United States Court of Appeals for the Federal Circuit

ARIOSA DIAGNOSTICS, INC., NATERA, INC.,
Plaintiffs-Appellees

DNA DIAGNOSTICS CENTER, INC.,
Counterclaim Defendant-Appellee

v.

SEQUENOM, INC., SEQUENOM CENTER FOR MOLECULAR MEDICINE, LLC,
Defendants-Appellants

ISIS INNOVATION LIMITED,
Defendant

2014-1139, 2014-1144

Appeals from the United States District Court for the Northern District of California in Nos. 3:11-cv-06391-SI, 3:12-cv-00132-SI, Judge Susan Y. Illston.

Decided: June 12, 2015

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Before REYNA, LINN, and WALLACH, *Circuit Judges.*

Opinion for the court filed by *Circuit Judge* REYNA.

Concurring Opinion filed by *Circuit Judge* LINN.

REYNA*, Circuit Judge.*

This appeal is from a grant of summary judgment of invalidity of the asserted claims of U.S. Patent No. 6,258,540 ("the '540 patent"). The United States District Court for the Northern District of California found that the asserted claims of the '540 patent are not directed to patent eligible subject matter and are therefore invalid under 35 U.S.C. § 101. For the reasons explained below, we *affirm*.

I

In 1996, Drs. Dennis Lo and James Wainscoat discovered cell-free fetal DNA ("cffDNA") in maternal plasma and serum, the portion of maternal blood samples that other researchers had previously discarded as medical waste. cffDNA is non-cellular fetal DNA that circulates freely in the blood stream of a pregnant woman. Applying a combination of known laboratory techniques to their discovery, Drs. Lo and Wainscoat implemented a method for detecting the small fraction of paternally inherited cffDNA in maternal plasma or serum to determine fetal characteristics, such as gender. The invention, commercialized by Sequenom as its MaterniT21 test, created an alternative for prenatal diagnosis of fetal DNA that avoids the risks of widely-used techniques that took samples from the fetus or placenta. In 2001, Drs. Lo and Wainscoat obtained the '540 patent, which relates to this discovery.

The parties agree that the patent does not claim cffDNA or paternally inherited cffDNA. Instead, the '540 patent claims certain methods of using cffDNA. The steps of the method of claim 1 of the '540 patent include amplifying the cffDNA contained in a sample of a plasma or serum from a pregnant female and detecting the paternally inherited cffDNA. Amplifying cffDNA results in a single copy, or a few copies, of a piece of cffDNA being multiplied across several orders of magnitude, generating thousands to millions of copies of that particular DNA sequence. In the amplification step, DNA is extracted from the serum or plasma samples and amplified by polymerase chain reaction ("PCR") or another method. PCR exponentially amplifies the cffDNA sample to detectable levels.

In the detecting step, the lab technician adds the amplified cffDNA to an agarose gel containing ethidium

bromide to stain and visualize the paternally inherited cffDNA.

The '540 patent also provides for making a diagnosis of certain fetal characteristics based on the detection of paternally inherited cffDNA. The specification explains that analysis of cffDNA permits more efficient determination of genetic defects and that a pregnant woman carrying a fetus with certain genetic defects will have more cffDNA in her blood than will a woman with a normal fetus. '540 patent col. 3 ll. 30-43.

Claims 1, 2, 4, 5, 8, 19-22, 24, and 25 of the '540 patent are at issue in this appeal.[1] Independent claim 1 requires:

> 1. A method for detecting a paternally inherited nucleic acid of fetal origin performed on a maternal serum or plasma sample from a pregnant female, which method comprises
>
> amplifying a paternally inherited nucleic acid from the serum or plasma sample and
>
> detecting the presence of a paternally inherited nucleic acid of fetal origin in the sample.

'540 patent col. 23 l. 61-67.

For comparison, independent claims 24 and 25 require:

> 24. A method for detecting a paternally inherited nucleic acid on a maternal blood sample, which method comprises:

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[1] The parties have stipulated that for the purposes of this appeal claims 1, 2, 4, 5, 8, 9-22, 24 and 25 are representative of claims 6, 7, 12, 13, 15, and 18 of the '540 patent. J.A. 24-25, 30-31.

> removing all or substantially all nucleated and anucleated cell populations from the blood sample,
>
> amplifying a paternally inherited nucleic acid from the remaining fluid and subjecting the amplified nucleic acid to a test for the Paternally [sic] inherited fetal nucleic acid.
>
> 25. A method for performing a prenatal diagnosis on a maternal blood sample, which method comprises
>
> obtaining a non-cellular fraction of the blood sample
>
> amplifying a paternally inherited nucleic acid from the non-cellular fraction
>
> and performing nucleic acid analysis on the amplified nucleic acid to detect paternally inherited fetal nucleic acid.

Id. at 26 ll. 20-36.

The remaining claims explain how the method of detection occurs or how it can be used. For example, claim 2 depends from claim 1 and claims amplification by polymerase chain reaction. *Id.* at col. 24 ll. 60-61. Claim 4 similarly depends from claim 1 and claims detection via a sequence specific probe. *Id.* col. 24 ll. 65-67. Claim 21 also depends from claim 1, but instead of focusing solely on a method for detecting, it focuses on a method for performing a prenatal diagnosis, using claim 1's method for detecting. *Id.* col. 26 ll. 4-14.

II

Appellee Ariosa Diagnostics, Inc. (formerly known as "Aria Diagnostics, Inc.") makes and sells the Harmony Test, a non-invasive test used for prenatal diagnosis of certain fetal characteristics. Natera, Inc. makes and sells

the Non-Invasive Paternity Test, which is intended to confirm the paternity or non-paternity of a gestating fetus from genetic information in fetal DNA available in the blood of the pregnant female. Diagnostics Center, Inc. is a licensee of Natera.

In response to letters threatening claims of infringement, Ariosa Diagnostics, Inc., Natera, Inc. and Diagnostics Center, Inc. each filed separate declaratory judgment actions from December 2011 through early 2012 against Sequenom alleging that they did not infringe the '540 patent. Sequenom counterclaimed alleging infringement in each case. The district court related the three actions for pretrial purposes.

In the *Ariosa* action, Sequenom filed a motion seeking to preliminarily enjoin Ariosa from selling the accused Harmony Prenatal Test. In July 2012, the district court issued an order denying Sequenom's motion for a preliminary injunction. In the context of doing so, the district court found that there was a substantial question over whether the subject matter of the asserted claims was directed to eligible subject matter. Sequenom appealed to this court.

On August 9, 2013, this court vacated and remanded the case, holding that the district court erred in certain respects not relevant to this appeal. *Aria Diagnostics, Inc. v. Sequenom, Inc.*, 726 F.3d 1296, 1305 (Fed. Cir. 2013). In addition, this Court noted that it offered no opinion "as to whether there is or is not a substantial question regarding the subject matter eligibility of the asserted claims" of the '540 patent, but remanded "for the district court to examine subject matter eligibility . . . . in light of *[Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 569 U.S. ___, 133 S. Ct. 2107, 2117 (2013)]." *Id.* at 1304.

After remand, the parties filed cross motions for summary judgment regarding invalidity under 35 U.S.C.

§ 101. The district court agreed with Ariosa's argument that the claims of the '540 patent were directed to the natural phenomenon of paternally inherited cffDNA and that the claims did not add enough to the natural phenomenon to make the claims patent eligible under § 101. The district court determined that the steps of amplifying and detecting were well-understood, routine, or conventional activity in 1997, when the application for the '540 patent was filed. The district court concluded that the '540 patent was not directed to patentable subject matter because "the only inventive component of the processes of the '540 patent is to apply those well-understood, routine processes to paternally inherited cffDNA, a natural phenomenon." J.A. 18. The district court also found that the claimed processes posed a risk of preempting a natural phenomenon. Sequenom appeals.

We have jurisdiction under 28 U.S.C. § 1295(a)(1).

III

We review the grant of summary judgment under the law of the regional circuit, in this case the Ninth Circuit. *Charles Mach. Works, Inc. v. Vermeer Mfg. Co.*, 723 F.3d 1376, 1378 (Fed. Cir. 2013). The Ninth Circuit reviews the grant or denial of summary judgment de novo. *Leever v. Carson City*, 360 F.3d 1014, 1017 (9th Cir. 2004). We also review de novo the question of whether a claim is invalid under section 101. *In re BRCA1- and BRCA2-Based Hereditary Cancer Test Patent Litig.*, 774 F.3d. 755, 759 (Fed. Cir. 2014).

Section 101 of the Patent Act defines patent eligible subject matter:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

35 U.S.C. § 101. The Supreme Court has long held that there are certain exceptions to this provision: laws of nature, natural phenomena, and abstract ideas. *Alice Corp. v. CLS Bank Int'l*, ___ U.S. ___, 134 S. Ct. 2347, 2354 (2014) (collecting cases).

In *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, 566 U.S. ___, 132 S. Ct. 1289 (2012), the Supreme Court set forth a framework for distinguishing patents that claim laws of nature, natural phenomena, and abstract ideas from those that claim patent-eligible applications of those concepts. First, we determine whether the claims at issue are directed to a patent-ineligible concept. *Id.* at 1297. If the answer is yes, then we next consider the elements of each claim both individually and "as an ordered combination" to determine whether additional elements "transform the nature of the claim" into a patent-eligible application. *Id.* at 1298. The Supreme Court has described the second step of this analysis as a search for an "inventive concept"—i.e., an element or combination of elements that is "sufficient to ensure that the patent in practice amounts to significantly more than a patent upon the [ineligible concept] itself." *Id.* at 1294; *see also Digitech Image Techs., LLC v. Elecs. For Imaging, Inc.*, 758 F.3d 1344, 1351 (Fed. Cir. 2014) ("Without additional limitations, a process that employs mathematical algorithms to manipulate existing information to generate additional information is not patent eligible.").

The claims of the '540 patent that are at issue in this appeal are method claims. Methods are generally eligible subject matter. In this case, the asserted claims of the '540 patent are directed to a multistep method that starts with cffDNA taken from a sample of maternal plasma or serum—a naturally occurring non-cellular fetal DNA that circulates freely in the blood stream of a pregnant woman. *See, e.g.*, '540 patent claims 1, 24, 25. It is undisputed that the existence of cffDNA in maternal blood is a natu-

ral phenomenon. Sequenom does not contend that Drs. Lo and Wainscoat created or altered any of the genetic information encoded in the cffDNA, and it is undisputed that the location of the nucleic acids existed in nature before Drs. Lo and Wainscoat found them. The method ends with paternally inherited cffDNA, which is also a natural phenomenon. The method therefore begins and ends with a natural phenomenon. Thus, the claims are directed to matter that is naturally occurring.

The written description supports the conclusion that the claims of the '540 patent are directed to a naturally occurring thing or natural phenomenon. In the Summary and Objects of the Invention section of the '540 patent, the patent states that "[i]t has now been discovered that foetal DNA is detectable in maternal serum or plasma samples."[2] '540 patent col. 1 ll. 50-51. The patent goes on to state that "[t]his is a surprising and unexpected finding; maternal plasma is the very material that is routinely discarded by investigators studying noninvasive prenatal diagnosis using foetal cells in maternal blood." *Id.* col. 1 ll. 51-55. In the discussion, the patent notes:

> In this study we have demonstrated the feasibility of performing non-invasive foetal RhD genotyping from maternal plasma. This represents the first description of single gene diagnosis from maternal plasma.

Id. col. 10 ll. 53-58. Further, the description of the invention notes: "[w]e have demonstrated that foetal DNA is present in maternal plasma and serum," *id.* col. 13 ll. 6-7, and "[t]hese observations indicate that maternal plasma/serum DNA may be a useful source of material for the

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[2] The term "fetal" and "foetal" are used interchangeably in the '540 patent and by the parties.

non-invasive prenatal diagnosis of certain genetic disorders," *id.* col. 13 ll. 11-13. The patent also states: "[t]he most important observation in this study is the very high concentration of foetal DNA in maternal plasma and serum." *Id.* col. 16 ll. 12-14. Thus, the claims at issue, as informed by the specification, are generally directed to detecting the presence of a naturally occurring thing or a natural phenomenon, cffDNA in maternal plasma or serum. As we noted above, the claimed method begins and ends with a naturally occurring phenomenon.

Because the claims at issue are directed to naturally occurring phenomena, we turn to the second step of *Mayo*'s framework. In the second step, we examine the elements of the claim to determine whether the claim contains an inventive concept sufficient to "transform" the claimed naturally occurring phenomenon into a patent-eligible application. 132 S. Ct. at 1294. We conclude that the practice of the method claims does not result in an inventive concept that transforms the natural phenomenon of cffDNA into a patentable invention.

Mayo made clear that transformation into a patent-eligible application requires "more than simply stat[ing] the law of nature while adding the words 'apply it.'" *Id.* at 1294. A claim that recites an abstract idea, law of nature, or natural phenomenon must include "additional features" to ensure "that the [claim] is more than a drafting effort designed to monopolize the [abstract idea, law of nature, or natural phenomenon]." *Id.* at 1297. For process claims that encompass natural phenomenon, the process steps are the additional features that must be new and useful. *See Parker v. Flook*, 437 U.S. 584, 591 (1978) ("The process itself, not merely the mathematical algorithm, must be new and useful.").

In *Mayo*, the patents at issue claimed a method for measuring metabolites in the bloodstream in order to calibrate the appropriate dosage of thiopurine drugs in

the treatment of autoimmune diseases. 132 S. Ct. at 1294. The respondent contended that the claimed method was a patent eligible application of a natural law that described the relationship between the concentration of certain metabolites and the likelihood that the drug dosage will be harmful or ineffective. Methods for determining metabolite levels, however, were already "well known in the art." *Id.* at 1298. Further, the process at issue amounted to "nothing significantly more than an instruction to doctors to apply the applicable laws when treating their patients." *Id.* In that case, "[s]imply appending conventional steps, specified at a high level of generality," was not enough to supply an inventive concept. *Id*. at 1300.

Like the patentee in *Mayo*, Sequenom contends that the claimed methods are patent eligible applications of a natural phenomenon, specifically a method for detecting paternally inherited cffDNA. Using methods like PCR to amplify and detect cffDNA was well-understood, routine, and conventional activity in 1997. The method at issue here amounts to a general instruction to doctors to apply routine, conventional techniques when seeking to detect cffDNA. Because the method steps were well-understood, conventional and routine, the method of detecting paternally inherited cffDNA is not new and useful. The only subject matter new and useful as of the date of the application was the discovery of the presence of cffDNA in maternal plasma or serum.

The specification of the '540 patent confirms that the preparation and amplification of DNA sequences in plasma or serum were well-understood, routine, conventional activities performed by doctors in 1997. The '540 patent provides that "[t]he preparation of serum or plasma from the maternal blood sample is carried out by standard techniques." '540 patent col. 2 ll. 27-28. It also provides that "[s]tandard nucleic acid amplification systems can be used, including PCR, the ligase chain reaction, nucleic

acid sequence based amplification (NASBA), branched DNA methods, and so on." *Id.* col. 2 ll. 44-47.

Other evidence supports this conclusion. For example, Sequenom's expert, Dr. Evans, testified at deposition that PCR and other methodologies for amplifying DNA were "already well known in science [in 1997]." J.A. 1092-93, 1995-96. Similarly, in a declaration filed during prosecution of the '540 patent, Dr. Lo testified that "[s]uitable amplification techniques can be ordinary PCR or more sophisticated developments thereof, but these techniques were all known in the literature before the date of my invention." J.A. 1109.

The detecting step was similarly well-understood, routine, and conventional. During prosecution of the application that became the '540 patent, the applicant stated:

> [O]ne skilled in the art is aware of a variety of techniques which might be used to detect different nucleic acid species. For example, there are numerous techniques which might be used to detect repeat expansions, single gene mutations, deletions or translocations. These techniques are a matter of routine for one skilled in the art for the analysis of DNA.

J.A. 1052. The applicant went on to note:

> [O]ne skilled in the art is readily able to apply the teachings of the present application to any one of the well-known techniques for detection of DNA with a view to analysis of foetal DNA in paternal [sic] plasma or serum.

J.A. 1055. Similarly, the applicant later added that "[t]he person skilled in the art has a broad range of techniques available for the detection of DNA in a sample." J.A. 1057.

The dependent claims are broad examples of how to detect cffDNA in maternal plasma. The dependent claims are focused on the use of the natural phenomenon in combination with well-understood, routine, and conventional activity. For example, claim 2 identifies the polymerase chain reaction as the amplification technique to be used in the detection method of claim 1. As noted above, this technique was well-understood, routine, and conventional in 1997, as specified by the patent itself. Like claim 1, claims 5 and 8 focus on detecting a specific chromosome within the cffDNA—a natural phenomenon—again, adding no inventive concept to the limitations of claim 1. None of the remaining asserted dependent or independent claims differ substantially from these claims. Thus, in this case, appending routine, conventional steps to a natural phenomenon, specified at a high level of generality, is not enough to supply an inventive concept. Where claims of a method patent are directed to an application that starts and ends with a naturally occurring phenomenon, the patent fails to disclose patent eligible subject matter if the methods themselves are conventional, routine and well understood applications in the art. The claims of the '540 patent at issue in this appeal are not directed to patent eligible subject matter and are, therefore, invalid.

IV

In its opinion, the district court addressed the principle of preemption. The district court noted:

> It is important to note that the '540 patent does not merely claim uses or applications of cffDNA, it claims methods for detecting the natural phenomenon. Because generally one must be able to find a natural phenomenon to use it and apply it, claims covering the only commercially viable way of detecting that phenomenon do carry a substantial risk of preempting all practical uses of it.

J.A. 19.

Sequenom argues that there are numerous other uses of cffDNA aside from those claimed in the '540 patent, and thus, the '540 patent does not preempt all uses of cffDNA, as shown by evidence in the record before the district court. Sequenom also argues that "a method applying or using a natural phenomenon in a manner that does not preclude alternative methods in the same field is non-preemptive, and, by definition, patent-eligible under Section 101." Appellants' Br. 30. Similarly, Sequenom and amici argue that because the particular application of the natural phenomena that the '540 patent claims embody are narrow and specific, the claims should be upheld. Ariosa argues that the principle of preemption does not alter the analysis. Ariosa argues that the claimed methods are not, as Sequenom asserts, limited and specific.

The Supreme Court has made clear that the principle of preemption is the basis for the judicial exceptions to patentability. *Alice*, 134 S. Ct at 2354 ("We have described the concern that drives this exclusionary principal as one of pre-emption"). For this reason, questions on preemption are inherent in and resolved by the § 101 analysis. The concern is that "patent law not inhibit further discovery by improperly tying up the future use of these building blocks of human ingenuity." *Id.* (internal quotations omitted). In other words, patent claims should not prevent the use of the basic building blocks of technology—abstract ideas, naturally occurring phenomena, and natural laws. While preemption may signal patent ineligible subject matter, the absence of complete preemption does not demonstrate patent eligibility. In this case, Sequenom's attempt to limit the breadth of the claims by showing alternative uses of cffDNA outside of the scope of the claims does not change the conclusion that the claims are directed to patent ineligible subject matter. Where a patent's claims are deemed only to disclose patent ineligible subject matter under the *Mayo* framework, as they are

in this case, preemption concerns are fully addressed and made moot.

Sequenom and amici encourage us to draw distinctions among natural phenomena based on whether or not they will interfere significantly with innovation in other fields now or in the future. The Supreme Court cases, however, have not distinguished among different laws of nature or natural phenomenon according to whether or not the principles they embody are sufficiently narrow. *See, e.g.*, *Parker v. Flook*, 437 U.S. 584 (1978) (holding narrow mathematical formula unpatentable). In *Parker v. Flook*, the Supreme Court stated the issue in the case as follows: "The question in this case is whether the identification of a limited category of useful, though conventional, post-solution applications of such a formula makes respondent's method eligible for patent protection." *Id.* at 585. The answer to that question was "no" because granting exclusive rights to the mathematical formula would be exempting it from any future use.

V

For completeness, we address Sequenom's remaining arguments. Sequenom argues that "before the '540 patent, *no one* was using the plasma or serum of pregnant mothers to amplify and detect paternally-inherited cffDNA." Appellants' Br. 49 (emphasis original). This argument implies that the inventive concept lies in the discovery of cffDNA in plasma or serum. Even if so, this is not the invention claimed by the '540 patent.

Sequenom further argues that "[o]ne simple measure of [Drs.] Lo and Wainscoat's contribution is that their 1997 Lancet publication has been cited over a thousand times." Appellants' Br. 25. Sequenom also notes that "the method reflects a significant human contribution in that [Drs.] Lo and Wainscoat combined and utilized man-made tools of biotechnology in a new way that revolutionized prenatal care." *Id.* We agree but note that the Supreme

Court instructs that "[g]roundbreaking, innovative, or even brilliant discovery does not by itself satisfy the § 101 inquiry." *Myriad Genetics, Inc.*, 133 S. Ct. at 2117. The discovery of the BRCA1 and BRCA2 genes was a significant contribution to the medical field, but it was not patentable. *Id.* at 2117. While Drs. Lo and Wainscoat's discovery regarding cffDNA may have been a significant contribution to the medical field, that alone does not make it patentable. We do not disagree that detecting cffDNA in maternal plasma or serum that before was discarded as waste material is a positive and valuable contribution to science. But even such valuable contributions can fall short of statutory patentable subject matter, as it does here.

VI

For each of the reasons stated above, we affirm the district court's summary judgment ruling.

AFFIRMED

COSTS

No costs.

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LINN, *Circuit Judge*, concurring.

I join the court's opinion invalidating the claims of the '540 patent only because I am bound by the sweeping language of the test set out in *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, 566 U.S. ___, 132 S. Ct. 1289 (2012). In my view, the breadth of the second part of the test was unnecessary to the decision reached

in *Mayo*. This case represents the consequence—perhaps unintended—of that broad language in excluding a meritorious invention from the patent protection it deserves and should have been entitled to retain.

It has long been established that "[l]aws of nature, natural phenomena, and abstract ideas are not patentable." *Alice Corp. v. CLS Bank Int'l*, 134 S. Ct. 2347, 2354 (2014) (citations omitted). In *Mayo*, the Supreme Court set forth a two-step framework for distinguishing patents that claim laws of nature, natural phenomena, and abstract ideas from those that claim patent-eligible applications of those concepts. The first step looks to determine whether claims are directed to a patent-ineligible concept. *Mayo*, 132 S. Ct. at 1297. If they are, the second step is to consider whether the additional elements recited in the claim "transform the nature of the claim" into a patent-eligible application by reciting an "inventive concept" that is "sufficient to ensure that the patent in practice amounts to significantly more than a patent upon the [ineligible concept] itself." *Id.* at 1294.

In applying the second part of the test, the Supreme Court in *Mayo* discounted, seemingly without qualification, any "[p]ost-solution activity that is purely conventional or obvious," *id.* at 1299 (original alterations omitted). This was unnecessary in *Mayo*, because doctors were already performing in combination all of the claimed steps of administering the drug at issue, measuring metabolite levels, and adjusting dosing based on the metabolite levels, *id*.

In *Diamond v. Diehr,* the Supreme Court held that "a new combination of steps in a process may be patentable even though all the constituents of the combination were well-known and in common use before the combination was made." 450 U.S. 175, 188 (1981). As *Mayo* explained: *Diehr* "pointed out that the basic mathematical equation, like a law of nature, was not patentable. But [*Diehr*]

found the overall process patent eligible because of the way the additional steps of the process integrated the equation into the process as a whole." *Mayo* 132 S. Ct. at 1298. Despite that recognition, *Mayo* discounted entirely the "conventional activity" recited in the claims in that case because the steps "add nothing specific to the laws of nature other than what is well-understood, routine, conventional activity, previously engaged in by those in the field." *Id.* at 1299. While that conclusion might have been warranted in that case, given the fact that the "conventional activities" in *Mayo* were the very steps that doctors were already doing—administering the drug at issue, measuring metabolite levels, and adjusting dosing based on the metabolite levels—the Supreme Court did not limit its ruling to those particular facts and circumstances.

The Supreme Court's blanket dismissal of conventional post-solution steps leaves no room to distinguish *Mayo* from this case, even though here *no one* was amplifying and detecting paternally-inherited cffDNA using the plasma or serum of pregnant mothers. Indeed, the maternal plasma used to be "routinely discarded," '540 patent col.1 ll.50–53, because, as Dr. Evans testified, "nobody thought that fetal cell-free DNA would be present."

It is hard to deny that Sequenom's invention is truly meritorious. Prior to the '540 patent, prenatal diagnoses required invasive methods, which "present[ed] a degree of risk to the mother and to the pregnancy." *Id.* at col.1 ll.16–17. The available "techniques [we]re time-consuming or require[d] expensive equipment." *Id.* at col.1 ll.17–37. Dr. Mark Evans testified that "despite years of trying by multiple methods, no one was ever able to achieve acceptable success and accuracy." In a groundbreaking invention, Drs. Lo and Wainscoat discovered that there was cell-free fetal DNA in the maternal plasma. The Royal Society lauded this discovery as "a para-

digm shift in non-invasive prenatal diagnosis," and the inventors' article describing this invention has been cited well over a thousand times. The commercial embodiment of the invention, the MaterniT21 test, was the first marketed non-invasive prenatal diagnostic test for fetal aneuploidies, such as Down's syndrome, and presented fewer risks and a more dependable rate of abnormality detection than other tests. Unlike in *Mayo*, the '540 patent claims a new method that should be patent eligible. While the instructions in the claims at issue in *Mayo* had been widely used by doctors—they had been measuring metabolites and recalculating dosages based on toxicity/inefficacy limits for years—here, the amplification and detection of cffDNA had never before been done. The new use of the previously discarded maternal plasma to achieve such an advantageous result is deserving of patent protection. *Cf.* Rebecca S. Eisenberg, *Prometheus Rebound: Diagnostics, Nature, and Mathematical Algorithms*, 122 Yale L.J. Online 341, 343–44 (2013) (noting that despite *Mayo*'s declaration that a claim to "a new way of using an existing drug" is patentable, *Mayo*, 132 S. Ct. at 1302, it is unclear how a claim to new uses for existing drugs would survive *Mayo*'s sweeping test).

In short, Sequenom's invention is nothing like the invention at issue in *Mayo*. Sequenom "effectuate[d] a practical result and benefit not previously attained," so its patent would traditionally have been valid. *Le Roy v. Tatham*, 63 U.S. 132, 135–36 (1859) (quoting *Household Coal & Iron Co. v. Neilson*, Webster's Patent Case 673, 683 (House of Lords 1843)); *Le Roy v. Tatham*, 55 U.S. 156, 175 (1852) (same); *see generally* Jeffrey A. Lefstin, *Inventive Application: a History*, 67 Fla. L. Rev. (forthcoming 2015), *available at* http://ssrn.com/abstract=2398696 (last visited June 10, 2015) (analyzing traditional notions of patent eligibility of newly discovered laws of nature). But for the sweeping language in the Supreme Court's *Mayo* opinion, I see no

reason, in policy or statute, why this breakthrough invention should be deemed patent ineligible.