

Meyer describes "methods for transcriptome sequencing using 454, as well as strategies for assembling a useful catalog of genes from the output." Ex. 1006, Abstract. These methods were "applied to sequence the transcriptome of planulae larvae from the coral *Acropora millepora*." *Id.*

Meyer describes one method for sequencing coral larval transcriptome. *Id.* at 2, 12–14, Fig. 1. In Additional File 4, Meyer describes a second method that includes minor modifications to improve reproducibility and further reduce the occurrence of adaptor concatenation. *Id.* at 14, 19–25. Meyer states that the protocol in additional File 4 "is recommended for researchers interested in using our methods for 454 sequencing of transcriptomes." *Id.* at 14.

Meyer's second method is schematically illustrated in the figure reproduced below.



The figure above is a color schematic showing an improved protocol for transcriptome analysis in emerging model organisms, as described in Meyer's Additional File 4. *Id.* at 20.

In the first step of this method, cDNA is synthesized and amplified from RNA using the SMART™ PCR cDNA Synthesis Kit from Clontech and a synthesis primer with a "cap" primer sequence at the 5′ end and a

"broken chain" polyT at the 3′ end. *Id.* at 19–20. The "broken chain" polyT primer is used "to reduce read artifacts during 454 pyrosequencing, which may get thrown out of calibration by too strong of a light signal produced from a long mononucleotide stretch (such as polyT or polyA)." *Id.*

In the second step, the cDNA may be normalized and reamplified using the "cap" primer, and is fragmented to an average size of 350–400 bp using sonication or nebulization. *Id.* at 19–20.

Third, the cDNA fragments are end-polished by incubation with a DNA polymerase and dNTPs, and then ligated to pseudo-double-stranded A+ and B+ adaptors at the "new" 5′ ends. *Id.* at 19, 20. The A+ and B+ adaptors each contain an equimolar mixture of: (1) a long oligo that gets ligated at its 3′ end and contains a suppression tag and the standard 454 A or B primer sequence, respectively; and (2) a short oligo that is complementary to the 3′ end of the long oligo to mimic the double-stranded blunt end for the ligase enzyme. *Id.* at 19. According to Meyer, "[t]he short oligo is not ligated since it lacks a 5′-phosphate." *Id.*

In the fourth step, the library is amplified using a mixture of the standard 454 A and B primers, as well as two long "step-out" primers (A+TrsaC and A+halfswitch) "to incorporate the A+ sequence at each of the original cDNA termini." *Id.* at 19–20. Meyer explains that "suppression tags" are used to "invoke a PCR suppression effect for the fragments that end up flanked by the same kind of adapter, which results in exclusive amplification of the fragments flanked by both A and B primers." *Id.* at 20. Meyer further discloses a "chase" step, in which the standard 454 A and B primers are used for "[e]xponential amplification." *Id.* at 20, 25.

In the final step, the library is sequenced using the B primer. *Id.* at 20.

Meyer states that its methods "resolve several challenges associated with 454 sequencing of transcriptomes." *Id.* at 9. According to Meyer,

> [b]ecause 454 sequencing does not efficiently process homopolymer regions greater than 8 bp in length, the poly-A tails at the 3' ends of intact transcripts present a problem, and would be expected to result in under-representation of the 3' ends of transcripts. In our method, this is resolved by simply interrupting the poly-T region with a single C. A single copy of this 'broken-T' adaptor was found in 98,276 of the raw reads (16% of the total), slightly more than the expectation (~10%) based on average read length (232 bp) and assuming an average transcript size of 2,200 bp. This comparison suggests that the 3' ends of transcripts were well-represented in our dataset, confirming the effectiveness of this solution for overcoming the homopolymer problem.

Id.

2. Claim 1

We focus our analysis on independent claim 1. Claim 1 is directed to a method for sequencing an enriched nucleic acid sequence of interest. Ex. 1002, 35:18–19. In particular, step (c) recites "amplifying the one or more oligonucleotide extension products . . . thereby enriching the nucleic acid sequence of interest, by generating amplified products comprising the enriched nucleic acid sequence of interest." *Id.* at 35:41–48.

Petitioner argues that Meyer discloses each limitation of claim 1. Pet. 42–50. According to Petitioner,

> The Meyer method was a method of enrichment in two senses. First, the Meyer method enriched for mRNA specifically, as opposed to other types of RNA or other nucleic acids in the original sample. EX1085.¶143; EX1006.0012-13, 0019-20. Second, through the use of the 3′ end anchored PCR, the Meyer method enriched for the 3′ end fragments compared to other mRNA. EX1085.¶144.

Id. at 31.

Patent Owner disagrees. PO Resp. 23–41. According to Patent Owner, "Meyer does not disclose enrichment of a target sequence through amplification as required by claim 1." *Id.* at 23 (heading normalized). Patent Owner contends that, in Meyer, it is the SMART protocol, and not any claimed step, that enriches the sample for mRNA over other types of RNA. *Id.* at 24. Patent Owner also argues that "the amplification step in Meyer was not designed to, and does not, enrich for the 3′ end fragments." *Id.* at 25–31.

On this record, we find Patent Owner's arguments more persuasive. We explain our reasoning below.

a. Alleged Enrichment of mRNA

Meyer discloses a method for sequencing the coral transcriptome. Ex. 1006, 1. Dr. Sims, Petitioner's declarant, opines that Meyer's full-transcriptome sequencing method is "a selective enrichment method, as it required selectively enriching for mRNA molecules over other types of RNA and other nucleic acids present in the original sample." Ex. 1085 ¶ 143 (citing Ex. 1006, 20). Although we agree with Petitioner and Dr. Sims that Meyer's method "enriched for mRNA specifically, as opposed to other types of RNA or other nucleic acids in the original sample" (Pet. 31), it does not satisfy the claimed "enrichment" under our construction.

As Petitioner recognizes, "Meyer used a commercially-available kit to isolate full-length strands of mRNA from other nucleic acids in the sample" and reverse transcribed those mRNA molecules to cDNA using the same kit via a method called the "SMART protocol." Pet. 31 (citing Ex. 1006, 12–13; Ex. 1034; Ex. 1085 ¶¶ 146–147). "[T]he SMART method is able to preferentially enrich for full-length cDNAs." Ex. 1034, 4; Ex. 2038 ¶¶ 176–178; Ex. 2287 ¶ 35. The Meyer reference shows, and Dr. Meyer, the

first author of the publication, confirms, that the SMART protocol process occurred before fragmentation and before the fragments are ligated to adaptors. Ex. 1006, 13; Ex. 2287 ¶¶ 37–40.

During his deposition, Dr. Sims testified that

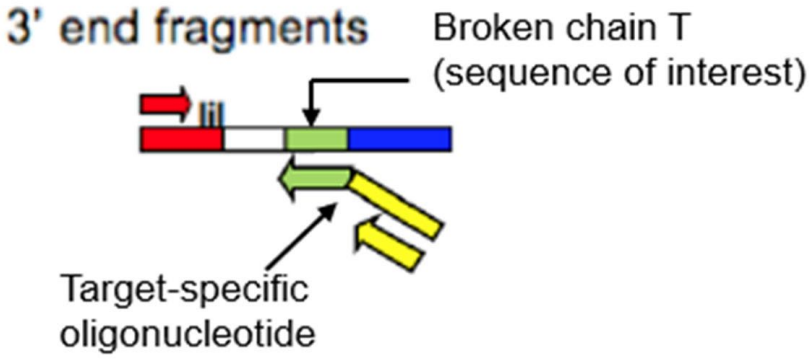
> [m]y interpretation is that claim 1 describes an enrichment process, and so overrepresentation of a nucleic acid sequence of interest at the beginning of the process doesn't satisfy the claim. The process described here [in claim 1] enriches. It's possible that other things are going on that also contribute to enrichment, but the process described here [in claim 1] is critical for enrichment.

Ex. 2037, 194:9–16.

We agree with Dr. Sims. As explained above, the amplification step must result in at least some enrichment of the sequence of interest, even though it does not have to be the only cause. *See supra* Section II.C.2.b. Indeed, Petitioner acknowledges that "at least ***some*** of the enrichment must result from the recited steps." Reply 12. Because Meyer's enrichment for mRNA using the SMART protocol occurred before any recited steps of claim 1, we find it does not meet the claimed "enrichment" under our construction.

b. Alleged Enrichment of the 3′ End Fragments

Petitioner asserts that "the Meyer method enriched for the 3′ end fragments compared to other mRNA." Pet. 31 (citing Ex. 1085 ¶ 144). Petitioner draws our attention to the following figure.



The figure above is Petitioner's annotation of a portion of the schematic illustration of the protocol described in Meyer's Additional File 4. *Id.* at 44. Petitioner argues that the broken chain T primer sequence (green box) is the claimed "nucleic acid sequence of interest." *Id.* at 45.

According to Petitioner, "[v]ia th[e] anchored PCR reaction and as part of the overall Meyer method, the 3′ fragments underwent every step recited in the '108 patent method." Pet. 30–31. Petitioner contends that, in Meyer, following ligation of the partial duplex adaptors (red), a target-specific oligonucleotide (green and yellow) was annealed to the nucleic acid sequence of interest (green). *Id.* at 44 (citing Ex. 1006, 20; Ex. 1085 ¶¶ 133, 190–196, 268–270). Petitioner contends that extending the green-yellow primer resulted in an extension product "comprised of a sequence complementary to the red adaptor sequence at one end, the complement of the target fragment in the middle, and the green-yellow primer sequence, including the yellow adaptor, on the other end." *Id.* at 47 (citing Ex. 1006, 20; Ex. 1085 ¶¶ 198, 271, 272).

Petitioner asserts that subsequent PCR reactions amplified the extension product using primers complementary to the red and yellow adaptors and generated "a library of double-stranded DNA products containing the 'sequence of interest' (green broken chain T primer) and the

adjacent mRNA fragment sequence." *Id.* at 48–50 (citing Ex. 1006, 20; Ex. 1085 ¶¶ 199, 200, 273, 274). Petitioner asserts that "these fragments were found at a greater prevalence than fragments at other portions of the strand, thus confirming that they were enriched compared to other mRNA fragments." *Id.* at 50; *see also id.* at 40 ("The result of that amplification was to enrich for the 3′ end fragments compared to other cDNA fragments present in the sample that lacked the requisite adaptors.") (citing Ex. 1006, 20; Ex. 1085 ¶¶ 143, 144, 266, 267, 168–175, 182).

On this record, we are not persuaded that the 3′ fragments in Meyer are "enriched" under our construction. We explain our reasoning below.

i. Reduce Read Artifacts During 454 Pyrosequencing

Meyer's method uses 454 pyrosequencing platform. Ex. 1006, 1, 19. "Because 454 sequencing does not efficiently process homopolymer regions greater than 8 bp in length, the poly-A tails at the 3' ends of intact transcripts present a problem, and would be expected to result in under-representation of the 3' ends of transcripts." *Id.* at 9. Meyer's method resolves this issue "by simply interrupting the poly-T region with a single C." *Id.* "The purpose of the 'broken chain' T-primer is to reduce read artifacts during 454 pyrosequencing, which may get thrown out of calibration by too strong of a light signal produced from a long mononucleotide stretch (such as polyT or polyA)." *Id.* at 19.

Dr. Meyer further explains that

> [i]n a typical nucleotide sequence where the sequence is varied, a single nucleotide would be added to the complementary sequence, emitting a single signal pulse. However, when several bases of the same kind appear in a row (a homopolymer comprising, for example, sequences CCCC or AAAAAA), the addition of the homopolymer-forming nucleotide in that round

> results in multiple base incorporations, generating a brighter light signal. The brightness of this signal is used by the 454 instrument to infer how many bases are repeated within the homopolymer sequence.
>
> This method can malfunction with the poly-A sequence found at the end of every protein-coding transcript. Assuming a typical library preparation protocol (such as the SMART cDNA amplification kit), the poly-A tail could be 30 bases long. Incorporation of that many nucleotides in the same 454 sequencing round would generate a far stronger burst of light than the 454 platform's sensors were equipped to handle. Such a burst would essentially blind the sensors, throwing off their calibration and leading the instrument to discard the whole read as well as reads in neighboring microwells, which could result in the failure of the whole sequencing run.
>
> Even though we ensured that sequencing always starts from the actual coral transcript part (Figure 1), due to the randomness of fragmentation, the coral part can be short enough for the read to run into the adaptor sequence, including the poly-A/T stretch. Even though we used a shorter poly-T-primer than standard (with only 13 "T" bases in a row, *see* EX1006.0013), any sequencing of that region would have led to us having to discard the poly-A/T containing reads and nearby wells.

Ex. 2287 ¶¶ 29–31.

Based on Meyer's disclosure and Dr. Meyer's unrebutted testimony, we find that the issue of "under-representation of the 3' ends of transcripts" occurs not in the physical sample, but in the data output from the 454 sequencer.

Dr. Meyer repeatedly testifies that the Meyer method employed the "broken-T" primer "solely to resolve the 'poly-A blinding' problem during 454 sequencing." Ex. 2287 ¶ 67 (citing Ex. 1006, 9, 19); *see also id.* ¶ 31 ("We did this to avoid the 'sensor-blinding' problem with the 454 sequencer."). According to Dr. Meyer, "[t]he breaking of the poly-T chain in

no way impacted the relative proportion of 3' end fragments that were amplified during library preparation." *Id.* ¶ 67.

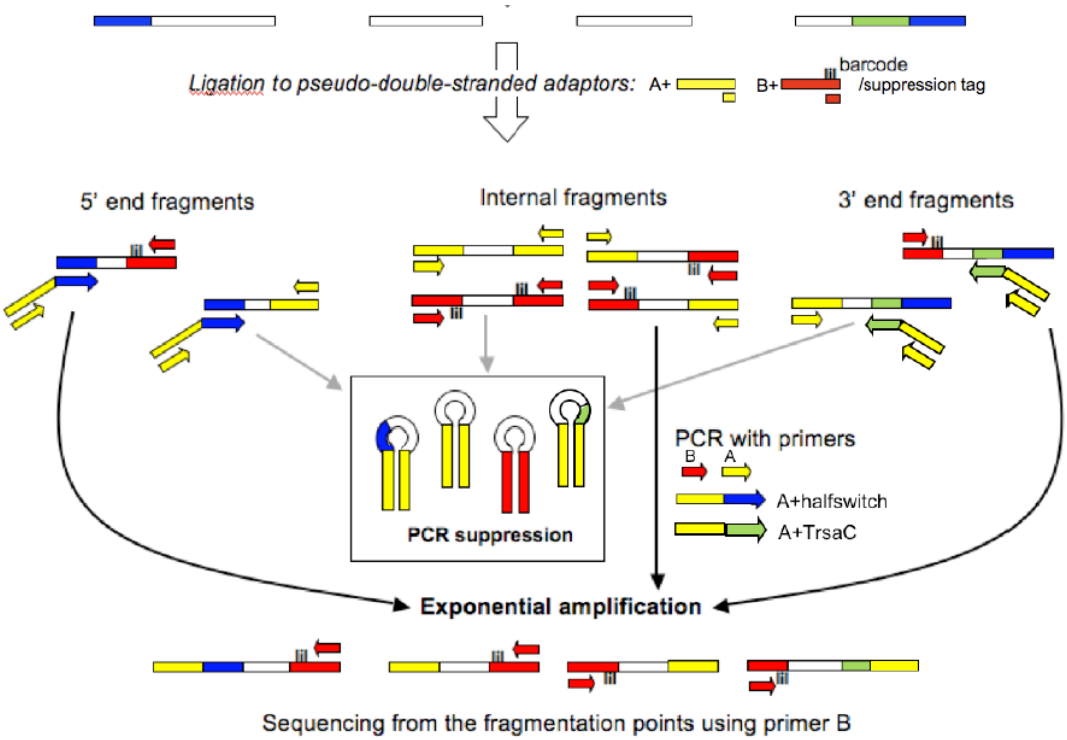
We credit Dr. Meyer's testimony, which is further supported by the disclosure of the Meyer reference. Indeed, Meyer reports that a single copy of this "broken-T" adaptor was found in 16% of the total raw reads, slightly more than the expected 10%. Ex. 1006, 9. Instead of supporting Petitioner's argument of enrichment of the 3' end fragments, Meyer explains that "[t]his comparison suggests that the 3' ends of transcripts were well-represented *in our dataset*, confirming the effectiveness of this solution for overcoming the homopolymer problem." *Id.* (emphasis added).

Employing a "broken-T" adaptor allows the 454 sequencer to *recognize more* 3' end fragments. Petitioner does not explain sufficiently why and how we should equate increased recognition, which leads to more reads, and thus, better representation of 3' ends of transcripts in the *dataset*, with increased proportion of the 3' end fragments in the *physical* library. For this reason alone, we find Meyer does not disclose enrichment of the 3' end fragments.

ii. Unbiased Amplification

Petitioner also contends that "through the use of the 3′ end anchored PCR, the Meyer method enriched for the 3′ end fragments compared to other mRNA." Pet. 31 (citing Ex. 1085 ¶ 144). We are not persuaded by this argument either.

Petitioner's arguments focus on the 3′ end fragments. Pet. 30–34, 38–40. Meyer's method, however, amplifies not only the 3′ end fragments, but also the 5′ end and the internal fragments, as shown in the following figure. Ex. 1006, 20.



The figure above is an excerpt of the protocol in Meyer's Additional File 4. As Patent Owner correctly points out,

> after the adapters are added, Meyer depicts ***eight*** types of fragments: two 5' end fragments that contain either the Primer A or Primer B sequence at one end and the cap primer on the other, four combinations of internal fragments with different sets of flanking primers, and two 3' end fragments that contain either the Primer A or Primer B sequence at one end and the modified cap primer on the other. Meyer does not disclose the relative proportions of these fragments. EX2287.¶75.

PO Resp. 27–28.

Meyer discloses amplifying the adaptor-ligated fragments using four primers: the standard 454 A (yellow) and B (red) primers, A+halfswitch (yellow and blue, with primer A and sequence complementary to the cap primer), and A+TrsaC (yellow and green, with primer A and sequence complementary to the broken-T chain). Ex. 1006, 19; Pet. 36; PO Resp. 28.

As Petitioner acknowledges, "these four primers annealed to their respective complementary sequences in the PCR reaction." Pet. 37 (citing Ex. 1085 ¶¶ 169, 173, 174). When discussing the polymerase extension step of PCR, however, Petitioner focuses exclusively on one of the four primers, "the annealed green-yellow primer is extended" to generate 3′ end fragments. *Id.* at 38; *see also* Reply 16 ("Meyer taught the use of an additional [A+TrsaC] primer to target and amplify 3′ end fragments.") (citing Ex. 1085 ¶ 144).

In reality, the polymerases, in the same reaction, also extended the primers annealed to the 5′ end fragments (blue-yellow) and the internal fragments (yellow). Ex. 1006, 19, 20, 25. As Dr. Meyer explains, after the primers anneal to their corresponding sequences on the fragments, extension products for both end fragments (5′ end and 3′ end), as well as the internal fragments were generated. Ex. 2287 ¶ 44. We find a POSA would readily understand this scientific fact about how the Meyer method works. Indeed, Petitioner's declarant, Dr. Sims, presents no persuasive response to Dr. Meyer on this point.

Thus, Petitioner's assertion that "Meyer extended the annealed fragments to generate 3′ fragments with adaptors on both ends" (Pet. 38, heading normalized), although not incorrect, paints an incomplete picture. Petitioner neglects to mention that Meyer also extended other annealed fragments to generate 5′ end fragments and internal fragments with adaptors on both ends.

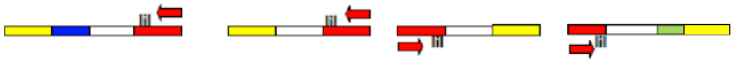
Petitioner maps claim 1's amplification step (c) to Meyer's "chase" step, in which the standard 454 A and B primers are used for "[e]xponential amplification." Pet. 48–50 ("[I]n subsequent rounds of the ongoing PCR reaction, the resulting extension product was further amplified in subsequent

cycles by primers to the red and yellow sequences.") (citing Ex. 1006, 19, 20; Ex. 1085 ¶¶ 168–175, 199, 273, 274); *see also* Ex. 1006, 20, 25 (showing conditions for the "chase" step).

Dr. Meyer testifies that "[a]ll fragments with a Primer A binding site on one end and a Primer B binding site on the other end were exponentially amplified." Ex. 2287 ¶ 45. In other words, the 5′ end fragments, the internal fragments, and the 3′ end fragments, as long as they have two different primer binding sites on the two ends, were all amplified. *See* Ex. 1006, 20 (disclosing "exclusive amplification of the fragments flanked by both A and B primers").

Petitioner does not dispute this point, agreeing that "Meyer amplified the extension products of the prior step using primers that were complementary to the red and yellow adaptors." Pet. 40 (citing Ex. 1006, 20; Ex. 1085 ¶ 174). Petitioner, however, asserts that "[t]he result of that amplification was to enrich for the 3′ end fragments compared to other cDNA fragments present in the sample that lacked the requisite adaptors." *Id.* (citing Ex. 1006, 20; Ex. 1085 ¶¶ 143, 144, 266, 267, 168–175, 182); *see also* Reply 16 (arguing "the amplification step in Meyer created exponentially more 3′ end fragments").

We are not persuaded by this argument because Petitioner, again, focuses on the 3′ extension products only, and ignores the 5′ and internal extension products. As shown in the figure below, the 5′ and internal extension products also have the red and yellow primers.



The figure above is an excerpt of the protocol in Meyer's Additional File 4. Ex. 1006, 20. It shows a 5′ extension product, two internal extension

products, and a 3′ extension product, each of which is flanked by both A (yellow) and B (red) primers. In view of this, we find Petitioner has not explained sufficiently why amplification "using primers that were complementary to the red and yellow adaptors" would "enrich for the 3′ end fragments compared to other cDNA fragments." *See* Pet. 40.

Petitioner's theory is flawed, but not simply because the 5′ end fragments and the internal fragments were amplified alongside the 3′ end fragments. As explained above, "[f]ragments with the sequence of interest are enriched as long as their proportion is increased relative to other fragments in the sample, regardless of whether the other fragments are amplified or not." *Supra* fn. 9. To prevail in this proceeding, however, Petitioner must show Meyer's amplification step results in at least some enrichment of the 3′ end fragments, even though it need not be solely responsible for the enrichment. *See supra* Section II.C.2.b. This, Petitioner has not done.

Petitioner contends that enrichment is nonetheless shown based on Meyer's disclosure that the 3′ end fragments were found in 16% of the total reads, "slightly more than the expectation (~10%)." Pet. 31 (citing Ex. 1006, 9; Ex. 1085 ¶¶ 145, 184); Reply 17 (citing Ex. 1006, 9). We are not persuaded that this comparison demonstrates Meyer discloses enrichment of the 3′ end fragments under our construction of "enrich."

First, as explained above, Meyer explicitly states that this comparison refers to the number of reads in the dataset, which, according to Dr. Meyer, does not correspond to the number of 3′ end fragments in the physical library due to "the 'sensor-blinding' problem with the 454 sequencer." *See supra* Section II.D.2.b.i (citing Ex. 1006, 9; Ex. 2287 ¶¶ 31, 67).

Second, under our construction of "enrich," the amplification step must result in at least some enrichment of the sequence of interest, even though it does not have to be the only cause. *See supra* Section II.C.2.b. Here, even if we consider the 16% to 10% comparison as reflecting the increase of 3′ end fragments in the physical library, Petitioner has not shown that increase, or at least part of that increase, is the result of the amplification step. After all, the library was first amplified in the same reaction using a mixture of primers to generate the 5′ extension products, the internal extension products, and the 3′ extension products, all of which were flanked by both A (yellow) and B (red) primers. Afterwards, those extension products were all amplified using the same primers, again, in the same reaction. Because these are unbiased amplifications, we find Petitioner has not shown it enriched the 3′ end fragments. *See* Tr. 13:7–9 (Petitioner "agree[d] that if it is truly unbiased amplification, that does not result in an increase in the proportion, and so that does not meet the plain meaning of enrich").

Third, Dr. Meyer testified that the Meyer method "was not designed to target specific regions of the mRNA transcripts. In order to accurately sequence the entire length of the transcripts, we specifically did not want to enrich certain targets within those transcripts." Ex. 2287 ¶ 70. According to Dr. Meyer, the observed 16% "was a good match" to the "very approximate 'ballpark' estimate" of 10%, indicating the method "was not off by several fold in terms of over- or under-representation of 3'-end fragments." *Id.* ¶ 58.

Dr. Meyer further testified that the 16% reads with broken-T sequence "was not a measure of enrichment but a way for confirming that the broken chain T sequence appeared within a reasonable amount of sequencing reads. Nor could it have been a measure of enrichment." *Id.* ¶ 74; *see also id.* ¶ 75

("The data does not reflect the inadvertent enrichment of the 3' end fragment over other cDNA fragments during amplification . . . [because] the approximate, back-of-the-envelope nature of our prediction of expected sequences (10%) simply cannot support such an inference.").

Petitioner argues that "Dr. Meyer was never provided the patent, never provided with the board's construction [of "enrich"], and never provided with Tecan's construction. So it's completely unclear what the single paragraph in Dr. Meyer's declaration was meant to mean, or what he thought enrichment meant, or what construction he thought he was applying." Tr. 26:2–6. We are not persuaded by this argument.

In denying that the observed 16% represents enrichment of the 3' end fragments over the observed 10%, Dr. Meyer specifically pointed out that the authors "never reported in Meyer on the number of 5' end fragments or internal fragments for comparison." Ex. 2287 ¶ 75. According to Dr. Meyer, the Meyer method "produced a sequence dataset that included 5' ends of genes, 3' ends of genes, and internal regions of genes," a "dataset that wasn't completely lacking in any one of those three categories." Ex. 1126, 179:19–180:2. He explained that although the Meyer method achieved the goal of representing all the regions of a gene "in terms of presence and absence," there was insufficient data to make "quantitative comparison," that is, to evaluate "whether the frequency of those fragments in the final pool was more or less than it started at or more or less than the other fragments." *Id.* at 180:3–181:5.

Dr. Meyer's testimony demonstrates that he understood and applied the plain and ordinary meaning of "enrich." As such, we credit Dr. Meyer's testimony that "[a]ny suggestion that the data reflects an enrichment of the 3' end fragments over the other cDNA fragments in our library of fragments

that were sequenced misinterprets what we actually reported in Meyer." Ex. 2287 ¶ 77.

c. Summary

In sum, we find Petitioner has not shown sufficiently Meyer discloses "amplifying the one or more oligonucleotide extension products . . . thereby enriching the nucleic acid sequence of interest, by generating amplified products comprising the enriched nucleic acid sequence of interest," as recited in step (c) of claim 1. Thus, Petitioner has not met its burden to show that Meyer anticipates claim 1.

3. Claims 3, 5–10, and 14–18

Petitioner also asserts that Meyer anticipates claims 3, 5–10, and 14–18. Pet. 50–60. Each of claims 3, 5–10, and 14–18 depends from claim 1. Because Petitioner has not shown that Meyer anticipates claim 1, we find Petitioner has not met its burden to show that Meyer anticipates claims 3, 5–10, and 14–18.

E. Alleged Obviousness over Meyer

Claim 8 depends from claim 1, and further recites "wherein the first adaptor sequence and/or the second adaptor sequence comprise a barcode sequence." Claim 17 depends from claim 1, and further recites "wherein the amplified products comprise a 3′ end with sequence complementary to a sequence on a surface." Claim 18 recites "[t]he method of claim 17, further comprising annealing a strand of the products of the amplifying to the sequence on the surface using the 3′ end with sequence complementary to the sequence on the surface prior to step d)."

Petitioner asserts that claims 8, 17, and 18 would have been obvious over Meyer. Pet. 61–62. In this challenge, Petitioner only addresses the

additional limitations of claims 8, 17, and 18. *Id.* Because Petitioner has not shown that Meyer discloses step (c) of claim 1, and Petitioner does not address that limitation in this ground, we find Petitioner has not met its burden to show that claims 8, 17, and 18 would have been obvious over Meyer.

F. Alleged Obviousness over Meyer and Siebert

Claim 2 depends from claim 1, and further recites "the nucleic acid fragment comprises genomic DNA." Petitioner asserts that claim 2 would have been obvious over the combination of Meyer and Siebert. Pet. 62–65. Petitioner relies on Siebert for teaching the additional limitation recited in claim 2 only. *Id.* Because Petitioner has not shown that Meyer discloses step (c) of claim 1, and Petitioner does not rely on Siebert for teaching that limitation, we find Petitioner has not met its burden to show that claim 2 would have been obvious over the combination of Meyer and Siebert.

G. Alleged Obviousness over Meyer, Caruccio, and Bronner

Each of claims 11, 12 depends from claim 1, and further recites "wherein the sequencing comprises the use of four labeled reversible terminators," and "wherein the sequencing comprises semiconductor sequencing," respectively. Claim 19 depends from claim 17, and further recites "wherein the surface is a surface of a flow cell."

Petitioner asserts that claims 11, 12, and 19 would have been obvious over the combination of Meyer, Caruccio, and Bronner. Pet. 66–69. Petitioner relies on Caruccio and Bronner for teaching the additional limitation recited in claims 11, 12, and 19 only. *Id.* Because Petitioner has not shown that Meyer discloses step (c) of claim 1, and Petitioner does not rely on Caruccio and Bronner for teaching that limitation, we find Petitioner

has not met its burden to show that claims 11, 12, and 19 would have been obvious over the combination of Meyer, Caruccio, and Bronner.

III. MOTION TO SEAL

Patent Owner moved to seal Exhibits 2200–2285 and limit access to these Exhibits to the Board and Patent Owner only. Paper 42. Patent Owner explained that these Exhibits were submitted for *in camera* review in connection with its request to substitute Dr. Meyer for Dr. Matz. *Id.* at 2. In the Order granting Patent Owner's request, the panel pointed out that there was no motion to seal concerning these Exhibits. Paper 37, 5. The panel explained that "[i]f Patent Owner intends to maintain those materials as confidential and available only for the Board's review, Patent Owner must file a motion to seal." *Id.*

There is a strong public policy for making all information filed in an *inter partes* review open to the public, especially because the proceeding determines the patentability of claims in an issued patent and, therefore, affects the rights of the public. Generally, all papers filed in an *inter partes* review shall be made available to the public. *See* 35 U.S.C. § 316(a)(1); 37 C.F.R. § 42.14. Our rules, however, "aim to strike a balance between the public's interest in maintaining a complete and understandable file history and the parties' interest in protecting truly sensitive information." Patent Trial and Appeal Board Consolidated Trial Practice Guide 19 (November 2019) ("TPG").[8] Thus, a party may move to seal certain information (37 C.F.R. § 42.14); but only "confidential information" is protected from disclosure (35 U.S.C. § 316(a)(7)).

[8] *Available at* https://www.uspto.gov/TrialPracticeGuideConsolidated.

The standard for granting a motion to seal is "for good cause." 37 C.F.R. § 42.54(a). The party moving to seal bears the burden of proof and must explain why the information sought to be sealed constitutes confidential information. *Id.* § 42.20(c).

Upon review of Exhibits 2200–2285, we agree with Patent Owner that "[t]hese documents contain or reflect privileged and confidential communications between [Patent Owner] Tecan and its retained witnesses. These documents also reflect privileged attorney work product as the documents contain litigation insight, attorney mental impressions, and draft reports." Paper 42, 2. Thus, we are persuaded that good cause exists to seal these Exhibits.

IV. CONCLUSION

After reviewing the entire record, we determine that Petitioner has not met its burden to show, by a preponderance of the evidence, that claims 1–3, 5–12, and 14–19 of the '108 patent are unpatentable.

In summary:

Claims	35 U.S.C. §	References	Claims Shown Unpatentable	Claims Not Shown Unpatentable
1, 3, 5–10, 14–18	102	Meyer		1, 3, 5–10, 14–18
8, 17, 18	103(a)	Meyer		8, 17, 18
2	103(a)	Meyer, Siebert		2
11, 12, 19	103(a)	Meyer, Caruccio, Bronner		11, 12, 19
Overall Outcome				1–3, 5–12, 14–19

V. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that Petitioner has not shown, by a preponderance of the evidence, that claims 1–3, 5–12, and 14–19 of the '108 patent are unpatentable;

FURTHER ORDERED that Patent Owner's Motion to Seal (Paper 42) is granted; and

FURTHER ORDERED that, because this is a Final Written Decision, parties to the proceeding seeking judicial review of the decision must comply with the notice and service requirements of 37 C.F.R. § 90.2.

FOR PETITIONER:

Thomas Fletcher
Nicholas Vincent
Jessamyn Berniker
WILLIAMS & CONNOLLY LLP
tfletcher@wc.com
nvincent@wc.com
jberniker@wc.com

FOR PATENT OWNER:

Linnea Cipriano
Scott Weingaertner
GOODWIN PROCTER LLP
lcipriano@goodwinlaw.com
sweingaertner@goodwinlaw.com