Articles + Publications | August 4, 2022

Federal Circuit Continues to Dismantle Diagnostic Patents

WRITTEN BY

Mark R. Bell, Ph.D. | Przemyslaw P. McEwan | Daniel M. Scolnick

Any new and useful process, machine, manufacture, or composition of matter may be patented in the United States.[1] However, the Supreme Court has held that "laws of nature, natural phenomena, and abstract ideas" are not eligible for patent protection, even though applications of such laws or phenomena may be patent eligible.[2] Despite a clear warning that these three exceptions must be carefully applied, else they "could eviscerate patent law," the Federal Circuit continues to routinely hold that patents directed to diagnostic methods, which often detect and/or measure biomarkers and the Federal Circuit routinely describes as detecting natural phenomena, are nevertheless invalid.[3] In its recent decision in *CareDx v. Natera*,[4] the Federal Circuit further dims this view by negating a trio of diagnostic patents owned by Stanford and exclusively licensed to CareDx, Inc.

The three Stanford patents were all titled "Non-Invasive Diagnosis of Graft Rejection in Organ Transplant."[5] The patents each describe methods of diagnosing or predicting organ transplant rejection by detecting levels of donor cell-free DNA (cfDNA) in the blood of the patient. When a transplanted organ is being rejected, the patient's immune system destroys the cells of the transplanted organ. These dying cells then release the cfDNA into the blood stream of the patient, which naturally increases as the organ rejection accelerates. By detecting the presence and increase of even small amounts of donor cfDNA in the blood, the methods provided in each patent allow for the potentially early detection and diagnosis of organ transplant rejection.[6]

The specifications of all three patents are identical, while the claims differ only by the technique used to detect the cfDNA: multiplex sequencing, high-throughput sequencing, digital polymerase chain reaction (PCR) with or without amplification. The Federal Circuit summarized the claims into four steps in the following quote:

1. "obtaining" or "providing" a "sample" from the recipient that contains cfDNA;

2. "genotyping" the transplant donor and/or recipient to develop "polymorphism" or "SNP" "profiles";

3. "sequencing" the cfDNA from the sample using "multiplex" or "high-throughput" sequencing, or performing "digital PCT"; and

4. "determining or "quantifying" the amount of donor cfDNA.[7]

The inclusion of the various methods of detection in the claims is important. Previously, the detection of cfDNA in the transplant recipient's blood was not possible with older detection techniques.

Despite many attempts over the following decade, even accomplished researchers could not invent a satisfactory way to measure donor cf-DNA in the recipient's bloodstream sufficient to monitor organ rejection. At best, preexisting techniques worked only in a small subset of cases. This decade of failure culminated in a discouraging announcement in 2008 by a prominent research group that using cf-DNA to monitor organ rejection was "difficult" and "impractical."[8]

According to the opinion, the inventors overcame this problem by applying the new and improved methods of gene sequencing and analysis, such as next-generation sequencing and digital PCR techniques, which were then specifically included in the claim language.

CareDx sued the defendants in district court, alleging that their various organ transplant rejection tests infringed the patents CareDx licensed from Stanford.[9] The alleged infringers moved to dismiss the complaints due to the patents being invalid as being directed to patent ineligible subject matter.[10] While the initial ruling by a magistrate judge held that the claims in question were new and unconventional, the district court overruled, holding that language in the specification concerning the conventional nature of the detection techniques raised doubts about the validity of the diagnostic claims.[11] After allowing for limited discovery on subject matter eligibility and expert testimony, the district court granted the motions to dismiss. The district court concluded that the claims in all three patents were directed to the detection of natural phenomena, specifically the presence of the cfDNA in the blood. Additionally, several statements in the specifications indicated, or even admitted, that the specific detection techniques recited in the claims were in fact conventional, and thus did not transform the claims into patent eligible subject matter.[12]

CareDx appealed to the Federal Circuit, arguing that the invention is not the natural correlation between transplant rejection and the cfDNA levels in the patient's blood, but rather the improved measurement methods recited in the claims that allowed the cfDNA to be detected.[13] CareDx also argued that using the next-generation sequencing and digital PCR techniques to detect the cfDNA was an inventive breakthrough that is specifically claimed.[14] However, the Federal Circuit affirmed the district court's judgement, stating that "[t]his is not a case involving a method of preparation or a new measurement technique."[15] The Federal Circuit further noted that CareDx did not discover the relationship between cfDNA and organ transplant rejection, and agreed with the district court that the multiple statements in the specifications of the patents in question stated that the next-generation sequencing and digital PCR techniques were merely conventional.[16]

Finally, the Federal Circuit found the claimed methods to be "indistinguishable from other diagnostic method claims the Supreme Court found ineligible in *Mayo*."[17] For example, the Federal Circuit proceeded to compare the claimed methods to those in *Ariosa Diagnostics v. Sequenom*, another cfDNA patent case invalidated on subject matter eligibility grounds.[18]

Here, as in Ariosa, the claims boil down to collecting a bodily sample, analyzing the cfDNA using conventional techniques, including PCR, identifying naturally occurring DNA from the donor organ, and then using the natural correlation between heightened cfDNA levels and transplant health to identify a potential rejection, none of which was inventive. The claims here are equally as ineligible as those in Ariosa.[19]

Although CareDx was unsuccessful in convincing the courts that their diagnostic patents were directed to eligible subject matter, this case holds at least one takeaway for the biotech industry. Care must be taken to ensure that

statements of what is conventional or known in the art — even, or especially, if those statements are "boilerplate" — are not and could not be applied to techniques that are utilized to solve new problems. Here, according to CareDx, cfDNA detection originating from a donor organ was previously not possible, and only development of new and improved methods of gene sequencing made such detection possible. Nevertheless, patent law in the United States continues to be unfavorable to diagnostic and prognostic patents. Thus, it is best not to give a court an easy excuse to invalidate a patent by pointing to admissions of conventionality. Ultimately, patent claims that recite the conventional use of existing techniques for the detection of "natural phenomena" are at risk of not being issued by the USPTO or being struck down as invalid and directed to ineligible subject matter if challenged in court.

---

[1] *See* 35 U.S.C. § 101. Often otherwise stated as "anything under the sun that is made by man." *Diamond v. Chakrabarty*, 447 U.S. 303, 308-09 (1980).

[2] *See Mayo Collaborative Servs. V. Prometheus Lab'ys, Inc.*, 566 U.S. 66, 70 (2012) (quoting *Diamond v. Diehr*, 450 U.S. 175, 185 (1981).

[3] *Id.* at 71.

[4] *CareDx, Inc. v. Natera, Inc.*, No. 2022-1027 (Fed. Cir. July 18, 2022).

[5] U.S. Patent Nos. 8,703,652, 9,845,497, and 10,329,607.

[6] *See CareDx*, No. 2022-1027 at 3.

[7] *Id.* at 8.

[8] *See Id*. (Appellant's Br. at 1-2).

[9] *See CareDx*, No. 2022-1027 at 8.

[10] *Id.*

[11] *Id.* at 9.

[12] *See, e.g.*, U.S. Patent No. 8,703,652 patent at column 5, lines 36-40 ("unless otherwise indicated, conventional techniques of immunology, biochemistry, chemistry, molecular biology, microbiology, cell biology, genomics, and recombinant DNA, which are well within the skill of art.").

[13] *See CareDx*, No. 2022-1027 at 11.

[14] *Id.* at 12.

[15] *Id.* at 13.

[16] *Id.* at 13-14.

[17] *Id.* at 15.

[18] *See Ariosa Diagnostics, Inc. v. Sequenom, Inc.*, 788 F.3d 1371 (Fed. Cir. 2015).

[19] *See CareDx*, No. 2022-1027 at 15-16.

RELATED INDUSTRIES + PRACTICES

- Health Care + Life Sciences
- Health Care + Life Sciences Intellectual Property