NOTE: This disposition is nonprecedential.

United States Court of Appeals for the Federal Circuit

GUARDANT HEALTH, INC.,
Appellant

v.

UNIVERSITY OF WASHINGTON,
Appellee

2024-1129

Appeal from the United States Patent and Trademark Office, Patent Trial and Appeal Board in No. IPR2022-00817.

Decided: January 23, 2026

E. JOSHUA ROSENKRANZ, Orrick, Herrington & Sutcliffe LLP, New York, NY, argued for appellant. Also represented by SAMANTHA MICHELLE LEFF; TRAVIS JENSEN, Menlo Park, CA; RAGHAV KRISHNAPRIYAN, ELIZABETH MOULTON, San Francisco, CA; SONJA ROCHELLE GERRARD, JAD ALLEN MILLS, MICHAEL T. ROSATO, Wilson, Sonsini, Goodrich & Rosati, PC, Seattle, WA; RICHARD TORCZON, Washington, DC.

WILLIAM MILLIKEN, Sterne Kessler Goldstein & Fox

PLLC, Washington, DC, argued for appellee. Also represented by RICHARD CRUDO, DAVID HOLMAN, BYRON LEROY PICKARD, RALPH WILSON POWERS, III.

Before MOORE, *Chief Judge*, HUGHES and STOLL, *Circuit Judges*.

STOLL, *Circuit Judge*.

Guardant Health Inc. appeals the final written decision of the Patent Trial and Appeal Board holding claims 1–30 of the University of Washington's U.S. Patent No. 10,760,127 not unpatentable under 35 U.S.C. § 103. On appeal, Guardant challenges the Board's decision requiring a motivation to combine and a reasonable expectation of success where the elements of amplification followed by sequencing were disclosed together in a single embodiment in a single reference. Guardant also asserts that substantial evidence does not support the Board's findings of no motivation to combine or reasonable expectation of success. We determine that the Board erred by requiring Guardant to show that a skilled artisan would have had a motivation to combine the steps of amplification followed by sequencing and would have had a reasonable expectation of success in performing the amplification and sequencing steps because the prior art reference expressly discloses performing those steps in sequence and the Petition did not rely on modifying these two steps to arrive at the claimed invention. Thus, we vacate the Board's unpatentability determination and remand for further proceedings consistent with this opinion.

BACKGROUND

I

The '127 patent is directed to a method for reducing the error rate in massively parallel DNA sequencing using Duplex Consensus Sequencing (DCS). U.S. Patent

No. 10,760,127 Title, Abstract, col. 17 ll. 3–10. The specification explains that massively parallel DNA sequencing has been used for clinical applications such as prenatal screening for aneuploidy and early detection of cancer and monitoring its response to therapy with nucleic acid-based serum biomarkers. The specification further states that massively parallel DNA sequencing has the "unique ability to detect minor variants within heterogenous mixtures." '127 patent col. 1 ll. 32–41. According to the specification, however, this type of sequencing has limitations, including errors that may occur during sample preparation and sequencing. These errors create "a practical limit of detection" leading to "approximately 1% of bases" being incorrectly identified. *Id.* at col. 1 l. 60–col. 2 l. 8. The specification goes on to state that "[t]his background level of artifactual heterogeneity establishes a limit below which the presence of true rare variants is obscured." *Id.* at col. 2 ll. 8–10. The specification then states that "[i]t would be desirable to develop an approach for tag-based error correction, which reduces or eliminates artifactual mutations arising from DNA damage, PCR errors, and sequencing errors; allows rare variants in heterogenous populations to be detected with unprecedented sensitivity; and . . . capitalizes on the redundant information stored in complexed double-stranded DNA." *Id.* at col. 2 l. 63–col. 3 l. 2.

The '127 patent then discloses the use of DCS for lowering the error rate of sequencing. The specification discloses that DCS involves: (1) "ligating [i.e., attaching] a double-stranded target nucleic acid molecule to at least one [single molecule identifier (SMI)] adaptor molecule to form a double-stranded SMI-target nucleic acid complex;" (2) "amplifying [i.e., copying] the double stranded SMI-target nucleic acid complex;" and (3) "sequencing [i.e., determining the linear sequence of] the amplified SMI-target nucleic acid products." *Id.* at col. 3 ll. 18–27.

Claim 1 is illustrative of the claims on appeal and recites:

> 1. A method of sequencing DNA comprising:
>
> a) attaching adapters to double-stranded DNA fragments to generate a plurality of partially-complementary, asymmetrical double-stranded adapter-DNA molecules, wherein the adapters comprise barcodes selected from a plurality of distinct barcode sequences;
>
> b) *amplifying original strands of at least a portion of the double-stranded adapter-DNA molecules to produce first and second strand copies*;
>
> c) *sequencing a plurality of first and second strand copies to obtain first and second strand sequence reads for at least a portion of the adapter-DNA molecules*; and
>
> d) for at least some of the adapter-DNA molecules comprising barcodes—
>
> confirming the presence of at least one sequence read derived from each of the original first and second strands of the adapter-DNA molecules;
>
> comparing at least one of the confirmed first and second strand sequence reads to a reference sequence; and
>
> analyzing one or more correspondences between at least one of the confirmed first and second strand sequence reads and the reference sequence to identify a sequence variation.

Id. at col. 37 ll. 31–52 (emphases added to highlight the claim limitations in dispute). Limitation 1.b, which involves "amplifying," and limitation 1.c, which involves "sequencing," are relevant on appeal.

II

The claims were challenged as unpatentable under 35 U.S.C. § 103 in light of four prior art references, though

not all four are relevant on appeal. We describe only the two prior art references necessary to address Guardant's challenges on appeal. The obviousness ground at issue on appeal is Travers '075[1] in view of Travers 2010.[2] We describe each reference below.

TRAVERS '075

Travers '075 is a patent application publication directed to compositions and methods for nucleic acid sequencing assigned to PacBio. J.A. 1501. Travers '075 mainly teaches Single Molecule Real Time (SMRT™) sequencing. J.A. 1522 ¶ 43. SMRT sequencing uses a nucleic acid synthesis complex comprising a polymerase enzyme, a template sequence, and a primer sequence, which is complementary to a portion of the template sequence. J.A. 1522 ¶ 43. This complex is immobilized within a confined illumination volume, or wells, which are part of a zero mode waveguide (ZMW) array. *Id.*; J.A. 1535 ¶ 141. The complex is surrounded by a reaction mixture containing the four different nucleotides (A, G, T, and C), each of which is labeled with a spectrally distinguishable fluorescent label attached to its terminal phosphate group. J.A. 1522 ¶ 44. The fluorescent label of the free nucleotides provides a short signal while a nucleotide incorporated by the polymerase in a primer extension provides a longer signal. *Id.* This technique allows the identity of each base to be detected in real time. J.A. 1522 ¶ 45.

One of the exemplary embodiments in Travers '075 teaches a circular template comprising a double-stranded

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[1] U.S. Patent Application No. 2009/0298075 A1.

[2] Kevin J. Travers et al., *A Flexible and Efficient Template Format for Circular Consensus Sequencing and SNP Detection*, 38 Nucleic Acids Research e159 (2010). Travers 2010 was authored by Pacific Biosciences (PacBio) employees.

portion linked by two single stranded portions. J.A. 1504 Fig. 2B; J.A. 1523 ¶ 50. Travers '075 teaches the application of the SMRT sequencing process to the circular template. J.A. 1505 Fig. 3B; J.A. 1523–24 ¶ 55.

Even though Travers '075 is mainly directed to SMRT sequencing, paragraph 122 discloses an embodiment in which replication occurs followed by SMRT sequencing as follows:

> Although the constructs of the invention are described primarily, and preferably, for use directly as templates for, e.g., sequencing applications, it will be appreciated that these structures may also serve as intermediate structures in the preparation of templates that provide for sequence redundancy in line with that provided by such constructs. For example, the structurally circular nucleic acid segments described herein, *may be used as templates in a rolling circle replication process* to produce concatemer molecules that include repeating copies of both the sense and antisense strands of the originating double stranded segment included within the circular nucleic acid. These replicated products *may then be employed directly as template molecules in a template dependent sequencing process* . . . .

J.A. 1532–33 ¶ 122 (emphases added).

Rolling circle replication (RCR) is only mentioned once in Travers '075—i.e., in paragraph 122—making this the sole disclosure of sequentially performing RCR amplification followed by sequencing.

TRAVERS 2010

As in Travers '075, Travers 2010 teaches the same SMRT sequencing method, using a SMRTbell template, similar to the circular template in Travers '075, for SMRT sequencing. J.A. 1585. Like the circular template in

Travers '075, the SMRTbell template taught by Travers 2010 has a double-stranded region flanked by two hairpin loops or single-stranded regions. *Id.* According to Travers 2010, "this format resembles a linear double-stranded molecule, and yet it is topologically circular." J.A. 1583, Abstract. Like Travers '075, Travers 2010 teaches applying the SMRTbell template to SMRT sequencing. J.A. 1585. Travers 2010 states that the SMRT sequencing process "does not depend on amplification." J.A. 1587.

III

Guardant petitioned for inter partes review of claims 1–30 of the '127 patent based on the combination of Travers '075 and Travers 2010. Guardant referred to Travers '075 and Travers 2010 collectively as the Travers Publications in its Petition. In its Petition, Guardant argued the Travers Publications disclose limitation 1.b, which involves "amplifying," and limitation 1.c, which involves "sequencing," and thus render claim 1 obvious. J.A. 183–85. Regarding limitation 1.b, Guardant cited paragraph 122 of Travers '075's disclosure of "rolling circle replication" of SMRT bell templates as evidence that Travers '075 discloses the amplification step. J.A. 183–84. Guardant argued that the sequencing step taught by limitation 1.c was also disclosed by paragraph 122 of Travers '075, where the products of RCR amplification are then employed in a sequencing process. J.A. 184–85. The Board instituted review. J.A. 333–55.

In its Patent Owner Response, UW argued that Guardant failed to show that a skilled artisan would have had a motivation to modify the SMRT sequencing process with the RCR amplification step disclosed in Travers '075 with a reasonable expectation of success. J.A. 426–66. UW also argued that Travers '075 did not enable RCR amplification followed by SMRT sequencing. J.A. 466–68.

In its Final Written Decision, the Board determined that Guardant did not demonstrate by preponderant evidence that a skilled artisan would have had a reason to combine, or a reasonable expectation of success in performing RCR amplification followed by SMRT sequencing. J.A. 21–22. Specifically, the Board found that a skilled artisan would not have modified the Travers Publications to perform RCR amplification followed by SMRT sequencing because it would render the SMRT sequencing on ZMWs disclosed in the Travers Publications unworkable. J.A. 45. The Board did not reach the issue of whether Travers '075 enabled RCR amplification followed by SMRT sequencing.

Guardant appeals. We have jurisdiction under 28 U.S.C. § 1295(a)(4)(A).

DISCUSSION

"We review the Board's legal conclusions de novo and its factual findings for substantial evidence." *Univ. of Strathclyde v. Clear-Vu Lighting LLC*, 17 F.4th 155, 160 (Fed. Cir. 2021). "The substantial evidence standard asks 'whether a reasonable fact finder could have arrived at the agency's decision,' and 'involves examination of the record as a whole, taking into account evidence that both justifies and detracts from an agency's decision.'" *OSI Pharms., LLC v. Apotex, Inc.*, 939 F.3d 1375, 1381–82 (Fed. Cir. 2019) (quoting *In re Gartside*, 203 F.3d 1305, 1312 (Fed. Cir. 2000)).

Obviousness is a legal question based on underlying findings of fact. *Strathclyde*, 17 F.4th at 160. A claim is unpatentable as obvious "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." 35 U.S.C. § 103(a).[3] The inquiries of whether the prior art discloses a claim limitation, whether a skilled artisan would have been motivated to modify or combine teachings in the prior art, and whether she would have had a reasonable expectation of success in doing so are questions of fact, reviewed for substantial evidence. *Strathclyde*, 17 F.4th at 160.

On appeal, Guardant asserts that the Board erred by requiring a motivation to combine and a reasonable expectation of success because the amplification and sequencing steps are both taught by paragraph 122 of Travers '075. We address these issues in turn.

I

Guardant argues that the Board erred when it required Guardant to show a persuasive motivation to modify Travers to perform RCR amplification before SMRT sequencing when those steps are disclosed in Travers '075. According to Guardant, a motivation to combine the steps was not required because the two steps were disclosed in a single embodiment in a single prior art reference. We agree. When the disputed elements of a claim are disclosed in a single embodiment in a single reference, no finding regarding a motivation to combine to arrive at those claimed elements is required. Our case law supports this conclusion. In *General Electric Co. v. Raytheon Technologies Corp.*, for example, we held that it is error to "require a motivation to combine each element of the claim—even those present together in a reference." 983 F.3d 1334, 1352 (Fed. Cir. 2020). We reasoned that such an approach "unduly

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[3] 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 '127 patent has an effective filing date before March 16, 2013, the pre-AIA version of § 103 applies.

dissects prior art references into collections of individual elements, requiring a party showing obviousness to re-do the work already done in the prior art reference." *Id.*

The Board erred when it required Guardant to show that a skilled artisan would have been motivated to combine the steps of performing RCR amplification followed by SMRT sequencing because both steps were expressly disclosed in a single embodiment in Travers '075 paragraph 122. It is undisputed that the claimed method requires the amplification step to occur before the sequencing step, and that the sequencing step requires sequencing the amplified adapter-DNA products from the amplification step. J.A. 10. The parties do not dispute that the RCR process taught by Travers '075 is a type of amplification process. Appellant's Br. 35; Appellee's Br. 25. The parties also do not dispute that the SMRT sequencing process is a type of sequencing process. Appellant's Br. 35; Appellee's Br. 25–26. The parties do not dispute that paragraph 122 of Travers '075 teaches amplification followed by sequencing. As such, there is no need to show that a skilled artisan would have been motivated to modify a reference to perform two claim steps one after the other when the reference itself already discloses those limitations together in the same sequence required by the claims.

UW argues that Guardant never presented an argument solely relying on Travers '075 before the Board, and thus the Board did not err in requiring that Guardant show a motivation to combine. Appellee's Br. 33–38. We disagree. In its Petition, Guardant cited the embodiment in paragraph 122 of Travers '075 that expressly teaches the steps of amplification followed by sequencing. Regarding claim limitation 1.b, Guardant's Petition specifically stated: "Travers['075] further describes amplification of template molecules prior to redundant sequencing. For example, Travers['075] explains that 'rolling circle replication' of SMRTbell templates produces concatemer molecules comprising 'repeating copies of both the sense

and antisense strands of the originating double stranded segment.'" J.A. 183–84 (quoting Travers '075 J.A. 1532–33, ¶ 122). The Petition also cited Figures 1 and 4 of Travers 2010, but Figures 1 and 4 are not directed to RCR or any other amplification process. J.A. 184; J.A. 1585, 1588. Instead, these figures illustrate and disclose the details regarding sequencing of the SMRTbell template. With respect to limitation 1.c, Guardant's Petition stated: "Travers['075] discloses that either SMRTbell templates or replication products therefrom (i.e., concatemers) may be sequenced using the disclosed template-dependent sequencing process." J.A. 184 (citing Travers '075 J.A. 1532–33, ¶ 122). The Petition also cited Travers 2010 for its teaching regarding SMRT sequencing. J.A. 166, 175–76.

The Petition, however, did not rely on modifying Travers '075 or Travers 2010 to perform RCR replication of SMRTbell templates followed by SMRT sequencing and the Board abused its discretion to the extent it found otherwise.[4] As such, the Board erred in requiring Guardant to provide a motivation to so modify the Travers Publications. Our decision in *Realtime Data, LLC v. Iancu*, 912 F.3d 1368 (Fed. Cir. 2019), is instructive. There, the petitioner argued that all the elements of challenged claim 1 were disclosed in a single prior art reference, O'Brien. *Realtime Data*, 912 F.3d at 1371. The petitioner alternatively argued that the claims would have been obvious in view of O'Brien combined with a secondary prior art reference—which did not disclose all elements of the claim on its own. *Id.* The Board agreed that O'Brien taught every limitation of the challenged claims and determined that the claims thus would have been unpatentable under both references. *Id.* at 1371–72. The patent owner appealed, arguing that

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[4] The Board never explicitly found that the Petition relied on modifying Travers '075 or Travers 2010.

the Board erred in determining a skilled artisan would have been motivated to combine the references. *Id.* at 1372. We held that the Board was free to conclude that O'Brien alone disclosed every element of the challenged claims. *Id.* at 1373. We further determined that, because the Board did not rely on the secondary reference as disclosing any particular claim element or teaching, there was no obligation for the Board to combine the references and no need to show a motivation to combine. *Id.*

Here, the Petition asserted that Travers '075 expressly disclosed performing amplification followed by sequencing by quoting paragraph 122 of Travers '075. As discussed, paragraph 122 of Travers '075 itself teaches not only limitations 1.b and 1.c, but the specific order of amplification followed by sequencing. Like *Realtime Data*, a single embodiment in Travers '075 teaches both the amplification and sequencing steps of claim 1, while Travers 2010 only teaches the sequencing step. And similar to *Realtime Data*, Guardant did not need to show a motivation to combine when relying on only the single reference. Accordingly, the Board erred here by treating the Petition as if it were relying on modifying the SMRT sequencing as disclosed in the Travers Publications by performing RCR amplification sequencing as disclosed in Travers '075.

We do, however, acknowledge that the Petition here could have been clearer. While the Petition relies on paragraph 122 of Travers '075, it also cites other parts of Travers '075 and Travers 2010 without expressly stating that it is presenting alternative theories or explaining how these different cites support its position. Despite these additional cites, however, the main theory in the Petition is that the steps of amplification followed by sequencing are taught by paragraph 122 of Travers '075 alone.

II

Guardant also argues that substantial evidence does not support the Board's finding that a person of ordinary

skill in the art would not have had a reasonable expectation of success in first performing RCR replication of SMRTbell templates and then performing SMRT sequencing. Like our conclusion regarding motivation to combine, however, we conclude that the Board erred by requiring Guardant to show that a skilled artisan would have had a reasonable expectation of success in performing RCR replication of SMRTbell templates followed by SMRT sequencing because Guardant's Petition relies on paragraph 122 of Travers '075 as disclosing these steps in sequence.

We have explained that "[t]he reasonable expectation of success requirement refers to the likelihood of success in combining references to meet the limitations of the claimed invention." *Intelligent Bio-Sys., Inc. v. Illumina Cambridge Ltd.*, 821 F.3d 1359, 1367 (Fed. Cir. 2016). And neither the Board nor UW has cited a case that requires a party to demonstrate a reasonable expectation of success in combining two elements to arrive at the claimed invention when those elements are disclosed in a single embodiment of a single prior art reference. UW cites *In re Stepan Co.*, 868 F.3d 1342 (Fed. Cir. 2017), to argue that Guardant had the burden to show that a skilled artisan would have been motivated to arrive at the claimed invention with a reasonable expectation of success:

> Whether a rejection is based on combining disclosures from multiple references, combining multiple embodiments from a single reference, or selecting from large lists of elements in a single reference, there must be a motivation to make the combination and a reasonable expectation that such a combination would be successful, otherwise a skilled artisan would not arrive at the claimed combination.

Stepan, 868 F.3d at 1346 n.1; *see also* Appellee's Br. 43–44. This quote is inapposite, however, because it addresses combinations. In other words, *Stepan* is distinguishable

from the present case because, here, the elements of the challenged claim are expressly taught by Travers '075. Travers '075 discloses performing RCR amplification followed by SMRT sequencing in a single embodiment. There is no combination of references, combination of multiple embodiments in a single reference, or selection from a large list of elements.

UW also argues that Travers '075 only provides a "passing mention" of performing RCR amplification prior to SMRT sequencing. Appellee's Br. 49. But a reference is prior art for all that it teaches, including less preferred embodiments. *See In re Inland Steel Co.*, 265 F.3d 1354, 1361 (Fed. Cir. 2001) (explaining that all disclosures of the prior art, including unpreferred embodiments, must be considered); *see also Beckman Instruments, Inc. v. LKB Produkter AB*, 892 F.2d 1547, 1551 (Fed. Cir. 1989) ("Even if a reference discloses an inoperative device, it is prior art for all that it teaches." (citation omitted)).

III

As an alternate ground for affirmance, UW asserts that the Board's fact findings are sufficient for this court to affirm the Board's final written decision on the basis that paragraph 122 of Travers '075 is not enabled. Appellee's Br. 67–68. Specifically, UW argues that "Travers '075 does not enable the sequencing of an RCR concatemer using PacBio's SMRT sequencing," and therefore because paragraph 122 is not enabled, it cannot be relied on for disclosing amplification followed by sequencing. Appellee's Br. 67. The Board did not reach this issue. As an appellate court, we will not address this issue in the first instance. *TriMed, Inc. v. Stryker Corp.*, 608 F.3d 1333, 1339 (Fed. Cir. 2010) ("A federal appellate court does not consider an issue not passed upon below." (quoting *Singleton v. Wulff,* 428 U.S. 106, 120 (1976))). Rather we remand the case for consideration of this issue by the Board in the first instance.

CONCLUSION

We have considered the parties' remaining arguments, and we find them unpersuasive. We vacate the Board's decision and remand the case to the Board for further proceedings consistent with this opinion.

VACATED AND REMANDED

COSTS

Costs to Appellant.