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

DAVID ISAAC GINDLER, Irell & Manella LLP, Los Angeles, CA, argued for plaintiff-appellee Ariosa Diagnostics, Inc. Also represented by ANDREI IANCU; AMIR NAINI, Russ August & Kabat, Los Angeles, CA.

WILLIAM PAUL SCHUCK, Bartko, Zankel, Bunzel & Miller, San Francisco, CA, for plaintiff-appellee Natera, Inc., counterclaim defendant-appellee DNA Diagnostics Center, Inc.

MICHAEL J. MALECEK, Kaye Scholer LLP, Palo Alto, CA, argued for defendants-appellants. Also represented by PETER E. ROOT, Menlo Park, CA; ATON ARBISSER, Los Angeles, CA.

RICHARD L. BLAYLOCK, Pillsbury Winthrop Shaw Pittman LLP, San Diego, CA, for amicus curiae Invitae Corporation. Also represented by KIRKE M. HASSON, COLIN TRAVERS KEMP, San Francisco, CA.

KEVIN EDWARD NOONAN, McDonnell, Boehnen Hulbert & Berghoff, LLP, Chicago, IL, for amicus curiae Biotechnology Industry Organization.

WILLIAM LARRY RESPESS, I, Sheppard, Mullin, Richter, & Hampton LLP, San Diego, CA, for amicus curiae The San Diego Intellectual Property Law Association.

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:

---

[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

---

[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.

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.

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.

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.

ON PETITION FOR REHEARING EN BANC

MICHAEL J. MALECEK, Kaye Scholer LLP, Palo Alto, CA, filed a petition for rehearing en banc for defendants-appellants. Also represented by PETER E. ROOT; ATON ARBISSER, Los Angeles, CA; THOMAS GOLDSTEIN, ERIC F. CITRON, Goldstein & Russell, P.C., Bethesda, MD.

DAVID ISAAC GINDLER, Irell & Manella LLP, Los Angeles, CA, filed a response to the petition for plaintiff-appellee Ariosa Diagnostics, Inc. Also represented by ANDREI IANCU, JOSHUA GORDON; AMIR NAINI, Russ August & Kabat, Los Angeles, CA.

MARK ANDREW PERRY, Gibson, Dunn & Crutcher LLP, Washington, DC, filed a response to the petition for plaintiff-appellee Natera, Inc. Also represented by TRACEY B. DAVIES, BRETT ROSENTHAL, MICHAEL A. VALEK, Dallas, TX.

WILLIAM PAUL SCHUCK, Bartko, Zankel, Bunzel & Miller, San Francisco, CA, for counterclaim defendant-appellee DNA Diagnostics Center, Inc.

GIDEON A. SCHOR, Wilson Sonsini Goodrich & Rosati, PC, New York, NY, for amici curiae Amarantus Bioscience Holdings, Inc., Personalis, Inc., Population Diagnostics, Inc. Also represented by MAYA SKUBATCH, Palo Alto, CA; RICHARD TORCZON, CHARLES J. ANDRES, JR., Washington, DC.

LANA GLADSTEIN, Nutter McClennen & Fish LLP, Boston, MA, for amicus curiae Bioindustry Association. Also represented by KONSTANTIN M. LINNIK, ISAAC A. HUBNER.

CHRISTOPHER MICHAEL HOLMAN, University of Missouri-Kansas City, Kansas City, MO, for amici curiae Biotechnology Industry Organization, Pharmaceutical Research and Manufacturers of America. Biotechnology Industry Organization also represented by BRIAN P. BARRETT, Eli Lilly and Company, Indianapolis, IN; LI WESTERLUND, Bavarian Nordic, Inc., Redwood City, CA.

BENJAMIN JACKSON, Myriad Genetics, Inc., Salt Lake City, UT, for amicus curiae The Coalition for 21st Century Medicine. Also represented by DAVID CARTER HOFFMAN, Genomic Health, Inc., Redwood City, CA.

DONALD LOUIS ZUHN, JR., McDonnell Boehnen Hulbert & Berghoff LLP, Chicago, IL, for amicus curiae Paul Gilbert Cole.

TEIGE P. SHEEHAN, Heslin, Rothenberg, Farley & Mesiti, P.C., Albany, NY, for amicus curiae Intellectual Property Owners Association. Also represented by PHILIP STATON JOHNSON, Johnson & Johnson, New Brunswick, NJ; KEVIN H. RHODES, 3M Innovative Properties Company, St. Paul, MN; HERBERT CLARE WAMSLEY, JR., Intellectual Property Owners Association, Washington, DC.

MATTHEW JAMES DOWD, Andrews Kurth LLP, Washington, DC, for amicus curiae JYANT Technologies, Inc. Also represented by ROBERT A. GUTKIN, SUSHILA CHANANA.

JEFFREY LEFSTIN, University of California Hastings College of Law, San Francisco, CA, for amici curiae Jeffrey Lefstin, Peter S. Menell.

JOHN D. MURNANE, Fitzpatrick, Cella, Harper & Scinto, New York, NY, for amicus curiae New York Intellectual Property Law Association. Also represented by ALICIA ALEXANDRA ROSE RUSSO, ERIN AUSTIN; DOROTHY R. AUTH, Cadwalader, Wickersham & Taft LLP, New York, NY; IRENA ROYZMAN, Patterson Belknap Webb & Tyler LLP, New York, NY; DAVID F. RYAN, Croton-on-Hudson, NY.

COREY A. SALSBERG, Novartis International AG, Basel, Switzerland, for amicus curiae Novartis AG.

KEVIN EDWARD NOONAN, McDonnell Boehnen Hulbert & Berghoff LLP, Chicago, IL, for amici curiae Twenty-Three Law Professors.

DAN L. BAGATELL, Perkins Coie LLP, Phoenix, AZ, for amici curiae Wisconsin Alumni Research Foundation, Marshfield Clinic, MCIS, Inc. Also represented by MICHELLE MARIE UMBERGER, Madison, WI; MICHAEL ROBERT OSTERHOFF, Chicago, IL.

Before PROST, *Chief Judge*, NEWMAN, LOURIE, DYK, MOORE, O'MALLEY, REYNA, WALLACH, TARANTO, CHEN, HUGHES, and STOLL, *Circuit Judges*.

LOURIE, *Circuit Judge*, with whom MOORE, *Circuit Judge*, joins, concurs with the denial of the petition for rehearing en banc.

DYK, *Circuit Judge*, concurs with the denial of the petition for rehearing en banc.

NEWMAN, *Circuit Judge*, dissents from the denial of the petition for rehearing en banc.

PER CURIAM.

O R D E R

A petition for rehearing en banc was filed by defendants-appellants Sequenom, Inc. and Sequenom Center for Molecular Medicine, LLC. The petition for rehearing was first referred to the panel that heard the appeal, and thereafter, to the circuit judges who are in regular active service. A response was invited by the court and filed by plaintiffs-appellees Ariosa Diagnostics, Inc. and Natera, Inc. A poll was requested, taken, and failed.

Upon consideration thereof,

IT IS ORDERED THAT:

(1) The petition for rehearing en banc is denied.

(2) The mandate of the court will issue on December 9, 2015.

FOR THE COURT

December 2, 2015
Date

/s/ Daniel E. O'Toole
Daniel E. O'Toole
Clerk of Court

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.

LOURIE, *Circuit Judge*, with whom MOORE, *Circuit Judge*, joins, concurring in the denial of the petition for rehearing en banc.

I concur in the court's denial of rehearing en banc in this case, based on the precedent of *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, 566 U.S. __, 132 S. Ct. 1289 (2012). I do so because I find no principled

basis to distinguish this case from *Mayo*, by which we are bound. I write separately to express some thoughts concerning laws of nature and abstract ideas, which seem to be at the heart of patent-eligibility issues in the medical sciences.

Since the Supreme Court's decision in *Bilski v. Kappos*, 561 U.S. __, 130 S. Ct. 3218 (2010), the issue of patent eligibility under § 101 has been of key importance in the adjudication of patent cases, particularly in the field of software. The Court's decisions in *Mayo*, *Association for Molecular Pathology v. Myriad Genetics, Inc.*, 569 U.S. __, 133 S. Ct. 2107 (2013), and *Alice Corp. v. CLS Bank International*, 573 U.S. __, 134 S. Ct. 2347 (2014), have further brought the focus onto the field of medical diagnostics.

The Supreme Court in *Mayo* determined that the claims in that patent "set forth laws of nature." It further held in *Mayo* that steps additional to those setting forth laws of nature in a claimed process must add something "that in terms of patent law's objectives ha[ve] significance" to the natural laws, such that those steps transform the process into an inventive application of those laws. *Mayo*, 132 S. Ct. at 1299. Moreover, the Court rejected "post-solution activity that is purely conventional or obvious" as not significant enough to bring a claimed invention within the realm of patent-eligible subject matter. *Id.* (internal quotation marks and alteration omitted).

Alice relates to the third specific exception to eligibility—abstract ideas—and its discussion also incorporates the requirement of an "inventive concept" beyond "conventional steps." It held that claims that amount to nothing more than *instruction to apply* an abstract idea are not patent eligible, although *application of the abstract idea may be*. In my view, neither of the traditional

preclusions of laws of nature or of abstract ideas ought to prohibit patenting of the subject matter in this case.

Laws of nature are *exact* statements of physical relationships, deduced from scientific observations of natural phenomena. They are often represented by equations, and include such laws as the relationship between energy and mass ($E=mc^2$), the relationship between current and resistance (Ohm's Law), that between force, mass, and acceleration ($F=ma$), Maxwell's equations, Newton's laws of motion, and many more. Those laws, all agree, are not and should not be patent-eligible subject matter. But methods that utilize laws of nature do not set forth or claim laws of nature. All physical steps of human ingenuity utilize natural laws or involve natural phenomena. Thus, those steps cannot be patent-ineligible solely on that basis because, under that reasoning, nothing in the physical universe would be patent-eligible.

Abstract steps are, axiomatically, the opposite of tangible steps; that which is not tangible is abstract. But steps that involve machines, which are tangible, steps that involve transformation of tangible subject matter, or tangible implementations of ideas or abstractions should not be considered to be abstract ideas. In *Bilski*, the Supreme Court supported this proposition when it described our earlier machine-or-transformation test as a useful clue, albeit not the only test, for eligibility.

Conversely, abstract ideas are essentially mental steps; they are not tangible even if they are written down or programmed into a physical machine. *Alice,* in affirming this court, held that claims that amount to nothing significantly more than *instruction to apply* an abstract idea are not patent eligible. But the fact that steps are well-known, although relevant to other statutory sections of the patent law, does not necessarily make them abstract.

The claims at issue in Sequenom's patent are directed to methods for detecting paternally-inherited fetal DNA in maternal blood samples, and performing a prenatal diagnosis based on such DNA. Following *Mayo*, which held that certain steps merely recite natural laws and that the remaining steps must be sufficiently innovative apart from the natural laws, the panel in this case held that the claims do not involve patent-eligible subject matter. Appellants and amici have argued before us in briefs that a broad range of claims of this sort appear to be in serious jeopardy. It is said that the whole category of diagnostic claims is at risk. It is also said that a crisis of patent law and medical innovation may be upon us, and there seems to be some truth in that concern.

The claims in this case perhaps should be in jeopardy, not because they recite natural laws or abstract ideas, but because they may be indefinite or too broad. But they should not be patent-ineligible on the ground that they set forth natural laws or are abstractions.

Claim 1 is directed to a method for detecting a paternally inherited nucleic acid of fetal origin from a pregnant female comprising amplifying a paternally inherited nucleic acid and detecting the presence of a paternally inherited nucleic acid. Claim 21 is directed to a method of performing a prenatal diagnosis comprising providing a maternal blood sample, separating the sample into a cellular and non-cellular fraction, detecting the presence of a nucleic acid, and providing a diagnosis. Both of these claims contain the nucleus of patent-eligible subject matter.

As the panel noted, the natural phenomenon here is the presence of cell-free fetal DNA ("cffDNA") in maternal plasma, which, when subjected to certain conventional steps, has led to an important new development: diagnosis of possible birth defects without using highly intrusive means. Applications of natural phenomena or laws to a

known process "may well be deserving of patent protection." *Diehr*, 450 U.S. at 187. And it is not disputed that this scientific work on its own seems like an important discovery and a valuable contribution to the medical field, although no one asserts that a claim directed to the mere existence of cffDNA is patent-eligible. But neither of the representative claims here merely recites a law of nature, a natural phenomenon, or an abstract idea. The claims rely on or operate by, but do not recite, a natural phenomenon or law. The claimed invention involves taking maternal serum, separating it, amplifying the genetic material to detect cffDNA, and running tests to identify certain genes or genetic defects; these are all physical, and not insignificant, steps requiring human intervention.

The claims might be indefinite or too broad in that they do not specify how to amplify and detect, or how to separate, detect, and diagnose. Or they perhaps attempt to claim all known methods of carrying out those steps. But the finer filter of § 112 might be better suited to treating these as questions of patentability, rather than reviewing them under the less-defined eligibility rules.

It is not disputed that fractionating blood, amplifying DNA, and analyzing DNA to detect specific gene sequences are known techniques in the art. As all other steps in the claims are individually well-known, the innovative aspect of the claims appears to be the improvement in the method of determining fetal genetic characteristics or diagnosing abnormalities of fetal DNA, consisting of *use of the non-cellular fraction of fetal DNA* obtained from a maternal blood sample.

The claim to this invention, then, might have been better drafted as a so-called Jepson claim, which recites what is in the prior art and what is the improvement. Such a claim might read, perhaps with more details added: "In a method of performing a prenatal diagnosis using techniques of fractionation and amplification, the

improvement consisting of using the non-cellular fraction of a maternal blood sample."

Regardless, we are not experts in drafting claims to protect new biological procedures and we are not in a position to rewrite claims or review a hypothetical claim. But against the accusation that such a claim to the invention might be considered mere draftsmanship and thus still ineligible under the seemingly expansive holding of *Mayo*, it must be said that a process, composition of matter, article of manufacture, and machine are different implementations of ideas, and differentiating among them in claim drafting is a laudable professional skill, not necessarily a devious device for avoiding prohibitions. This is true despite the Supreme Court's affirmance of this court in *Alice*, where we had held, by a 7–3 vote, that method and media claims in inventions *of the type claimed there* were essentially the same.

But focusing on the claims we have rather than those we might have had, the claims here are directed to an actual use of the natural material of cffDNA. They recite innovative and practical *uses* for it, particularly for diagnostic testing: blood typing, sex typing, and screening for genetic abnormalities. And it is undisputed that before this invention, the amplification and detection *of cffDNA from maternal blood*, and use of these methods for prenatal diagnoses, were *not* routine and conventional. But applying *Mayo*, we are unfortunately obliged to divorce the additional steps from the asserted natural phenomenon to arrive at a conclusion that they add nothing innovative to the process.

Moreover, the claims here are not abstract. There is nothing abstract about performing actual physical steps on a physical material. And if the concern is preemption of a natural phenomenon, this is, apparently, a novel process and that is what patents are intended to incentivize and be awarded for. The panel here also noted that

there were other uses for cffDNA and other methods of prenatal diagnostic testing using cffDNA that do not involve the steps recited in the various claims. That fact should sufficiently address the concern of improperly tying up future use of natural phenomena and laws.

In sum, it is unsound to have a rule that takes inventions of this nature out of the realm of patent-eligibility on grounds that they only claim a natural phenomenon plus conventional steps, or that they claim abstract concepts. But I agree that the panel did not err in its conclusion that under Supreme Court precedent it had no option other than to affirm the district court.

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.

DYK, *Circuit Judge*, concurring in the denial of the petition for rehearing en banc.

I concur in the court's denial of rehearing en banc. In my view the framework of *Mayo* and *Alice* is an essential ingredient of a healthy patent system, allowing the inval-

idation of improperly issued and highly anticompetitive patents without the need for protracted and expensive litigation. Yet I share the concerns of some of my colleagues that a too restrictive test for patent eligibility under 35 U.S.C. § 101 with respect to laws of nature (reflected in some of the language in *Mayo*) may discourage development and disclosure of new diagnostic and therapeutic methods in the life sciences, which are often driven by discovery of new natural laws and phenomena. This leads me to think that some further illumination as to the scope of *Mayo* would be beneficial in one limited aspect. At the same time I think that we are bound by the language of *Mayo*, and any further guidance must come from the Supreme Court, not this court.

I

The language of *Mayo* is clear. The *Mayo* Court found that prior Supreme Court decisions "insist that a process that focuses upon the use of a natural law also contain other elements or a combination of elements, sometimes referred to as an 'inventive concept,' sufficient to ensure that the patent in practice amounts to significantly more than a patent upon the natural law itself." *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 132 S. Ct. 1289, 1294 (2012) (quoting *Parker v. Flook*, 437 U.S. 584, 594 (1978)). Patent claims directed to laws of nature are ineligible under 35 U.S.C. § 101 when, "(*apart* from the natural laws themselves) [they] involve well-understood, routine, conventional activity previously engaged in by researchers in the field." *Id.* (emphasis added). Reviewing the Court's earlier *Flook* decision, the *Mayo* Court determined that Flook's claim to a chemical process applying an "apparently novel mathematical algorithm," *id.* at 1298, was ineligible under § 101 because the steps of the process "were all 'well known,' to the point where, *putting the formula to the side*, there was no 'inventive concept' in the claimed application of the formula," *id.* at

1299 (quoting *Flook*, 437 U.S. at 594) (emphasis added). "[S]imply appending conventional steps, specified at a high level of generality, to laws of nature, natural phenomena, and abstract ideas cannot make those laws, phenomena, and ideas patentable." *Id.* at 1300. In other words, *Mayo* states that the inventive concept necessary for eligibility must come in the application analyzed at step two, rather than from the discovery of the law of nature itself.

Alice subsequently confirmed that the two-step framework articulated in *Mayo* is a unitary rule that applies equally "for distinguishing patents that claim laws of nature, natural phenomena, and abstract ideas from those that claim patent-eligible applications of those concepts." *Alice Corp. Pty. Ltd. v. CLS Bank Int'l*, 134 S. Ct. 2347, 2355 (2014) (citing *Mayo*). *Alice* explained,

> First, we determine whether the claims at issue are directed to one of those patent-ineligible concepts. If so, we then ask, what else is there in the claims before us? . . . *We have described step two 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. (emphasis added) (alterations, citations, and quotation marks omitted). "*At Mayo step two*, we must examine the elements of the claim to determine whether it contains an 'inventive concept' sufficient to 'transform' the claimed abstract idea into a patent-eligible application." *Id.* at 2357 (emphasis added) (quotation marks omitted). Thus *Alice* also holds that inventive concept must be found at step two of the framework.

Mayo has unambiguously announced a generally applicable test for determining subject-matter eligibility

under § 101 with respect to laws of nature, and we are bound to follow it. We cannot confine *Mayo* to its facts or otherwise cabin a clear statement from the Supreme Court. "[O]nce the Court has spoken, it is the duty of other courts to respect that understanding of the governing rule of law." *Rivers v. Roadway Express, Inc.*, 511 U.S. 298, 312 (1994). A court of appeals must not "confus[e] the factual contours of [a Supreme Court decision] for its unmistakable holding" to arrive at a "novel interpretation" of that decision. *Thurston Motor Lines, Inc. v. Jordan K. Rand, Ltd.*, 460 U.S. 533, 534–35 (1983) (per curiam). As we have recognized, "[a]s a subordinate federal court, we may not so easily dismiss [the Supreme Court's] statements as dicta but are bound to follow them." *Ariad Pharm., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1347 (Fed. Cir. 2010) (en banc) (citing *Stone Container Corp. v. United States*, 229 F.3d 1345, 1349–50 (Fed. Cir. 2000)).

The panel thus held correctly that *Mayo* is controlling precedent that governs the outcome here. The panel's opinion aptly states and applies the two-step framework of *Mayo*. "First, we determine whether the claims at issue are directed to a patent-ineligible concept." *Ariosa Diagnostics, Inc. v. Sequenom, Inc.*, 788 F.3d 1371, 1375 (Fed. Cir. 2015) (citing *Mayo*, 566 U.S. at 1292). "[T]he 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. . . . [T]he claimed method begins and ends with a naturally occurring phenomenon." *Id.* at 1376. At the second step of the *Mayo* framework, the panel determined that "[t]he method at issue here amounts to a general instruction to doctors to apply routine, conventional techniques when seeking to detect cffDNA." *Id.* at 1377. The panel therefore found that the claims were not patent eligible under § 101. *Id.* at 1378.

II

The *Mayo*/*Alice* framework works well when the abstract idea or law of nature in question is well known and longstanding, as was the situation in *Mayo* itself (as discussed below), earlier Supreme Court cases,[1] and in many of our own recent cases where we have found claims patent ineligible under § 101.[2] Where the abstract idea or

---

[1] *See, e.g.*, *Bilski v. Kappos*, 561 U.S. 593, 611 (2010) ("Hedging is a fundamental economic practice *long prevalent* in our system of commerce and taught in any introductory finance class.") (quoting *In re Bilski*, 545 F.3d 943, 1013 (Fed. Cir. 2008) (Rader, J., dissenting)) (emphasis added); *Diamond v. Diehr*, 450 U.S. 175, 177 n.2 (1981) (noting that the Arrhenius equation "*has long been used* to calculate the cure time in rubber-molding processes") (emphasis added); *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127, 129 (1948) ("Methods of selecting the strong strains [of nitrogen-fixing root-nodule bacteria] and of producing a bacterial culture from them *have long been known*.") (emphasis added); *see also* the influential English patent case discussed in *Mayo*, 132 S. Ct. at 1300, *Neilson v. Harford*, Webster's Patent Cases 295, 371 (1841) ("We think the case must be considered as if the principle [that hot air promotes ignition better than cold air is] *well known* . . . .") (emphasis added).

[2] *See*, *e.g.*, *Intellectual Ventures I LLC v. Capital One Bank*, 792 F.3d 1363, 1369 (Fed. Cir. 2015) (invalidating claims that applied an abstract idea—tailoring of advertising to individual customers—which "had often been" used before); *OIP Techs., Inc. v. Amazon.com, Inc.*, 788 F.3d 1359, 1362, 1364 (Fed. Cir. 2015) (invalidating claims to computerized methods of offer-based price optimization and noting that the abstract idea implicated was a "fundamental economic concept[]"); *Ultramercial,*

law of nature is well known and longstanding, there is no basis for attributing novelty to that aspect of the claimed invention.

Also, it seems to me that the *Mayo*/*Alice* framework works well with respect to abstract ideas. In my view, claims to business methods and other processes that merely organize human activity should not be patent eligible under any circumstances. *See Alice*, 134 S. Ct. at 2360 (Sotomayor, J., concurring); *In re Bilski*, 545 F.3d 943, 972 (Fed. Cir. 2008) (en banc) (Dyk, J., concurring). In any event, departing from the *Mayo*/*Alice* framework with respect to abstract ideas (as opposed to discoveries of natural laws and phenomena) would create serious risks of undue preemption because of the difficulty in distinguishing between new and established abstract ideas.

But, as I see it, there is a problem with *Mayo* insofar as it concludes that inventive concept cannot come from discovering something new in nature—*e.g.*, identification of a previously unknown natural relationship or property. In my view, *Mayo* did not fully take into account the fact that an inventive concept can come not just from creative,

---

Inc. v. Hulu, LLC, 772 F3d 709, 715 (Fed. Cir. 2014) (invalidating a claim to routine, conventional application of the abstract idea of "using advertising as an exchange or currency" and rejecting the patentee's argument that the idea was new); *buySAFE, Inc. v. Google, Inc.*, 765 F.3d 1350, 1351, 1355 (Fed. Cir. 2014) (invalidating a claim to a method of guaranteeing a party's performance in an online transaction and finding that the abstract idea implicated was "beyond question of ancient lineage"); *SmartGene, Inc. v. Advanced Biological Labs., SA*, 555 F. App'x 950 (Fed. Cir. 2014) (invalidating a claim to computerized application of a mental process for treating medical patients that "doctors do routinely").

unconventional application of a natural law, but also from the creativity and novelty of the discovery of the law itself. This is especially true in the life sciences, where development of useful new diagnostic and therapeutic methods is driven by investigation of complex biological systems. I worry that method claims that apply newly discovered natural laws and phenomena in somewhat conventional ways are screened out by the *Mayo* test. In this regard I think that *Mayo* may not be entirely consistent with the Supreme Court's decision in *Myriad*.[3]

In *Myriad* the patent applicant discovered a previously unknown natural phenomenon: the sequences of the BRCA1 and BRCA2 genes and their connection with cancer. *Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 133 S. Ct. 2107, 2112–13 (2013). While the Court found ineligible Myriad's claims to naturally occurring gDNA sequences, it suggested that "new *applications* of knowledge about the BRCA1 and BRCA2 genes" could generally be eligible, with reference to claim 21 of U.S. Patent No. 5,753,441 (discussed further below).[4] *Id.* at 2120. *Myriad* thus appeared to recognize that an inventive concept can sometimes come from discovery of an

---

[3] Any tension between *Mayo* and *Myriad* does not, of course, change our obligation to respect the sweeping precedent of *Mayo*, as the panel did. Supreme Court "decisions remain binding precedent until [the Court] see[s] fit to reconsider them, regardless of whether subsequent cases have raised doubts about their continuing vitality." *Hohn v. United States*, 524 U.S. 236, 252–53 (1998) (citation omitted).

[4] The "new applications" referred to by the Court must have meant applications of the newly discovered genes rather than inventive concepts at step two of the *Mayo*/*Alice* framework.

unknown natural phenomenon, not just from unconventional application of a phenomenon. As *Myriad* emphasized, the first party with knowledge of a law of nature, natural phenomenon, or abstract idea should be "in an excellent position to claim applications of that knowledge." *Id.* (quoting *Ass'n. for Molecular Pathology v. USPTO*, 689 F.3d 1303, 1349 (Fed. Cir. 2012) (Bryson, J., concurring in part and dissenting in part)).

III

Of course, I do not suggest that a newly discovered law of nature should be patent eligible in its entirety. Laws of nature are never patentable as such, even when first discovered by the patent applicant. As *Mayo* recognized, "Einstein could not patent his celebrated law that $E=mc^2$." 132 U.S. at 1293 (quoting *Diamond v. Chakrabarty*, 447 U.S. 303, 309 (1980)); *see also Flook*, 437 U.S. at 591; *Gottschalk v. Benson*, 409 U.S. 63, 72 (1972) (holding that claims to methods of using a new mathematical algorithm were unpatentable because they "in practical effect would be a patent on the algorithm itself"). *Myriad* itself reminded us that "[g]roundbreaking, innovative, or even brilliant discovery does not by itself satisfy the § 101 inquiry." *Myriad*, 133 S. Ct. at 2117; *see also Ariosa*, 788 F.3d at 1379.

The primary concern with a patent on a law of nature is undue preemption—the fear that others' innovative future applications of the law will be foreclosed. *See O'Reilly v. Morse*, 56 U.S. 62, 113 (1853); *Mayo*, 132 S. Ct. at 1301. As *Mayo* emphasized, "there is a danger that the grant of patents that tie up the[] use [of laws of nature] will inhibit future innovation premised upon them . . . ." 132 S. Ct. at 1301; *see also id.* at 1304 (highlighting "the kind of risk that underlies the law of nature exception, namely the risk that a patent on the law would significantly impede future innovation").

As far back as *O'Reilly v. Morse*, the Supreme Court found unpatentable Morse's sweeping claim to all "marking or printing [of] intelligible characters, signs, or letters, at any distances" via "the use of the motive power of the electric or galvanic current, which I call electro-magnetism," holding that "the claim is too broad, and not warranted by law." 56 U.S. at 112, 113. *Morse*, like *Mayo*, was concerned with undue preemption of the building blocks of human ingenuity. "[W]hile he shuts the door against inventions of other persons, the patentee would be able to avail himself of new discoveries in the properties and powers of electro-magnetism which scientific men might bring to light." *Id.* at 113.

Similarly, in an aspect of our original *Myriad* decision that was not reversed by the Supreme Court, *Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 133 S. Ct. 694 (2012), and again in our court's recent *In re BRCA1- & BRCA2-Based Hereditary Cancer Test* decision, we found genetic testing claims that sought to capture "all comparisons between the patient's BRCA genes and the wild-type BRCA genes" to be overbroad and thus ineligible under § 101, noting that "[t]he covered comparisons are not restricted by the purpose of the comparison or the alteration being detected." 774 F.3d 755, 763, 765 (Fed. Cir. 2014).

However, if the breadth of the claim is sufficiently limited to a specific application of the new law of nature discovered by the patent applicant and reduced to practice, I think that the novelty of the discovery should be enough to supply the necessary inventive concept. My proposed approach would require that the claimed application be both narrow in scope and actually reduced to practice, not merely "constructively" reduced to practice by filing of a patent application replete with prophetic examples.

In my view, the breadth of the claim should be critical. Even when a patent applicant has demonstrated some particular utility for a newly discovered law of nature and reduced it to practice, the claim should be invalid unless narrowly tailored to the particular application of the law that has been developed. Claims that extend far beyond the utility demonstrated by the patent applicant and reduced to practice should be invalid, as they "too broadly preempt the use" of the underlying idea by others. *Mayo*, 132 S. Ct. at 1294; *see also Diamond v. Diehr*, 450 U.S. 175, 191–92 (1981). But, so long as a claim is narrowly tailored to what the patent applicant has actually invented and reduced to practice, there is limited risk of undue preemption of the underlying idea. In *Myriad* the Court noted, 133 S. Ct. at 2120, that an example of a meritorious claim might be claim 21 of Myriad's U.S. Patent No. 5,753,441 ("the '441 patent"), which was not at issue in the case and which Judge Bryson discussed in his concurring opinion on our court's decision below, *Ass'n for Molecular Pathology*, 689 F.3d at 1348 (Bryson, J., concurring). Claim 21 of the '441 patent covers a method of detecting any of several specific mutations in the BRCA1 gene, newly discovered by the patent applicant and shown to increase a person's risk of developing particular cancers, using conventional methods. *See In re BRCA1 & BRCA2*, 774 F.3d at 765.

This approach appears also to be supported by *Morse*. The Supreme Court established in *Morse* that the extent to which a patentee can claim is the extent to which he has actually made some concrete use of the discovery and reduced it to practice. "The specification of this patentee describes his invention or discovery, and the manner and process of constructing and using it; and his patent . . . covers nothing more." *Morse*, 56 U.S. at 119. Limiting patentees to narrow applications they have actually developed and reduced to practice would be in

keeping with *Mayo*'s commandment that "simply appending conventional steps, *specified at a high level of generality*, to laws of nature, natural phenomena, and abstract ideas cannot make those laws, phenomena, and ideas patentable." *Mayo*, 132 S. Ct. at 1300 (emphasis added).

This proposed approach, limiting the scope of patents based on new discoveries to narrow claims covering applications actually reduced to practice, would allow the inventor to enjoy an exclusive right to what he himself has invented and put into practice, but not to prevent new applications of the natural law by others.[5] This would ensure that the scope of the patent claims would not "foreclose[] more future invention than the underlying

---

[5] It has been suggested that the requirements of enablement and written description will guard against the dangers of overclaiming a law of nature. Those doctrines, important as they are, generally require only that one or a handful of representative embodiments be described by the patentee. *See, e.g.*, Donald S. Chisum, *Chisum on Patents*, § 7.03 at 7-15 (2015) ("An enabling *disclosure* is all that is required [for enablement]. The applicant need not describe actual embodiments or examples. Indeed, an applicant need not have reduced the invention to practice prior to filing."); *Id.* § 7.04[1][e] at 7-309–7-310.1 ("In *Ariad Pharmaceuticals, Inc. v. Eli Lilly & Co.* (2010), the Federal Circuit, sitting en banc, reaffirmed that written description of the invention is a requirement distinct from enablement . . . . [The court] declined to set forth 'bright-line rules,' including rules on the number of species needed to support a generic claim.") (citing and quoting *Ariad*, 598 F.3d at 1351–52). Therefore, the doctrines of enablement and written description would not entirely prevent claims that preempt future applications of the law of nature by others.

discovery could reasonably justify." *Id.* at 1301. Limiting the scope of the patent also would avoid the problem that "the more abstractly [a process patent's] claims are stated, the more difficult it is to determine precisely what they cover." *Mayo*, 132 S. Ct. at 1302 (quoting Christina Bohannan & Herbert Hovenkamp, *Creation without Restraint: Promoting Liberty and Rivalry in Innovation* 112 (2012)).

To be sure, determination of whether a claim applying a new law of nature is overbroad could present difficulties of definition and line drawing. But allowing narrow claims that have been actually reduced to practice when those claims embody an inventive, newly discovered law of nature would promote the fundamental policies underlying § 101. Requiring narrow claims and actual reduction to practice would be a reasonable accommodation in return for a more permissive inventive concept requirement. The approach would, I think, ensure that only diagnostic and therapeutic method patents limited in their claim scope would survive. These patents would provide the world with disclosure and useful applications of previously unknown natural laws, and the opportunity to obtain such patents would help to restore the incentive to make those discoveries that the patent system has historically provided.

IV

To be clear, I do not suggest that *Mayo* was incorrectly decided on its particular facts. The claims at issue in *Mayo* contributed only routine application to a law of nature that was already well known. "At the time the discoveries embodied in the patents were made, scientists *already understood* that the levels in a patient's blood of certain metabolites, including, in particular, [the individual metabolites measured in the claimed methods], were correlated with the likelihood that a particular dosage of a

thiopurine drug could cause harm or prove ineffective." 132 S. Ct. at 1295 (emphasis added). While "those in the field did not know the precise correlations between metabolite levels and likely harm or ineffectiveness," *id.*, "scientists *routinely* measured metabolites as part of their investigations into the relationships between metabolite levels and efficacy and toxicity of thiopurine compounds," *id.* at 1298 (emphasis added). In *Mayo*, the application of the natural law was merely routine optimization of drug dosage to maximize therapeutic effect.[6] As discussed above, *Mayo* thus forms part of a long line of Supreme Court decisions invalidating patent claims to conventional applications of well-known laws of nature.

V

Finally, it seems to me that the approach I suggest would not change the result in this case. Sequenom's challenged claims embody a newly discovered natural phenomenon, the presence of paternally inherited cell-free fetal DNA (cffDNA) in a mother's bloodstream. Judge Linn's concurrence notes that "the amplification and detection of cffDNA had never before been done." *Ariosa*, 788 F.3d at 1381 (Linn, J., concurring). But the major defect is not that the claims lack inventive concept but rather that they are overbroad. *See Mayo*, 132 S. Ct. at 1294.

---

[6] *Cf. Pfizer, Inc., v. Apotex, Inc.*, 480 F.3d 1348, 1368 (Fed. Cir. 2007) ("[D]iscovery of an optimum value of a variable in a known process is usually obvious."); *In re Geisler*, 116 F.3d 1465, 1470 (Fed. Cir. 1997) (noting that generally, in the context of obviousness, "it is not inventive to discover the optimum or workable ranges by routine experimentation") (quoting *In re Aller*, 220 F.2d 454, 456 (CCPA 1955)).

For example, claim 1 of the '540 patent broadly covers any method of detecting paternally inherited cffDNA from maternal serum or plasma via amplification and detection of that cffDNA. '540 patent, col. 23, ll. 61–67. Even the somewhat narrower claim 21 of the '540 patent, which recites a method of performing a prenatal diagnosis based on the presence, quantity, or sequence of paternally inherited cffDNA detected by the method of claim 1, still broadly encompasses *any* diagnosis of *any* disease, disorder, or condition. '540 patent, col. 26, ll. 4–14. Such claims appear to be impermissible attempts to capture the entire natural phenomenon of cffDNA rather than any particular applications thereof developed and actually reduced to practice by the inventors.

A future case is likely to present a patent claim where the inventive concept resides in a newly discovered law of nature or natural phenomenon, but the claim is narrowly drawn and actually reduced to practice. That case will, I hope, provide the Supreme Court with an opportunity to revisit the *Mayo*/*Alice* framework in this one limited aspect.

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.

NEWMAN, *Circuit Judge*, dissenting from denial of the petition for rehearing en banc.

I agree with my colleagues that this case is wrongly decided. However, I do not share their view that this incorrect decision is required by Supreme Court precedent. The facts of this case diverge significantly from the

facts and rulings in *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, 132 S. Ct. 1289 (2012), and in *Association for Molecular Pathology v. Myriad Genetics*, 133 S. Ct. 2107 (2013).

In *Mayo,* both the medicinal product and its metabolites were previously known, leaving sparse room for innovative advance in using this information as a diagnostic dosage tool. Nonetheless, the Court recognized the principle that patent eligibility is not disabled when science is put to practical use, stating that "a new way of using an existing drug" is patent-eligible under Section 101. 132 S. Ct. at 1302.

Whether or not *Mayo* drew an appropriate line in that case, particularly in view of the specificity of the diagnostic method that was developed, this decision does not require the drawing of a different line on quite different facts. In the case now before us, the claimed method was not previously known, nor the diagnostic knowledge and benefit implemented by the method.

Similar caveats accompanied the Court's decision in *Association for Molecular Pathology v. Myriad Genetics*, with the Court stating that "this case does not involve patents on new *applications* of knowledge about the BRCA1 and BRCA2 genes." 133 S. Ct. at 2120 (emphasis original). The Court further explained its holding, stating that: "We merely hold that genes and the information they encode are not patent eligible under § 101 simply because they have been isolated from the surrounding genetic material." *Id.*

In the case at bar, the inventors are not claiming the scientific fact of the discovery of paternal DNA in the blood of a pregnant woman; they are claiming the discovery and development of a new diagnostic method of using this information. As the panel recognized, this is a "breakthrough," for this information can now be learned not only earlier in the gestation period than was previous-

ly available, but without the risks of the previously required invasive procedures of penetrating the amniotic sac.

Precedent does not require that all discoveries of natural phenomena or their application in new ways or for new uses are ineligible for patenting; the Court has cautioned against such generalizations. Such caution takes hold for the case at bar. The new diagnostic method here is novel and unforeseen, and is of profound public benefit—"a significant contribution to the medical field," Panel Maj. Op. at 16—a "breakthrough," Panel Conc. Op. at 5. The panel's decision to withhold access to patenting, now endorsed by the en banc court's refusal to rehear the case, is devoid of support.

Nor does patenting of this new diagnostic method preempt further study of this science, nor the development of additional applications. Patenting does, however, facilitate the public benefit of provision of this method through medical diagnostic commerce, rather than remaining a laboratory curiosity.

This subject matter is not ineligible under Section 101, but warrants standard legal analysis for compliance with the requirements of patentability, that is, novelty, unobviousness, specificity of written description, enablement, etc., and whether the claims are appropriately limited, as discussed many years ago in *O'Reilly v. Morse*, 56 U.S. 62, 112 (1853) ("We perceive no well-founded objection to the description which is given of the whole invention and its separate parts, nor to his right to a patent for the first seven inventions set forth in the specification of his claims.").

I respectfully dissent from my colleagues' conclusion that Supreme Court precedent on Section 101 excludes this invention from eligibility for patenting. The subject matter should be reviewed for compliance with Sections

102, 103, and 112, and any other relevant provisions of the patent law.