IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

NATERA, INC., Plaintiff, v. CAREDX, INC., Defendant.	Civil Action No. 20-38-CFC-CJB (CONSOLIDATED)

Jack B. Blumenfeld, Derek J. Fahnestock, Anthony D. Raucci, MORRIS, NICHOLS, ARSHT, & TUNNELL LLP, Wilmington Delaware; Kevin P.B. Johnson, QUINN EMANUEL URQUHART & SULLIVAN, LLP, Redwood Shores, California; Andrew M. Holmes, Jeff Nardinelli, QUINN EMANUEL URQUHART & SULLIVAN, LLP, San Francisco, California

Counsel for Plaintiff

Brian E. Farnan, Michael J. Farnan, FARNAN LLP, Wilmington, Delaware; Edward R. Reines, Derek C. Walter, WEIL, GOTSHAL & MANGES LLP, Redwood Shores, California; W. Sutton Ansley, WEIL, GOTSHAL & MANGES LLP, Washington, D.C.

Counsel for Defendant

MEMORANDUM OPINION

December 11, 2023
Wilmington, Delaware

COLM F. CONNOLLY
CHIEF JUDGE

Plaintiff Natera, Inc. has sued CareDx, Inc. for infringement of U.S. Patent Nos. 10,597,724 (the #724 patent), 10,655,180 (the #180 patent), and 11,111,544 (the #544 patent). D.I. 118; D.I. 119; D.I. 120. The #724 and #180 patents are directed to methods of observing DNA in samples taken from patients. *See* D.I. 118 ¶ 24; D.I. 119 ¶ 26. The #544 patent is directed to a method of "preparing a preparation of amplified DNA" from the sample of one individual to make possible the observation of the DNA of a second individual in the sample. *See* D.I. 120 ¶ 28; #214 patent at claim 21 ("A method for preparing a preparation of amplified DNA derived from a biological sample of a second individual useful for determining genetic data for DNA from a first individual in the biological sample, the method comprising."). Pending before me is CareDx's Motion #1 for Summary Judgment that Natera's Patents Claim Ineligible Subject Matter (D.I. 249).

It is now well settled under Federal Circuit case law that the use of conventional techniques in a standard way to observe DNA in a biological sample is not eligible for patentability under 35 U.S.C. § 101. *CareDx, Inc. v. Natera, Inc.*, 40 F.4th 1371, 1380 (Fed. Cir. 2022), *cert. denied*, No. 22-1066, 2023 WL 6379010 (U.S. Oct. 2, 2023). "[M]ethods for preparing a fraction of cell-free DNA

that is enriched in fetal DNA" to make possible the observation of DNA, however, are patent eligible under § 101. *Illumina, Inc. v. Ariosa Diagnostics, Inc.*, 967 F.3d 1319, 1326 (Fed. Cir. 2020).

CareDx argues that the claims in the three asserted patents "fail to describe any non-conventional technique," and are therefore ineligible under § 101. D.I. 250 at 1. Natera counters that the patents' subject matters are not barred from patentability by § 101 because the #724 and #180 patents teach "concrete steps that improve over prior art laboratory techniques," and because the #544 patent teaches the "prepar[ation] [of] non-naturally occurring preparations useful for determining genetic data for cell-free DNA [i.e., cfDNA] in a mixed-cfDNA sample . . . ." D.I. 327 at 1.

I. LEGAL STANDARDS

A court must grant summary judgment "if the movant shows that there is no genuine dispute as to any material fact and the movant is entitled to judgment as a matter of law." Fed. R. Civ. P. 56(a). Material facts are those "that could affect the outcome" of the proceeding. *Lamont v. New Jersey*, 637 F.3d 177, 181 (3d Cir. 2011). "[A] dispute about a material fact is genuine if the evidence is sufficient to permit a reasonable jury to return a verdict for the non-moving party." *Id.* (internal quotation marks omitted). A non-moving party asserting that a fact is genuinely disputed must support such an assertion by: "(A) citing to particular parts of

materials in the record, including depositions, documents, electronically stored information, affidavits or declarations, stipulations, . . . admissions, interrogatory answers, or other materials; or (B) showing that the materials cited [by the opposing party] do not establish the absence . . . of a genuine dispute . . . ." Fed. R. Civ. P. 56(c)(1). The non-moving party's evidence "must amount to more than a scintilla, but may amount to less (in the evaluation of the court) than a preponderance." *Williams v. Borough of West Chester, Pa.*, 891 F.2d 458, 460–61 (3d Cir. 1989).

II. DISCUSSION

A. The #724 Patent

Natera alleges in relevant part, and CareDx does not dispute, that the claims of the #724 patent "are directed to a[] . . . method for determining genetic data for DNA from a first individual in a biological sample of a second individual using synthetic pieces of DNA, including amplification products, which are produced using synthetic tools to . . . amplify[]and measur[e] small amounts of DNA from one individual or organism in a biological sample of another individual or organism." D.I. 118 ¶ 24.

1. Claim 1 is Representative

Claim 1 of the #724 patent, the only asserted independent claim of that patent, recites:

> A method for determining genetic data for DNA from a first individual in a biological sample of a second individual, the method comprising:
>
> > (a) amplifying a plurality of polymorphic loci on cell-free DNA extracted from the biological sample to generate amplified products;
> >
> > (b) measuring an amount of the amplified products by sequencing-by-synthesis to obtain genetic data at the plurality of polymorphic loci;
> >
> > (c) determining the most likely genetic data for DNA from the first individual based on allele frequencies in the genetic data at the plurality of polymorphic loci.

#724 patent at claim 1.

CareDx argues, and I agree, that claim 1 of the #724 patent is a representative claim for § 101 purposes. D.I. 250 at 3–4. Courts can treat a claim as representative if "the patentee does not present any meaningful argument for the distinctive significance of any claim limitations not found in the representative claim." *Berkheimer v. HP Inc.*, 881 F.3d 1360, 1365 (Fed. Cir. 2018). Natera disputes that claim 1 is representative, but it does not point to any limitation in any other claim of the patent that by itself or in combination with any other limitation meaningfully distinguishes claim 1 from another claim for § 101 purposes. *See* D.I. 327 at 22–23. Instead, Natera argues that the patent's "written description[] teach[es] embodiments corresponding to the various dependent claims and that they are independent improvements, showing that the allegedly 'representative

claim[]' [is] not representative." D.I. 327 at 22–23. Natera, however, offers no elaboration of this argument; and, in any event, the relevant question is whether the patent's other claims, not its written description, meaningfully differ from the alleged representative claim. *See Synopsys, Inc. v. Mentor Graphics Corp.*, 839 F.3d 1138, 1149 (Fed. Cir. 2016) ("The § 101 inquiry must focus on the language of the Asserted Claims themselves."); *Accenture Glob. Servs., GmbH v. Guidewire Software, Inc.*, 728 F.3d 1336, 1345 (Fed. Cir. 2013) ("[T]he important inquiry for a § 101 analysis is to look to the claim.").

Where, as here, the patent's "claims are substantially similar and linked to the same law of nature, analyzing representative claims is proper." *Cleveland Clinic Foundation v. True Health Diagnostics LLC*, 859 F.3d 1352, 1360 (Fed. Cir. 2017) (internal quotation marks and citation omitted). Claim 1 is the only asserted independent claim of the #724 patent. The remaining, dependent claims of the patent add limitations that have no bearing on whether the patent is directed to ineligible subject matter. The dependent claims are substantially similar to claim 1 and are linked to the same law of nature because they are all directed to detecting genetic data for DNA from one individual in a biological sample of another individual. *See Cleveland Clinic Foundation*, 859 F.3d at 1360. Claim 2, for example, simply requires that the "polymorphic loci" in claim 1 be "SNP loci." #724 patent at claim 2. Claim 4 explains that the "amplifying" in claim 1

"comprises targeted PCR." #724 patent at claim 4. And claim 7 recites that the "biological sample" in claim 1 is a "blood sample." #724 patent at claim 7. None of these limitations affect the analysis of whether the #724 patent is directed to a law of nature. Accordingly, I will treat claim 1 of the #724 patent as representative.

2. There is No Genuine Issue of Fact with Respect to Whether Claim 1 Recites Only Conventional Techniques

CareDx argues that the #724 patent recites two techniques for observing DNA—PCR amplification and sequencing by synthesis—and that both techniques "were conventional well before the claimed November 26, 2005 priority date" of the patent. D.I. 250 at 9–10. Natera does not dispute that these techniques are the only techniques recited in the claim; nor does it dispute that both techniques were conventional as of the patent's priority date. *See generally* D.I. 327.

Instead, Natera argues that claim 1 teaches a combination of these techniques that was not conventional at the time of the patent's priority date. D.I. 327 at 12–13. According to Natera, the #724 patent "teach[es] specific combinations including targeted amplification and subsequent analysis of the amplification products using allele frequencies" that were not present as of the 2005 priority date. D.I. 327 at 15. But Natera cites, and there is, nothing in the claims of the #724 patent that teach these alleged "specific combinations." *See Synopsys*, 839 F.3d at 1149 ("The § 101 inquiry must focus on the language of the

Asserted Claims themselves."); *Accenture*, 728 F.3d at 1345 ("[T]he important inquiry for a § 101 analysis is to look to the claim."). The claims do not disclose any "specific combination" of these techniques or even anything specific about any one of the techniques. On the contrary, the claims discuss merely "amplifying *a plurality of* polymorphic loci," "measuring *an amount of* the amplified products," and "determining *the most likely* genetic data . . . *based on allele frequencies* in the genetic data *at the plurality* of polymorphic loci." #724 patent at claim 1 (emphasis added). Moreover, the mental process of "subsequent analysis" to what are admittedly conventional techniques cannot save the #724 patent from § 101's bar. *See Genetic Technologies Ltd. v. Merial L.L.C.*, 818 F.3d 1369, 1380 (Fed. Cir. 2016) ("We thus hold that the simple mental process step of 'detect[ing] the allele' in [the asserted] claim 1, either alone or in combination with [conventional techniques, including DNA amplification], does not supply sufficient inventive concept to make the claim patent-eligible under § 101.").

There being no genuine issue of fact about whether the claims of the #724 patent teach a method of observation of DNA that employs only conventional techniques, I will grant CareDx's motion insofar as it seeks summary judgment of invalidity of the #724 patent under § 101.

B. The #180 Patent

Natera alleges that the claims of the #180 patent

> are directed to measuring DNA in a sample using synthetic pieces of DNA, including amplification products, which are produced using synthetic tools such as primers, to provide a novel and innovative solution to problems peculiar to the particular problem of amplifying and measuring small amounts of DNA from one individual or organism in a biological sample of another individual or organism.

D.I. 119 ¶ 26.

1. Claim 14 is Representative

Claim 14 of the #180 patent, the only asserted independent claim of that patent, recites:

> A method for measuring an amount of DNA in a biological sample, the method comprising:
>
> > (a) performing a targeted PCR amplification for more than 100 SNP loci on one or more chromosomes expected to be disomic in a single reaction mixture using more than 100 PCR primer pairs, wherein the reaction mixture comprises cell-free DNA extracted from a biological sample of a subject comprising DNA of mixed origin, wherein the DNA of mixed origin comprises DNA from the subject and DNA from a genetically distinct individual, wherein neither the subject nor the genetically distinct individual is a fetus, wherein the DNA of mixed origin comprises DNA from a transplant, and wherein the amplified SNP loci comprise SNP loci on at least chromosome 1, 2, or 3;
> >
> > (b) measuring a quantity of each allele at a plurality of amplified SNP loci that comprise an allele present in the genetically distinct individual but not the subject, wherein the quantity of each

> allele at a plurality of amplified SNP loci are measured by high-throughput sequencing;
>
> (c) measuring an amount of the DNA from the genetically distinct individual in the biological sample using the quantity of each allele at the SNP loci and an expected quantity of each allele at the SNP loci for different DNA fractions,
>
> wherein the method is performed without prior knowledge of genotypes of the genetically distinct individual.

#180 patent at claim 14.

CareDx argues, and I agree, that claim 14 is representative for § 101 purposes. D.I. 250 at 3–5. All the other asserted claims of the patent are substantially similar and linked to the observation of DNA in a patient through the same techniques recited in claim 14. *See Cleveland Clinic Foundation*, 859 F.3d at 1360. Natera argues that claim 14 is not representative because claim 15 of the patent "teaches the determining bias for statistical correction . . . ." D.I. 327 at 23. Claim 15 recites:

> The method of claim 14, further comprising determining a bias of the PCR amplification, and using the bias to statistically correct the determined quantity of each allele at the plurality of SNP loci on the one or more chromosomes expected to be disomic before the quantity of each allele is used to determine the amount of the DNA from the genetically distinct individual.

#180 patent at claim 15. Thus, "determining the bias" is simply math—i.e., counting and calculating. It is not an unconventional technique or other

requirement that meaningfully differentiates claim 15 from claim 14 for § 101 purposes. Indeed, claiming math in the abstract is quintessential ineligible subject matter. *See, e.g., Parker v. Flook*, 437 U.S. 584, 595 (1978) ("[I]f a claim is directed essentially to a method of calculating, using a mathematical formula, even if the solution is for a specific purpose, the claimed method is nonstatutory") (quotation marks and citation omitted); *see also In re Stanford Univ.*, 991 F.3d 1245, 1251 (Fed. Cir. 2021) (holding that mathematical calculations included in claim terms that merely "yield[] different or better results[] [do] not render patent eligible subject matter.").

Accordingly, I will treat claim 14 as representative.

2. Whether the Techniques Taught by Claim 14 are Conventional is Disputed

As noted above, CareDx argues that none of the techniques used to observe DNA taught by claim 14 are unconventional and that, therefore, the claim is ineligible for patentability under § 101. D.I. 250 at 10–12. Natera counters that amplifying more than 100 targets simultaneously in a single mixture was unconventional at the time of the patent's priority date, and it supports this contention with the opinion (albeit conclusory) of its expert witness, Dr. Quackenbush. D.I. 327 at 17 n.57; D.I. 330-32 at ¶¶ 291–98. CareDx points out that Dr. Quackenbush's current position is directly contradicted by his prior testimony and by the testimony of Natera's inventor. *See* D.I. 250 at 11–12; D.I.

251-5 at 4 (Dr. Quackenbush testifying in previous cases that "[w]hen [he] was at Stanford between 1994 and 1997, we would do over 10,000 PCRs every night overnight. . . . You could amplify 10,000 SNPs with conventional technology . . . ."); D.I. 251-7 at 3–4 (Natera's inventor admitting during his deposition that amplifying "5,000 targets in a single PCR and a single reaction volume" occurred as early as 2009). But Dr. Quackenbush's credibility is a jury question, not an issue for the court to resolve in addressing a motion for summary judgment.

There being a disputed fact about whether the techniques taught by claim 14 were conventional as of the #180 patent's priority date, I will deny CareDx's motion insofar as it seeks summary judgment of invalidity of the #180 patent under § 101.

C. The #544 Patent

With respect to the #544 patent, the parties address in their briefing only claims 21 and 38. Claim 21 recites:

> A method for preparing a preparation of amplified DNA derived from a biological sample of a second individual useful for determining genetic data for DNA from a first individual in the biological sample, the method comprising:
>
> > (a) extracting cell-free DNA from the biological sample;

(b) preparing a preparation of amplified DNA by amplifying a plurality of target loci on the cell-free DNA extracted from the biological sample to generate amplified DNA;

(c) analyzing the preparation of amplified DNA by sequencing the amplified DNA using sequencing-by-synthesis to obtain genetic data of the plurality of target loci, and determining the most likely genetic data for DNA from the first individual based on allele frequencies in the genetic data at the plurality of target loci.

#544 patent at claim 21.

Claim 38 recites:

A method for preparing a preparation of amplified DNA derived from a biological sample of a second individual useful for determining genetic data for DNA from a first individual in the blood sample, the method comprising:

(a) extracting cell-free DNA from the biological sample;

(b) preparing a preparation of amplified DNA by performing targeted PCR to amplify a plurality of SNP loci on the cell-free DNA extracted from the blood sample to generate amplified DNA, wherein the SNP loci are on a plurality of chromosomes;

(c) analyzing the preparation of amplified DNA by sequencing the amplified DNA using sequencing-by-synthesis to obtain genetic data of the plurality of SNP loci, wherein the sequencing-by-synthesis comprises clonal amplification of the amplified DNA and measurement of sequences of the clonally amplified DNA, and determining the most likely genetic data for DNA from the first

> individual based on allele frequencies in the genetic data at the plurality of SNP loci.

#544 patent at claim 38.

The two claims are in all material respects identical for purposes of this motion because they teach "methods for preparing preparations" for DNA observation. As such, under *Illumina*, they are not *per se* directed to ineligible patentable subject matter. *Illumina*, 967 F.3d at 1326 (Fed. Cir. 2020).

CareDx argues that "other than th[e] preamble label[s] [of claims 21 and 38 of the #544 patent] there is no material difference between the method steps of the [#]544 and [#]724 Patents" and that "[i]t is illogical that the same basic method could be directed to different things merely because of a preamble label that is not even claim-limiting." D.I. 356 at 2. But CareDx cites nothing in the record to support this assertion, and, to my knowledge, Natera has not said that the preambles of claims 21 and 38 are not limiting. On the contrary, Natera emphasized in its briefing that the claims are "method of preparation" claims that fall within *Illumina*. D.I. 327 at 2–6. Because CareDx mischaracterizes the #544 as a "method of detection" patent, its argument that the claims of the #544 patent recite conventional techniques is irrelevant to whether the patent is eligible under § 101. *See* D.I. 250 at 6–9. By its terms, the #544 patent is a "method of preparation" patent that falls under *Illumina*.

Accordingly, I will deny CareDx's motion for summary judgment insofar as it seeks a judgment that the #544 patent is invalid under § 101.

III. CONCLUSION

For the reasons discussed above, I will grant CareDx's motion for summary judgment insofar as it seeks a judgment that the #724 patent is invalid under § 101. I will otherwise deny the motion.

The Court will issue an Order consistent with this Memorandum Opinion.

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FOR THE DISTRICT OF DELAWARE

NATERA, INC., Plaintiff, v. CAREDX, INC., Defendant.	Civil Action No. 20-38-CFC-CJB (CONSOLIDATED)

ORDER

At Wilmington on this Eleventh day of December in 2023,

For the reasons set forth in the Memorandum Opinion issued this day, IT IS HEREBY ORDERED that Defendant CareDx, Inc.'s Motion #1 for Summary Judgment that Natera's Patents Claim Ineligible Subject Matter (D.I. 249) is GRANTED IN PART AND DENIED IN PART.

CHIEF JUDGE