APPENDIX A

UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

2019-1419

ILLUMINA, INC., SEQUENOM, INC.,
Plaintiffs-Appellants,
v.

ARIOSA DIAGNOSTICS, INC.,
ROCHE SEQUENCING SOLUTIONS, INC.,
ROCHE MOLECULAR SYSTEMS, INC.,
Defendants-Appellees.

OPINION ISSUED: March 17, 2020
OPINION MODIFIED: August 3, 2020[*]

Appeal from the United States District Court
for the Northern District of California in
No. 3:18-cv-02847-SI, Senior Judge Susan Y. Illston.

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* * *

Before LOURIE, MOORE, and REYNA,
Circuit Judges.

Opinion for the court filed by
Circuit Judge LOURIE.

Dissenting opinion filed by *Circuit Judge* REYNA.

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[*] This opinion has been modified and reissued following a petition for rehearing filed by Defendants-Appellees.

LOURIE, *Circuit Judge.*

Illumina, Inc. and Sequenom, Inc. (collectively, "Illumina") appeal from a decision of the United States District Court for the Northern District of California that claims 12, 4-5, and 9-10 of U.S. Patent 9,580,751 (the "'751 patent") and claims 1-2 and 10-14 of U.S. Patent 9,738,931 (the "'931 patent") are invalid under 35 U.S.C. § 101 as directed to an ineligible natural phenomenon. *Illumina, Inc. v. Ariosa Diagnostics, Inc.*, 356 F. Supp. 3d 925 (N.D. Cal. 2018) ("*Decision*"). Because we conclude that the claims are directed to patent-eligible subject matter, we reverse.

BACKGROUND

"In 1996, Drs. Dennis Lo and James Wainscoat discovered cell-free fetal DNA in maternal plasma and serum, the portion of maternal blood samples that other researchers had previously discarded as medical waste." *Ariosa Diagnostics, Inc. v. Sequenom, Inc.*, 788 F.3d 1371, 1373 (Fed. Cir. 2015). They applied for a patent, and, in 2001, they obtained U.S. Patent 6,258,540, which claimed a method for detecting the small fraction of paternally inherited cell-free fetal DNA in the plasma and serum of a pregnant woman. *Id.* In 2015, we held that the claims of that patent were invalid under 35 U.S.C. § 101 because they were directed to "matter that is naturally occurring"—*i.e.*, the natural phenomenon that cell-free fetal DNA exists in maternal blood. *Id.* at 1376.

The present case involves two patents that are unrelated to the patent held invalid in *Ariosa*, but rather claim priority from a European patent application filed in 2003. The '751 and '931 patents at issue in this case, which are related to each other and have largely identical specifications, begin by acknowledging the natural

phenomenon that was at issue in *Ariosa*: "[I]t has been shown that in the case of a pregnant woman extracellular fetal DNA is present in the maternal circulation and can be detected in maternal plasma … ." '751 patent col. 1 ll. 23-25. The patents then identify a problem that was the subject of further research on cell-free fetal DNA in maternal blood:

> [T]he major proportion (generally >90%) of the extracellular DNA in the maternal circulation is derived from the mother. This vast bulk of maternal circulatory extracellular DNA renders it difficult, if not impossible, to determine fetal genetic alternations [sic] … from the small amount of circulatory extracellular fetal DNA.

Id. col. 1 ll. 42-50. In simple terms, the problem that the inventors encountered was that, although it was known that cell-free fetal DNA existed in the mother's bloodstream, there was no known way to distinguish and separate the tiny amount of fetal DNA from the vast amount of maternal DNA.

The inventors of the '751 and '931 patents attempted to find a solution to that problem. First, they made a discovery:

> An examination of circulatory extracellular fetal DNA and circulatory extracellular maternal DNA in maternal plasma has now shown that, surprisingly, the majority of the circulatory extracellular fetal DNA has a relatively small size of approximately 500 base pairs or less, whereas the majority of circulatory extracellular maternal DNA in maternal plasma has a size greater than approximately 500 base pairs.

Id. col. 1 ll. 54-61. To arrive at that discovery, the inventors examined five pregnancies and found that cell-free fetal DNA fragments "were almost completely of sizes smaller than 500 base pairs." '751 patent col. 4 ll. 50-53. Moreover, the inventors found that 70% of all DNA fragments smaller than 300 base pairs were fetal. *Id.*

Having made that discovery regarding the relative size distributions of cell-free fetal and maternal DNA fragments in a pregnant mother's bloodstream, the inventors used their discovery to develop a solution to the identified problem of distinguishing the fetal DNA from the maternal DNA:

> This surprising finding forms the basis of the present invention according to which separation of circulatory extracellular DNA fragments which are smaller than approximately 500 base pairs provides a possibility to enrich for fetal DNA sequences from the vast bulk of circulatory extracellular maternal DNA.

Id. col. 2 ll. 1-6.

The claims of the '751 and '931 patents are directed to that solution. Specifically, they claim methods of preparing a fraction of cell-free DNA that is enriched in fetal DNA. The methods of preparation include size discrimination of the DNA based on size parameters that the inventors selected to balance the need to remove enough longer maternal DNA fragments to enrich the sample but also leave behind enough shorter fetal DNA fragments to allow for testing. As explained in the patent, "depending on the downstream application" of the enriched mixture, the size parameter is not fixed at either 500 or 300 base pairs but can be even smaller. *See* '751 patent col. 4 ll. 57-59.

Claim 1 of the '751 patent, the only independent claim, includes an inventor-chosen size parameter of 500 base pairs to allow for selective removal of longer DNA fragments from the mixture:

> 1. A method for preparing a deoxyribonucleic acid (DNA) fraction from a pregnant human female useful for analyzing a genetic locus involved in a fetal chromosomal aberration, comprising:
>
> (a) extracting DNA from a substantially cell-free sample of blood plasma or blood serum of a pregnant human female to obtain extracellular circulatory fetal and maternal DNA fragments;
>
> (b) producing a fraction of the DNA extracted in (a) by:
>
> (i) size discrimination of extracellular circulatory DNA fragments, and
>
> (ii) selectively removing the DNA fragments greater than approximately 500 base pairs,
>
> wherein the DNA fraction after (b) comprises a plurality of genetic loci of the extracellular circulatory fetal and maternal DNA; and
>
> (c) analyzing a genetic locus in the fraction of DNA produced in (b).

'751 patent col. 7 l. 54-col. 8 l. 57. In contrast, claim 1 of the '931 patent imposes a different size parameter, namely, 300 base pairs:

1. A method, comprising:

(a) extracting DNA comprising maternal and fetal DNA fragments from a substantially cell-free sample of blood plasma or blood serum of a pregnant human female;

(b) producing a fraction of the DNA extracted in (a) by:

(i) size discrimination of extracellular circulatory fetal and maternal DNA fragments, and

(ii) selectively removing the DNA fragments greater than approximately 300 base pairs,

wherein the DNA fraction after (b) comprises extracellular circulatory fetal and maternal DNA fragments of approximately 300 base pairs and less and a plurality of genetic loci of the extracellular circulatory fetal and maternal DNA fragments; and

(c) analyzing DNA fragments in the fraction of DNA produced in (b).

'931 patent col. 7 l. 58-col. 8 l. 63.

Dependent claims in each patent place further limitations on the size discrimination and selective removal processes recited in step (b) of the method claims. For example, dependent claim 7 of the '751 patent recites that "the size discrimination in (b) comprises centrifugation," and claim 8 further limits it to "density gradient centrifugation." '751 patent col. 9 ll. 1-4. Likewise, dependent claims 4-10 of the '931 patent recite that step (b) can comprise "chromatography," "electrophoresis,"

"centrifugation," and/or "nanotechnological means." '931 patent col. 9 ll. 1-14.

Illumina filed suit against Ariosa Diagnostics, Inc., Roche Sequencing Solutions, Inc., and Roche Molecular Systems, Inc. (collectively, "Roche") alleging infringement of the '751 and '931 patents. Roche moved for summary judgment that the asserted claims are invalid under 35 U.S.C. § 101. The district court granted Roche's motion for summary judgment, holding that the claims of the '751 and '931 patents are directed to ineligible subject matter. *Decision*, 356 F. Supp. 3d at 935. The court entered judgment in favor of Roche, and Illumina appealed. We have jurisdiction under 28 U.S.C. § 1295(a)(1).

DISCUSSION

We review a grant of summary judgment according to the law of the regional circuit. *Kaneka Corp. v. Xiamen Kingdomway Grp. Co.*, 790 F.3d 1298, 1303 (Fed. Cir. 2015) (citing *Halo Elecs., Inc. v. Pulse Elecs., Inc.*, 769 F.3d 1371, 1377 (Fed. Cir. 2014)). In the Ninth Circuit, a grant of summary judgment is reviewed *de novo*. *Leever v. Carson City*, 360 F.3d 1014, 1017 (9th Cir. 2004) (citing *Hargis v. Foster*, 312 F.3d 404, 409 (9th Cir. 2002)). Summary judgment is appropriate when "there is no genuine dispute as to any material fact and the movant is entitled to judgment as a matter of law." Fed. R. Civ. P. 56.

I

Section 101 provides that "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 … ." 35 U.S.C. § 101. Given the expansive terms of

§ 101, "Congress plainly contemplated that the patent laws would be given wide scope"; the legislative history likewise indicated that "Congress intended statutory subject matter to 'include anything under the sun that is made by man.'" *Diamond v. Chakrabarty*, 447 U.S. 303, 308-09 (1980) (internal citation omitted).

The Supreme Court has held that § 101 "contains an important implicit exception. '[L]aws of nature, natural phenomena, and abstract ideas' are not patentable." *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 566 U.S. 66, 70 (2012) (alteration in original) (quoting *Diamond v. Diehr*, 450 U.S. 175, 185 (1981)). These exceptions exist because monopolizing the basic tools of scientific work "might tend to impede innovation more than it would tend to promote it." *Id.* at 71. However, the Supreme Court has advised that these exceptions must be applied cautiously, as "too broad an interpretation of this exclusionary principle could eviscerate patent law." *Id.*

Laws of nature and natural phenomena are not patentable, but applications and uses of such laws and phenomena may be patentable. A claim to otherwise statutory subject matter does not become ineligible by its use of a law of nature or natural phenomenon. *See Diehr*, 450 U.S. at 187; *Parker v. Flook*, 437 U.S. 584, 590 (1978). On the other hand, adding "conventional steps, specified at a high level of generality," to a law of nature or natural phenomenon does not make a claim to the law or phenomenon patentable. *Mayo*, 566 U.S. at 82.

To distinguish claims to patent-eligible applications of laws of nature and natural phenomena from claims that impermissibly tie up such laws and phenomena, we apply the two-part test set forth by the Supreme

Court. First, we examine whether the claims are "directed to" a law of nature or natural phenomenon. *Alice Corp. Pty. Ltd. v. CLS Bank Int'l*, 573 U.S. 208, 217 (2014). If—and only if—they are, then we proceed to the second inquiry, where we examine whether the limitations of the claim apart from the law of nature or natural phenomenon, considered individually and as an ordered combination, "'transform the nature of the claim' into a patent-eligible application." *Id.* (quoting *Mayo*, 566 U.S. at 78).

II

This is not a diagnostic case. And it is not a method of treatment case. It is a method of preparation case.

Under *Mayo*, we have consistently held diagnostic claims unpatentable as directed to ineligible subject matter. *See Athena Diagnostics, Inc. v. Mayo Collaborative Servs., LLC*, 927 F.3d 1333, 1352 (Fed. Cir. 2019) (Moore, J., dissenting from denial of rehearing *en banc*) ("Since *Mayo*, we have held every single diagnostic claim in every case before us ineligible."); *see also, e.g.*, *Athena Diagnostics, Inc. v. Mayo Collaborative Servs., LLC*, 915 F.3d 743 (Fed. Cir. 2019); *Cleveland Clinic Found. v. True Health Diagnostics LLC*, 859 F.3d 1352 (Fed. Cir. 2017); *Cleveland Clinic Found. v. True Health Diagnostics LLC*, 760 F. App'x 1013 (Fed. Cir. 2019). In contrast, we have held that method of treatment claims are patent-eligible. *See Endo Pharm. Inc. v. Teva Pharm. USA, Inc., 919 F.3d 1347 (Fed. Cir. 2019); Natural Alternatives Int'l, Inc. v. Creative Compounds, LLC*, 918 F.3d 1338 (Fed. Cir. 2019); *Vanda Pharm. Inc. v. West-Ward Pharm. Int'l Ltd.*, 887 F.3d. 1117 (Fed. Cir. 2018). The claims in this case do not fall into either bucket, and we consider the claims under the *Alice/Mayo* test.

Here, it is undisputed that the inventors of the '751 and '931 patents discovered a natural phenomenon. But at step one of the *Alice/Mayo* test, "it is not enough to merely identify a patent-ineligible concept underlying the claim; we must determine whether that patent-ineligible concept is what the claim is 'directed to.'" *Rapid Litig. Mgmt. Ltd. v. CellzDirect, Inc.*, 827 F.3d 1042, 1050 (Fed. Cir. 2016). The focus of the dispute in this case is whether the claims of the '751 and '931 patents are "directed to" the natural phenomenon, *i.e.*, whether they claim the discovered natural phenomenon itself versus eligible subject matter that exploits the discovery of the natural phenomenon.

As an initial matter, there are differences between the district court and the parties about how to articulate the natural phenomenon that the inventors discovered. The district court appeared to find that the relevant natural phenomenon is either the "testable quantity" of fetal DNA or "test results" obtained from that fetal DNA. *Decision*, 356 F. Supp. 3d at 933. Roche's articulation of the natural phenomenon was a moving target throughout its briefing and at oral argument, but appears to be the "size distribution" of fetal to maternal cell-free DNA in a mother's blood reflected in Table 1 of the specification, with a particular focus on the number "500 base pairs" as the critical dividing line between the two. *See* Appellee's Br. 14, 18, 21; Oral Arg. 27:58, 28:35, 29:16. And Illumina asserts more simply that the inventors' discovery was that "fetal cell-free DNA tends to be shorter than maternal cell-free DNA." Appellant's Br. 24; *see also id.* at 8 ("[I]n a sample of cell-free DNA from a pregnant woman, the DNA that arises from the fetus is smaller on average than the DNA that arises from the mother.").

We take note of Roche's inability—despite its status as the party challenging the validity of the patents—to clearly identify the natural phenomenon that forms the basis of its challenge. But, ultimately, we find that the parties' respective articulations reflect distinctions without differences. For simplicity, we adopt Illumina's articulation of the natural phenomenon, *i.e.*, that cell-free fetal DNA tends to be shorter than cell-free maternal DNA in a mother's bloodstream. We thus turn to the crucial question on which this case depends: whether the claims are "directed to" that natural phenomenon. We conclude that the claims are *not* directed to that natural phenomenon but rather to a patent-eligible method that utilizes it.

The claims in this case are directed to methods for preparing a fraction of cell-free DNA that is enriched in fetal DNA. The methods include specific process steps—size discriminating and selectively removing DNA fragments that are above a specified size threshold—to increase the relative amount of fetal DNA as compared to maternal DNA in the sample. '751 patent col. 7 ll. 63-67. The size thresholds in the claims—500 base pairs in the '751 patent and 300 base pairs in the '931 patent—are not dictated by any natural phenomenon, particularly because the size distributions of fetal and maternal cell-free DNA overlap each other (*i.e.*, there are maternal DNA fragments shorter than 300 base pairs). The claimed size thresholds are human-engineered parameters that optimize the amount of maternal DNA that is removed from the mixture and the amount of fetal DNA that remains in the mixture in order to create an improved end product that is more useful for genetic testing than the original natural extracted blood sample.

Moreover, the claimed methods achieve more than simply observing that fetal DNA is shorter than maternal DNA or detecting the presence of that phenomenon. The claims include physical process steps that change the composition of the mixture, resulting in a DNA fraction that is different from the naturally occurring fraction in the mother's blood. The dependent claims further illustrate the concrete nature of the claimed process steps. For ex-ample, claims 7-8 of the '751 patent and claims 8-9 of the '931 patent require that the size discrimination step comprise "centrifugation," and specifically "density gradient centrifugation." '751 patent col. 9 ll. 1-4; '931 patent col. 9 ll. 9-12. Other dependent claims in the '931 patent comprise other discrimination and separation means, such as "high performance liquid chromatography" (claims 4-5), "capillary electrophoresis" (claims 6-7), or "nanotechnological means" (claim 10). These dependent claims are supported by the specification's description of the physical means by which the size discrimination and selective removal step of the claims can be achieved:

> The size separation of the extracellular DNA in said serum or plasma sample can be brought about by a variety of methods, including but not limited to: chromatography or electrophoresis such as chromatography on agarose or polyacrylamide gels, ion-pair reversed-phase high performance liquid chromatography [], capillary electrophoresis in a self-coating, low-viscosity polymer matrix [], selective extraction in microfabricated electrophoresis devices [], microchip electrophoresis on reduced viscosity polymer matrices [], adsorptive membrane chromatography [] and the like; density gradient centrifugation []; and methods utilising [sic]

> nanotechnological means such as microfabricated entropic trap arrays [] and the like.

'931 patent col. 2 l. 61-col. 3 l. 18 (citations omitted); *see also id.* col. 4 ll. 15-22 ("3. The gel was electrophoresed at 80 Volt for 1 hour. 4. The Gel [sic] was cut into pieces corresponding to specific DNA sizes … ."). As described by the specification, the inventors used these concrete process steps, not merely to observe the presence of the phenomenon that fetal DNA is shorter than maternal DNA, but rather to exploit that discovery in a method for preparation of a mixture enriched in fetal DNA.

Roche insists that the claims in this case are no more eligible than the claims at issue in *Ariosa*. We disagree. In *Ariosa*, the relevant independent claims were directed to a method "for detecting a paternally inherited nucleic acid" (claims 1 and 24) or a method "for performing a prenatal diagnosis" (claim 25). *See Ariosa*, 788 F.3d at 1373-74. The only operative steps in the claims were "amplifying" (*i.e.*, making more of) the cell-free fetal DNA and then "detecting [it]," "subjecting [it] … to a test," or "performing nucleic acid analysis on [it] to detect [it]." *Id.* We found those claims ineligible because, like the invalid diagnostic claims at issue in *Mayo*, *Athena*, and *Cleveland Clinic*, they were directed to detecting a natural phenomenon after a sample has been prepared or extracted. In essence, the inventors in *Ariosa* discovered that cell-free fetal DNA exists, and then obtained patent claims that covered a method directed to starting with a sample that contains cell-free fetal DNA and seeing that that the cell-free fetal DNA exists.

Here, in contrast, the claims are directed to more than just the correlation between a DNA fragment's

size and its tendency to be either fetal or maternal, a correlation which is not even mentioned in the claims. The claims do not cover a method for detecting whether a cell-free DNA fragment in a previously-prepared sample is fetal or maternal based on the natural size distribution of cell-free DNA fragments; rather, the claimed methods exploit that natural size distribution *during* the sample preparation steps to remove some maternal DNA from the mother's blood. Even the "analyzing" step of the claims is *not* directed to analyzing the discovered natural phenomenon, but to analyzing something else entirely, namely, "fetal chromosomal aberrations." *See* '751 patent col. 7 ll. 55-56, col. 8 ll. 56-57, col. 9 ll. 5-8; '931 patent col. 9 ll. 17-24. Thus, the claims in this case are different from the claims that we held invalid in *Ariosa*.

Roche also argues, based on the Supreme Court's decision in *Association for Molecular Pathology v. Myriad Genetics, Inc.*, that "a naturally occurring DNA segment is a product of nature and not patent eligible merely because it has been isolated." 569 U.S. 576, 580 (2013). But the claims here are not directed to the cell-free fetal DNA itself. The Supreme Court in *Myriad* expressly declined to extend its holding to method claims reciting a process used to isolate DNA. *See id.* at 595-96. The Court stated:

> It is important to note what is *not* implicated by this decision. First, there are no method claims before this Court. Had Myriad created an innovative method of manipulating genes while searching for the BRCA1 and BRCA2 genes, it could possibly have sought a method patent. But the processes used by Myriad to isolate DNA were well understood by geneticists at the time of Myriad's patents, were well

> understood, widely used, and fairly uniform insofar as any scientist engaged in the search for a gene would likely have utilized a similar approach, and are not at issue in this case..

Id. (internal quotation marks omitted). Thus, in *Myriad*, the claims were ineligible because they covered a gene that the inventors isolated but did not invent, rather than an innovative process for isolating a gene.

Here, we encounter the opposite situation, *i.e.*, the claims do not cover separated cell-free fetal DNA itself but rather a process for selective removal of non-fetal DNA to enrich a mixture in fetal DNA. That process includes size parameters that the inventors engineered to balance the practicalities of the specific problem that they were facing, namely, removing enough cell-free maternal DNA to enrich the mixture while leaving enough cell-free fetal DNA to allow for testing. Thus, the Supreme Court's decision in *Myriad* is not on point in this case where the inventors claimed to have conceived and reduced to practice, not the separated DNA, but a method that uses unconventional size parameters to perform the separation.

In our view, *CellzDirect*, while not directly on point, is instructive. In *CellzDirect*, the inventors discovered the natural phenomenon "that some fraction of hepatocytes are capable of surviving multiple freeze-thaw cycles." 827 F.3d at 1045. Having made that discovery, they patented an "improved process of preserving hepatocytes," that comprises freezing hepatocytes, thawing the hepatocytes, removing the non-viable hepatocytes, and refreezing the viable hepatocytes. *Id.* We found that their claimed invention was patent-eligible because it was "not simply an observation or detection of the ability of hepatocytes to survive multi-

ple freeze-thaw cycles. Rather, the claims are directed to a new and useful method of preserving hepatocyte cells." *Id.* at 1048.

The inventors in *CellzDirect* did not invent hepatocytes or impart to hepatocytes an ability to survive cycles of freezing and thawing. *Id.* at 1045. Rather, they discovered that hepatocytes naturally have that ability, and they exploited that phenomenon in a patent-eligible method. So too here, the inventors of the '751 and '931 patents obviously did not invent cell-free fetal DNA or the relative size distribution of fetal and maternal cell-free DNA in maternal blood. And, like in *CellzDirect*, the inventors used their discovery to invent a method of preparing a fraction of DNA that includes physical process steps to selectively remove some maternal DNA in blood to produce a mixture enriched in fetal DNA.

Roche argues that the techniques for size discriminating and selectively removing DNA fragments that are used to practice the invention were well-known and conventional. And we recognize, of course, that the inventors of the '751 and '931 patents did not invent centrifugation, chromatography, electrophoresis, or nanotechnology.[1] But conventional separation technologies can be used in unconventional ways. And Roche, the party challenging the validity of the patents and thus bearing the burden of proof on its § 101 challenge, has presented no evidence that thresholds of 500 base pairs and 300 base pairs were conventional for separating different types of cell-free DNA fragments. Thus, the

[1] We note, without deciding, that Illumina argues that claim 11 of the '931 patent requires the use of microarrays, which it claims was a methodology not previously used with cell-free DNA. Appellant's Br. 40.

claims are directed to a human-engineered method rather than the natural size distributions of cell-free DNA. Moreover, while such conventionality considerations may be relevant to the inquiry under *Alice/Mayo* step two, or to other statutory considerations such as obviousness that are not at issue before us in this case, they do not impact the *Alice/Mayo* step one question whether the claims themselves are directed to a natural phenomenon. Again, *CellzDirect* is instructive, where we acknowledged that the inventors had not invented the well-known processes of "freezing" and "thawing," but only in the context of the *Alice/Mayo* step two inquiry. 827 F.3d at 1050-51.

Rather than focusing on what the inventors of the '751 and '931 patents did not invent, we focus our *Alice/Mayo* step one analysis on what the inventors *did* purport to invent and what they claimed in their patents: methods for preparing a fraction of cell-free DNA by the physical process of size discriminating and selectively removing DNA fragments longer than a specified threshold. Those methods are "directed to" more than merely the natural phenomenon that the inventors discovered. Accordingly, we conclude at step one of the *Alice/Mayo* test that the claims are not directed to a patent-ineligible concept, and we need not reach step two of the test.

III

In *Ariosa*, we recognized that the inventors had made a discovery with implications that would allow what had previously been discarded as medical waste to be used as a tool for determining fetal characteristics. 788 F.3d at 1373. We acknowledged the profound impact that the discovery had on the field of prenatal medicine, including that it "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." *Id.* Nevertheless, under guidance from the Supreme Court, we determined that the discovery of that natural phenomenon, no matter how significant it was to the medical field, was not itself patentable, and neither was a method for detecting it. *Id.* at 1379-80.

The invention in this case is the product of further research on cell-free fetal DNA. This time, the inventors discovered that, not only does the fetal DNA exist in the bloodstream of a pregnant mother, but it has characteristics that make it distinguishable, and therefore separable, from the maternal DNA. Again, regardless how groundbreaking this additional discovery may have been, the inventors were not entitled to patent the natural phenomenon that cell-free fetal DNA tends to be shorter than cell-free maternal DNA. "Groundbreaking, innovative, or even brilliant discovery does not by itself satisfy the § 101 inquiry." *Myriad*, 569 U.S. at 591. Thus, they could not claim a method directed to the natural phenomenon, *e.g.*, a method for determining whether a fragment of cell-free DNA is fetal or maternal based on its length. And they did not attempt to patent such a method.

The inventors here patented methods of preparing a DNA fraction. The claimed methods utilize the natural phenomenon that the inventors discovered by employing physical process steps to selectively remove larger fragments of cell-free DNA and thus enrich a mixture in cell-free fetal DNA. Though we make no comment on whether the claims at issue will pass muster under challenges based on any other portion of the patent statute, under § 101 the claimed methods are patent-eligible subject matter.

CONCLUSION

We conclude that the claims of the '751 and '931 patents are directed to patent-eligible subject matter under 35 U.S.C. § 101. We therefore reverse the district court's grant of summary judgment and remand for further proceedings.

REVERSED AND REMANDED

UNITED STATES COURT OF APPEALS
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2019-1419

ILLUMINA, INC., SEQUENOM, INC.,
Plaintiffs-Appellants,

v.

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ROCHE SEQUENCING SOLUTIONS, INC.,
ROCHE MOLECULAR SYSTEMS, INC.,
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Appeal from the United States District Court
for the Northern District of California in
No. 3:18-cv-02847-SI, Senior Judge Susan Y. Illston.

REYNA, *Circuit Judge*, dissenting.

The claims, written description, and legal precedent converge to a conclusion that the '751 and '931 patents[1] cover patent ineligible subject matter. The asserted claims are directed to a natural phenomenon, the patents' sole claimed advance is the discovery of that natural phenomenon, and the application of the natural phenomenon utilizes routine steps and conventional procedures that are well known in the art.

[1] U.S. Patent Nos. 9,580,751 and 9,738,931. The patents contain nearly identical written descriptions and claims. For economy, this opinion will reference only the '751 patent.

The patents in this appeal proclaim a surprising discovery that has advanced the medical arts in an area of great need. Without doubt, scientists are entitled to great credit and recognition for such a discovery. But, under U.S. patent law, they are not entitled to a patent.

DISCUSSION

I. The Claims are Directed to a Natural Phenomenon

At the time of the invention, skilled artisans knew that cell-free fetal DNA ("cff-DNA") existed, that it could be detected in a sample of a pregnant woman's blood or serum, and that it was useful for reliably analyzing fetal genetic markers (for detecting certain diseases and disorders). '751 patent col. 1 ll. 22-34. But for some genetic markers that are found in the genomes of both the mother and the fetus, skilled artisans faced a problem: the relatively small amount of cff-DNA compared to maternal extracellular DNA in the mother's blood made it difficult to identify and analyze genetic alterations in the fetus. *Id.* at col. 1 ll. 41-50.

The patent maintains that the problem was overcome when the inventors made a "surprising" discovery. *Id.* at col. 1 ll. 54-61. The inventors discovered that cff-DNA tends to be shorter than cell-free maternal DNA in a mother's blood. *See* '751 patent at col. 1 ll. 54-67; *see also* Maj. Op. at 3-4, 8. The written description explains that the majority of cff-DNA in the mother's blood plasma "has a relatively small size of approximately 500 base pairs or less, whereas the majority of circulatory extracellular maternal DNA in maternal plasma has a size greater than approximately 500 base pairs." *Id.* at col. 1 ll. 54-61. The written description states that "[t]his surprising finding *forms the basis* of the present invention." *Id.* at col. 2 ll. 1-2 (emphasis added).

As explained in detail below, it is to this precise surprising discovery of size discrepancy of cff-DNA in a mother's blood—an undisputed natural phenomenon—that the claims at issue are directed. These claims, thus, do not escape *Alice* step one.

A. The Claimed Method Steps Involve a Natural Phenomenon

The first step of the Alice test requires that we determine whether the claims at issue are "directed to" a natural phenomenon. *Alice Corp. Pty. Ltd. v. CLS Bank Intern*, 573 U.S. 208, 217-18 (2014). To make this determination, the Supreme Court has analyzed whether the claims "in-volved" patent-ineligible subject matter. *Id.* at 219; *see also id.* at 218-20 (citing *Gottschalk v. Benson*, 409 U.S. 63, 71-72 (1972), and *Bilski v. Kappos*, 561 U.S. 593, 599 (2010)). In *Alice*, the Court determined that the claims were directed to an abstract idea because the claims "involve" the abstract idea of "intermediated settlement," a concept the Court deemed a "fundamental economic practice." *Alice*, 573 U.S. at 219. Like in *Alice*, the claims here are directed to a natural phenomenon because they involve a fundamental natural phenomenon, that cff-DNA tends to be shorter than cell-free maternal DNA in a mother's blood, to produce a "mixture" of naturally-occurring substances.

For example, the preamble of claim 1 of the '751 patent informs us that the patent claims a method for preparing a DNA "fraction" from a pregnant human female that can be used for diagnostic purposes.[2] The

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[2] Claim 1 recites:

> A method for preparing a deoxyribonucleic acid (DNA) fraction from a pregnant human female useful for analyzing a ge-

remainder of claim 1 recites the method steps for producing the fraction and analyzing it. Each step involves the DNA taken from the blood plasma or serum of a pregnant human female. The DNA itself is not changed or altered.

The first step is achieved by (a) *extracting* DNA from a substantially cell-free sample of blood plasma or blood serum taken from a pregnant female. That sample is then used to (b) produce a "fraction" of the DNA extracted in the first step (a). The fraction is produced via (i) *size discrimination* of the extracellular circulatory DNA fragments, and (ii) *selective removal* of DNA fragments greater than approximately 500 base pairs. Claim 1 states that after the extraction, size discrimination, and selection and removal steps are completed, the fraction comprises "a plurality of genetic loci of the

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netic locus involved in a fetal chromosomal aberration, comprising:

> (a) extracting DNA from a substantially cell-free sample of blood plasma or blood serum of a pregnant human female to obtain extracellular circulatory fetal and maternal DNA fragments;
>
> (b) producing a fraction of the DNA extracted in (a) by:
>
> > (i) size discrimination of extracellular circulatory DNA fragments, and
> >
> > (ii) selectively removing the DNA fragments greater than approximately 500 base pairs, wherein the DNA fraction after (b) comprises a plurality of genetic loci of the extracellular circulatory fetal and maternal DNA; and
>
> (c) analyzing a genetic locus in the fraction of DNA produced in (b).

'751 patent at col. 7 ll. 54-67, col. 8 ll. 53-57; *cf.* '931 patent at col. 7 ll. 58-67, col. 8 ll. 57-63 (claim 1).

extracellular circulator fetal and maternal DNA." '751 patent at col. 8 ll. 53-55. The Majority describes the resulting fraction as "a mixture enriched in fetal DNA." Maj. Op. at 12. But this mixture is made of the same natural substances present in the original sample.

In sum, the claimed method begins with extracting a sample of blood plasma or serum from a pregnant mother that consists wholly of various naturally occurring substances, including cff-DNA. '751 patent at col. 7. ll. 58-61. The claimed method separates those naturally occurring substances by size, leaving a "fraction" of the original sample that is predominantly cff-DNA. *Id.* at col. 7 ll. 63-67, col. 8 ll. 53-55. The claimed method ends with analyzing the components of the "fraction," which contains cff-DNA. *Id.* at col. 8 ll. 56-57. The substances present throughout the process are naturally occurring substances, and the claimed method steps do not alter those substances. Thus, under the Supreme Court's step-one analysis, the claimed method steps "involve" natural phenomenon and are, therefore, directed to a natural phenomenon.[3]

B. The Claimed Advance is a Natural Phenomenon

My conclusion that the method steps are directed to a natural phenomenon is bolstered by our precedent that looks to the "claimed advance" for determining whether a claim is directed to patent ineligible subject matter. *E.g.*, *Athena*, 915 F.3d 743, 750 (Fed. Cir. 2019) (Lourie, J.); *Genetic Techs. Ltd. v. Merial L.L.C.*, 818

[3] The dependent claims add detail such as techniques for conducting each method step and the detection of specific chromosomal aberrations. For example, claim 7 of the '751 patent specifies centrifugation for the size discrimination step and claim 10 specifies for the detection of a fetal chromosomal aberration causing Down Syndrome. '751 patent at col. 9 ll. 1-2, 7-8.

F.3d 1369, 1375 (Fed. Cir. 2016); *Ariosa Diagnostics, Inc. v. Sequenom, Inc.*, 788 F.3d 1371 (Fed. Cir. 2015).

In *Ariosa*, we concluded that the claims were directed to a natural phenomenon relying, in part, on the patent's disclosure that the natural phenomenon was a "surprising and unexpected finding." 788 F.3d at 1376 (citation and quotation omitted). In *Athena*, we concluded that the claimed advance was "only in the discovery of the natural law" by relying, in part, on the patent's disclosure that the inventors "surprisingly found" the natural law. 915 F.3d at 751 (citation and quotation omitted). In *Cleveland Clinic*, we concluded that the claims were directed to a natural law relying, in part, on the patent's disclosure that "the inventions are 'based on the discovery'" of the natural law. 859 F.3d at 1360-61 (citation omitted).

Here, the claimed advance is the inventors' "surprising[]" discovery of a natural phenomenon—that cff-DNA tends to be shorter than cell-free maternal DNA in a mother's bloodstream. *See* '751 patent at col. 1 ll. 54-61. Like in *Ariosa* and *Athena*, the patent's written description identifies only the natural phenomenon as the "surprising finding." *Id.* at col. 1 l. 54-col. 2 l. 6. And the patent explains that the natural phenomenon "forms the basis of the present invention," like the patent in *Cleveland Clinic*. *Id.* at col. 2 ll. 1-6. It is undisputed that the surprising discovery is a natural phenomenon. *See* Maj. Op. at 3-4, 9. The claimed advance is, therefore, the discovery of the natural phenomenon.

The conclusion that the claimed advance is the discovery of a natural phenomenon is supported by the fact that the claimed method steps begin and end with a naturally occurring substance. *See Ariosa*, 788 F.3d at 1376. In *Ariosa*, we found ineligible process claims di-

rected to a method of detecting paternally inherited cff-DNA. *Id.* The claimed method steps began with a naturally occurring blood sample and ended with cff-DNA, itself a naturally occurring substances. *Id.* In this case, as in *Ariosa*, the inventors did not create or alter via the claimed method steps any of the genetic information encoded in the cff-DNA in the claimed method steps. *Id.*

The Majority avoids our claimed advance precedent by reasoning that these claims belong in a distinct category of process claims for "method[s] of preparation." [4] *See* Maj. Op. at 8. But characterizing the claims as a "method of preparation" does not render inapplicable this court's precedent including *Athena*, *Roche Molecular*, *Cleveland Clinic*, *Genetic Techs.*, and *Ariosa.* [5] *Id.* Our precedent does not support such cherry picking. A "method of preparation" is treated no differently than any other process claim under our law. The statute provides that the term "process" in § 101 encompasses all "process, art or method" claims. 35 U.S.C. § 100(b). It makes no distinction based on how the process or method is characterized.

Here, the Majority fails to adequately address the claimed advance inquiry. *E.g.*, Maj. Op. at 8-13. Yet,

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[4] *Cf., Rapid Litig. Mgmt. Ltd. v. CellzDirect, Inc.*, 827 F.3d 1042, 1046 (Fed. Cir. 2016) (reciting in claim 1's preamble "[a] method of producing a desired preparation").

[5] *Athena Diagnostics, Inc. v. Mayo Collaborative Servs., LLC*, 915 F.3d 743 (Fed. Cir. 2019); *Roche Molecular Sys., Inc. v. Cepheid*, 905 F.3d 1363 (Fed. Cir. 2018); *Cleveland Clinic Found. v. True Health Diagnostics LLC*, 859 F.3d 1352 (Fed. Cir. 2017); *Genetic Techs. Ltd. v. Merial L.L.C.*, 818 F.3d 1369 (Fed. Cir. 2016); *Ariosa Diagnostics, Inc. v. Sequenom, Inc.*, 788 F.3d 1371 (Fed. Cir. 2015).

the Majority maintains that the claimed methods are not directed to the natural phenomenon—under the *Alice/Mayo* step-one inquiry—because they "include physical process steps" that "achieve more than simply observing that fetal DNA is shorter than maternal DNA or detecting the presence of that phenomenon." Maj. Op. at 11. The problem with this approach is that it conflates the *Alice/Mayo* step-one analysis with the step-two analysis by focusing on whether and how the claimed "physical process steps" transform the invention into more than an observation of the natural phenomenon. *See Alice*, 573 U.S. 217-18. The Supreme Court describes step two of the analysis as "a search for an 'inventive concept'—i.e., an element or combination of elements that is '*sufficient to ensure that the pa-tent in practice amounts to significantly more than a patent upon the [ineligible concept] itself*.'" *Id.* (emphasis added) (quoting *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, 566 U.S. 66, 72-73 (2012)).

The Majority also suggests that the claimed advance is an improvement in "size discriminat[ion]" and "selective[] remov[al]" techniques. *See* Maj. Op. at 9-11. The Majority reasons that the inventors used "specific process steps" of "size discriminating and selectively removing DNA fragments that are above a specified size threshold" and that these "concrete process steps … exploit [the natural phenomenon] in a method for preparation of a mixture enriched in fetal DNA." *Id.* at 9-10, 12. But whether the claimed method steps are specific and concrete is not the point of analysis for the "directed to" inquiry or for deter-mining the claimed advance at step one. *See Athena*, 915 F.3d at 752 (concluding that the claims' specific and concrete nature "does not disturb our conclusion at step one").

The claimed advance suggested by the Majority, an improvement in the underlying DNA-processing technology, is not supported by the claims or the written description. As discussed below, the written description identifies the claimed method steps as well-known or performed using commercially available tools or kits. *See* '751 patent at col. 2 l. 49-col. 3 l. 18, col. 3 ll. 49-50, col. 3 l. 65-col. 4 l. 13, col. 5 ll. 45-50. Where a written description identifies a technology as well-known or performed using commercially available tools or kits, that technology cannot logically constitute a claimed advance. *Ariosa*, 788 F.3d at 751; *see also Athena*, 915 F.3d at 751 (identifying the claimed "immunological assay techniques [as] known per se in the art" and therefore not the claimed advance); *Cleveland Clinic*, 859 F.3d at 1361 (relying on the patent's disclosure of "commercially available testing kits" for detecting the natural law).

Table 1, below, highlights the commercially available tools and kits that are identified in the written description as used to perform each claimed method step.

Table 1: Performance of Claimed Method Steps

Claimed Method Step	**Commercially Available Tool or Kit**
Claim 1(a), "extracting DNA"	QIAgen Maxi kit ('751 patent col. 3 ll. 49-50)
Claim 1(b)(i), "size discrimination"	Invitrogen 1% agarose gel ('751 patent col. 3 ll. 66-67)
Claim 1(b)(ii), "selectively removing"	New England Biolabs 100 base pair ladder (*id.* at col. 4 ll. 4-5)

	Lamda Hind III digest ('751 patent col. 4 ll. 5-6) QIAEX Gel Extraction kit (*id.* at col. 4 ll. 10-12)
Step (c), "analyzing a genetic locus"	Applied Biosystems (ABI) 7000 Sequence Detection System ('751 patent col. 4 ll. 14-38) TaqMan System and TaqMan Minor Groove Binder (*id.* at col. 4 ll. 19-38)

The Majority turns to attorney argument to save these claims. It reasons that Roche "has presented no evidence that thresholds of 500 base pairs and 300 base pairs were conventional for separating different types of cell-free DNA fragments." Maj. Op. at 15. But whether a claim is directed to patent ineligible subject matter depends on the claims and the written description, and not attorney argument. The absence, or silence, of conventionality of an aspect of an invention in the written description does not render that aspect *un*-conventional. There is nothing in the patent itself to indicate that size selection based on 500 and 300 base pairs was an unconventional human engineered parameter or that this aspect of the invention is the claimed advance. This explains why the Majority's repeated statements concerning human engineered parameters are unsupported by citations to the specification. *See*

Maj. Op. at 10, 14-17. The claimed DNA-processing technologies do not, therefore, constitute the claimed advance. *See Cleveland Clinic*, 859 F.3d at 1361.

The Majority relies on *CellzDirect*. *See* Maj. Op. at 14-15. But *CellzDirect* is distinct from this case. In *CellzDirect*, the inventors created a new and useful cryopreservation technique comprising multiple free-thaw cycles. 827 F.3d at 1048. The claimed invention went beyond applying a known laboratory technique to a newly discovered natural phenomenon and, instead, created an entirely new laboratory technique. *Id.* Unlike in *CellzDirect*, the claimed method steps here are not new, nor are the claimed techniques used in a new or unconventional way. The method steps do not recite or recognize the creation of a new laboratory technique. The Majority recognizes that the inventors "did not invent centrifugation, chromatography, electrophoresis, or nanotechnology"—the claimed techniques described in the written description. Maj. Op. at 15.

The Majority further reasons that the claimed method steps of size discrimination and selective removal "change the composition of the mixture, resulting in a DNA fraction that is different from the naturally-occurring fraction in the mother's blood." *Id.* at 9-10. On this basis, the Majority concludes that the claimed method in the patent "achieves more than simply observing that fetal DNA is shorter than maternal DNA, or detecting the presence of that phenomenon." *Id.*

The Majority's position is declaratory, but not logical. That the claimed process changes the *composition* of a sample of naturally occurring substances, but does not alter the naturally occurring substances themselves, is not sufficient to render the claimed process patent eligible. *See Genetic Techs.*, 818 F.3d at 1374

(holding ineligible the claimed process for using PCR to amplify genomic DNA in a sample before detecting it); *Ariosa*, 788 F.3d at 1373 (holding ineligible the claimed process for using PCR to amplify cff-DNA in a sample before detecting it).

Here, the claimed method steps of size discrimination and selective removal do not alter the naturally occurring substances in the sample of blood plasma or serum from a pregnant mother. Importantly, the majority correctly understands that the patent does not claim the fraction in terms of chemical composition, as a naturally occurring substance that has been chemically altered by the method steps. *Cf. Association for Molecular Pathology v. Myriad Genetics, Inc.*, 569 U.S. 576, 593 (2013) ("Myriad's claims are simply not expressed in terms of chemical composition, nor do they rely in any way on the chemical changes that result from the isolation of a particular section of DNA.").

The Majority also suggests that the claimed methods are not directed to the natural phenomenon because the "correlation" that "a DNA fragment's size and its tendency to be either fetal or maternal" is not recited in the claim. Maj. Op. at 12-13. Neither our precedent nor that of the Supreme Court imposes such a requirement. Requiring a recitation of the natural phenomenon leads to the "drafts-man's art" problem, where a claim drafter has written a claim that is devoted to an ineligible concept, but the drafter managed to avoid reciting the ineligible concept itself. It was this recognition of "the draftsman's art" that motivated the Supreme Court to adopt the step-two, inventive concept inquiry. *Mayo*, 566 U.S. at 72 (citing *Parker v. Flook*, 437 U.S. 584, 593 (1978)); *see also Diamond v. Diehr*, 450 U.S. 175, 188-89 (1981).

The Majority's category-based approach also allows claim draftsmanship to evade § 101's safeguard at the step-one inquiry. In *Myriad*, the Court concluded that the claims at issue were "concerned primarily" with a patent-ineligible product of nature and recognized that "separating [a] gene from its surrounding genetic material is not an act of invention." 569 U.S. at 591. Here, the separation of genetic material from its surroundings is plainly the focus of the claims at issue. Yet, the Majority distinguishes *Myriad* on the sole ground that these claims have been drafted as method claims rather than composition of matter claims. In any event, whether a patent claim recites a process or a composition of matter does not impact the step-one, "directed to" inquiry because this inquiry applies equally to composition of matter and process claims.[6] I see no principled reason why under the facts of this case *Myriad* should or should not apply simply because this case presents a method claim and not a composition of matter claim. Regardless of whether the asserted claims are to a composition of matter or a "method of preparation," the purpose of § 101 remains the same: to safeguard against claims that monopolize a law of nature, natural phenomenon, or abstract idea. *See Alice*, 573 U.S. at 216.

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[6] *E.g.*, *Myriad*, 569 U.S. at 591 (analyzing the "focus" of the relevant composition of matter claims), *Mayo*, 566 U.S. at 72-73 (analyzing the "focus" of the relevant process claims); *Bilski*, 561 U.S. at 609—13 (analyzing whether the process claims involved an abstract idea); *Diehr*, 450 U.S. at 192 (analyzing whether the process claims were "drawn to" a mathematical formula or a patent-eligible process applying that formula); *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127, 132 (1948) (analyzing eligibility of "product claims").

II. The Claims Are Do Not Survive Step Two

Step two of the *Alice* inquiry is a search for other elements that transform ineligible claims into significantly more than a patent upon the natural law or phenomenon. *See Mayo*, 566 U.S. at 72-73. *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 72.

In step two, we ask: "[w]hat else is there in the claims before us?" *Id.* at 78. This question is a lifeline, one that is limited to "additional features" of the claim that transforms the nature of the claim into a patent-eligible application. *Id.* at 77; *Ariosa*, 788 F.3d at 1377.

For method claims that encompass natural phenomena, the method 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."). We must assess whether the additional features are new and useful within the field generally, not in the context of their particular application to the newly discovered phenomenon. *See Roche Molecular*, 905 F.3d at 1372; *see also Athena*, 915 F.3d at 754.

The method steps under review do not transform the nature of the claims into patent-eligible applications. The three claimed method steps of (a) extracting DNA, (b) producing a fraction of DNA by size discrimination, and (c) analyzing a genetic locus are not new, either alone or in combination. As illustrated above in Table 1, the written description indicates that the laboratory techniques of the claimed method are commercially available. And the written description explains that step (b)'s requirement of producing a frac-

tion by size discrimination "can be brought about by a variety of methods." '751 patent at col. 2 ll. 49-51.

Contrary to the majority's belief, that the size discrimination and selective removal method steps were applied for the first time to the newly discovered natural phenomenon does not render those steps transformative, new and useful, under the *Alice/Mayo* step-two inquiry. *See Roche Molecular*, 905 F.3d at 1372; *see also Athena*, 915 F.3d at 754. In *Roche Molecular*, we held that the method claims at issue, which involved PCR amplification of DNA, did not contain an inventive concept even though the inventors were the first to use PCR to detect the claimed natural phenomenon. 905 F.3d at 1372. We reasoned that the claims did not contain an inventive concept because they did not "disclose any 'new and useful' improvement to PCR protocols or DNA amplification techniques in general." *Id. see also Athena*, 915 F.3d at 754 (noting that "to supply an inventive concept, the sequence of claimed steps must do more than adapt a conventional assay to a newly discovered natural law").

Like in *Roche Molecular*, the claimed method steps here do not disclose any new and useful improvement to DNA separation techniques. And they do not disclose an unconventional assay to apply the newly discovered natural phenomenon. As noted above in the step-one discussion, the Majority reasons that Roche has presented "no evidence that thresholds of 500 base pairs and 300 base pairs were conventional for separating different types of cell-free DNA fragments." Maj. Op. at 15. But, like in *Roche*, the addition of these so-called thresholds—which are claimed as approximations conforming to the natural phenomenon—are nothing more than an adaptation of commercially available

DNA separation techniques to the natural phenomenon.

The dependent claims also fail to transform the nature of the claims because they too rely on the same commercially available, routine, and conventional techniques as claim 1, only they provide more specificity on which techniques to use (e.g., '751 patent, claim 7, identifying "density gradient centrifugation" for the size discrimination method).

For example, the written description describes two examples where experiments illustrate the application of the natural phenomenon. '751 patent at col. 3 l. 30-col. 6 l. 46. The results of Example 1, as captured in Table 1, demonstrate that "DNA fragments originating from the fetus were almost completely of sizes smaller than 500 base pairs with around 70% being of fetal origin for sizes smaller than 300 base pairs." *Id.* at col. 4 l. 50-col. 5 l. 7. The results of Example 2 demonstrate that fetal alleles for "D21S11," a genetic marker found in the human chromosome related to Down Syndrome, could be detected in cell-free DNA samples from which fragments greater than 500 base pairs or 300 base pairs had been removed. The patent explains that both experiments were conducted using known laboratory techniques and commercially available testing kits. *E.g.*, *id.* at col. 3 ll. 49-50, col. 3 l. 65-col. 4 l. 13, col. 5 ll. 45-50; *see also id.* at col. 2 l. 61-col. 3 l. 18.

Simply appending routine, conventional steps to a natural phenomenon, specified at a high level of generality, is not enough to supply an inventive concept. Thus, the claims of the patent in this appeal that are directed to patent ineligible subject matter are not transformed into significantly more than a patent upon

the natural law or phenomenon. *See Mayo*, 566 U.S. at 72-73.

III. Preemption

The Supreme Court has made clear that the principle of preemption is the basis for the judicial exceptions to patentability. *Alice*, 573 U.S. at 216-17. 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." 566 U.S. at 86.

Here, the claims are drafted in a manner that tie up future innovations premised upon the natural phenomenon because no skilled artisan would be entitled to rely on the natural phenomenon to isolate cff-DNA. That a skilled artisan could isolate or enrich cff-DNA using some unclaimed technique is not dispositive for preemption. *See Athena Diagnostics, Inc. v. Mayo Collaborative Servs.*, 927 F.3d 1333, 1351 (Fed. Cir. 2019) (Chen, J., concurring in the denial of the petition for rehearing en banc) ("That claims 7 and 9 do not preempt all ways of observing the law of nature isn't decisive, as none of the steps recited therein add anything inventive to the claims."). As in *Athena*, the only claimed advance here is the discovery of the natural phenomenon, and as drafted, these claims significantly preempt use of that natural phenomenon.

CONCLUSION

Much of what we are as humans has its source in our respective DNA, including particular genetic aberrations. The development of medical and scientific procedures to detect and diagnose genetic aberrations, like those involved in the patents in this appeal, count among the great discoveries of modern medicine. Such procedures may qualify for a patent, but DNA itself, or

a segment of DNA that discloses an aberration, like the entirety of the human genome, does not.

I dissent because while I do not doubt that process claims that are directed to natural phenomenon could be patent eligible subject matter, this is not such a case.

APPENDIX B

UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

2019-1419

ILLUMINA, INC., SEQUENOM, INC.,
Plaintiffs-Appellants,

v.

ARIOSA DIAGNOSTICS, INC.,
ROCHE SEQUENCING SOLUTIONS, INC.,
ROCHE MOLECULAR SYSTEMS, INC.,
Defendants-Appellees.

Decided: March 17, 2020

Appeal from the United States District Court
for the Northern District of California in
No. 3:18-cv-02847-SI, Senior Judge Susan Y. Illston.

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* * *

Before LOURIE, MOORE, and REYNA,
Circuit Judges.

Opinion for the court filed by
Circuit Judge LOURIE.

Dissenting opinion filed by *Circuit Judge* REYNA.

LOURIE, *Circuit Judge*.

Illumina, Inc. and Sequenom, Inc. (collectively, "Illumina") appeal from a decision of the United States

District Court for the Northern District of California that claims 12, 4-5, and 9-10 of U.S. Patent 9,580,751 (the "'751 patent") and claims 1-2 and 10-14 of U.S. Patent 9,738,931 (the "'931 patent") are invalid under 35 U.S.C. § 101 as directed to an ineligible natural phenomenon. *Illumina, Inc. v. Ariosa Diagnostics, Inc.*, 356 F. Supp. 3d 925 (N.D. Cal. 2018) ("*Decision*"). Because we conclude that the claims are directed to patent-eligible subject matter, we reverse.

BACKGROUND

"In 1996, Drs. Dennis Lo and James Wainscoat discovered cell-free fetal DNA in maternal plasma and serum, the portion of maternal blood samples that other researchers had previously discarded as medical waste." *Ariosa Diagnostics, Inc. v. Sequenom, Inc.*, 788 F.3d 1371, 1373 (Fed. Cir. 2015). They applied for a patent, and, in 2001, they obtained U.S. Patent 6,258,540, which claimed a method for detecting the small fraction of paternally inherited cell-free fetal DNA in the plasma and serum of a pregnant woman. *Id.* In 2015, we held that the claims of that patent were invalid under 35 U.S.C. § 101 because they were directed to "matter that is naturally occurring"—*i.e.*, the natural phenomenon that cell-free fetal DNA exists in maternal blood. *Id.* at 1376.

The present case involves two patents that are unrelated to the patent held invalid in *Ariosa*, but rather claim priority from a European patent application filed in 2003. The '751 and '931 patents at issue in this case, which are related to each other and have largely identical specifications, begin by acknowledging the natural phenomenon that was at issue in *Ariosa*: "[I]t has been shown that in the case of a pregnant woman extracellular fetal DNA is present in the maternal circulation and

can be detected in maternal plasma . … " '751 patent col. 1 ll. 23-25. The patents then identify a problem that was the subject of further research on cell-free fetal DNA in maternal blood:

> [T]he major proportion (generally >90%) of the extracellular DNA in the maternal circulation is derived from the mother. This vast bulk of maternal circulatory extracellular DNA renders it difficult, if not impossible, to determine fetal genetic alternations [sic] … from the small amount of circulatory extracellular fetal DNA.

Id. col. 1 ll. 42-50. In simple terms, the problem that the inventors encountered was that, although it was known that cell-free fetal DNA existed in the mother's bloodstream, there was no known way to distinguish and separate the tiny amount of fetal DNA from the vast amount of maternal DNA.

The inventors of the '751 and '931 patents attempted to find a solution to that problem. First, they made a discovery:

> An examination of circulatory extracellular fetal DNA and circulatory extracellular maternal DNA in maternal plasma has now shown that, surprisingly, the majority of the circulatory extracellular fetal DNA has a relatively small size of approximately 500 base pairs or less, whereas the majority of circulatory extracellular maternal DNA in maternal plasma has a size greater than approximately 500 base pairs.

Id. col. 1 ll. 54-61. Having made that discovery, they used it to develop a solution to the identified problem of distinguishing fetal DNA from maternal DNA in the mother's bloodstream:

> This surprising finding forms the basis of the present invention according to which separation of circulatory extracellular DNA fragments which are smaller than approximately 500 base pairs provides a possibility to enrich for fetal DNA sequences from the vast bulk of circulatory extracellular maternal DNA.

Id. col. 2 ll. 1-6.

The claims of the '751 and '931 patents are directed to that solution. Specifically, they claim methods of preparing a fraction of cell-free DNA that is enriched in fetal DNA. Claim 1 is the only independent claim in each patent:

> 1. A method for preparing a deoxyribonucleic acid (DNA) fraction from a pregnant human female useful for analyzing a genetic locus involved in a fetal chromosomal aberration, comprising:
>
> (a) extracting DNA from a substantially cell-free sample of blood plasma or blood serum of a pregnant human female to obtain extracellular circulatory fetal and maternal DNA fragments;
>
> (b) producing a fraction of the DNA extracted in (a) by:
>
> (i) size discrimination of extracellular circulatory DNA fragments, and
>
> (ii) selectively removing the DNA fragments greater than approximately 500 base pairs,

wherein the DNA fraction after (b) comprises a plurality of genetic loci of the extracellular circulatory fetal and maternal DNA; and

(c) analyzing a genetic locus in the fraction of DNA produced in (b).

'751 patent col. 7 l. 54-col. 8 l. 57.

1. A method, comprising:

(a) extracting DNA comprising maternal and fetal DNA fragments from a substantially cell-free sample of blood plasma or blood serum of a pregnant human female;

(b) producing a fraction of the DNA extracted in (a) by:

(i) size discrimination of extracellular circulatory fetal and maternal DNA fragments, and

(ii) selectively removing the DNA fragments greater than approximately 300 base pairs,

wherein the DNA fraction after (b) comprises extracellular circulatory fetal and maternal DNA fragments of approximately 300 base pairs and less and a plurality of genetic loci of the extracellular circulatory fetal and maternal DNA fragments; and

(c) analyzing DNA fragments in the fraction of DNA produced in (b).

'931 patent col. 7 l. 58-col. 8 l. 63.

Dependent claims in each patent place further limitations on the size discrimination and selective removal processes recited in step (b) of the method claims. For

example, dependent claim 7 of the '751 patent recites that "the size discrimination in (b) comprises centrifugation," and claim 8 further limits it to "density gradient centrifugation." '751 patent col. 9 ll. 1-4. Likewise, dependent claims 4-10 of the '931 patent recite that step (b) can comprise "chromatography," "electrophoresis," "centrifugation," and/or "nanotechnological means." '931 patent col. 9 ll. 1-14.

Illumina filed suit against Ariosa Diagnostics, Inc., Roche Sequencing Solutions, Inc., and Roche Molecular Systems, Inc. (collectively, "Roche") alleging infringement of the '751 and '931 patents. Roche moved for summary judgment that the asserted claims are invalid under 35 U.S.C. § 101. The district court granted Roche's motion for summary judgment, holding that the claims of the '751 and '931 patents are directed to ineligible subject matter. *Decision*, 356 F. Supp. 3d at 935. The court entered judgment in favor of Roche, and Illumina appealed. We have jurisdiction under 28 U.S.C. § 1295(a)(1).

DISCUSSION

We review a grant of summary judgment according to the law of the regional circuit. *Kaneka Corp. v. Xiamen Kingdomway Grp. Co.*, 790 F.3d 1298, 1303 (Fed. Cir. 2015) (citing *Halo Elecs., Inc. v. Pulse Elecs., Inc.*, 769 F.3d 1371, 1377 (Fed. Cir. 2014)). In the Ninth Circuit, a grant of summary judgment is reviewed *de novo*. *Leever v. Carson City*, 360 F.3d 1014, 1017 (9th Cir. 2004) (citing *Hargis v. Foster*, 312 F.3d 404, 409 (9th Cir. 2002)). Summary judgment is appropriate when "there is no genuine dispute as to any material fact and the movant is entitled to judgment as a matter of law." Fed. R. Civ. P. 56.

I

Section 101 provides that "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 … ." 35 U.S.C. § 101. Given the expansive terms of § 101, "Congress plainly contemplated that the patent laws would be given wide scope"; the legislative history likewise indicated that "Congress intended statutory subject matter to 'include anything under the sun that is made by man.'" *Diamond v. Chakrabarty*, 447 U.S. 303, 308-09 (1980) (internal citation omitted).

The Supreme Court has held that § 101 "contains an important implicit exception. '[L]aws of nature, natural phenomena, and abstract ideas' are not patentable." *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 566 U.S. 66, 70 (2012) (alteration in original) (quoting *Diamond v. Diehr*, 450 U.S. 175, 185 (1981)). These exceptions exist because monopolizing the basic tools of scientific work "might tend to impede innovation more than it would tend to promote it." *Id.* at 71. However, the Supreme Court has advised that these exceptions must be applied cautiously, as "too broad an interpretation of this exclusionary principle could eviscerate patent law." *Id.*

Laws of nature and natural phenomena are not patentable, but applications and uses of such laws and phenomena may be patentable. A claim to otherwise statutory subject matter does not become ineligible by its use of a law of nature or natural phenomenon. *See Diehr*, 450 U.S. at 187; *Parker v. Flook*, 437 U.S. 584, 590 (1978). On the other hand, adding "conventional steps, specified at a high level of generality," to a law of nature or natural phenomenon does not make a claim to

the law or phenomenon patentable. *Mayo*, 566 U.S. at 82.

To distinguish claims to patent-eligible applications of laws of nature and natural phenomena from claims that impermissibly tie up such laws and phenomena, we apply the two-part test set forth by the Supreme Court. First, we examine whether the claims are "directed to" a law of nature or natural phenomenon. *Alice Corp. Pty. Ltd. v. CLS Bank Int'l*, 573 U.S. 208, 217 (2014). If—and only if—they are, then we proceed to the second inquiry, where we examine whether the limitations of the claim apart from the law of nature or natural phenomenon, considered individually and as an ordered combination, "'transform the nature of the claim' into a patent-eligible application." *Id.* (quoting *Mayo*, 566 U.S. at 78).

II

This is not a diagnostic case. And it is not a method of treatment case. It is a method of preparation case.

Under *Mayo*, we have consistently held diagnostic claims unpatentable as directed to ineligible subject matter. *See Athena Diagnostics, Inc. v. Mayo Collaborative Servs., LLC*, 927 F.3d 1333, 1352 (Fed. Cir. 2019) (Moore, J., dissenting from denial of rehearing *en banc*) ("Since *Mayo*, we have held every single diagnostic claim in every case before us ineligible."); *see also, e.g.*, *Athena Diagnostics, Inc. v. Mayo Collaborative Servs., LLC*, 915 F.3d 743 (Fed. Cir. 2019); *Cleveland Clinic Found. v. True Health Diagnostics LLC*, 859 F.3d 1352 (Fed. Cir. 2017); *Cleveland Clinic Found. v. True Health Diagnostics LLC*, 760 F. App'x 1013 (Fed. Cir. 2019). In contrast, we have held that method of treatment claims are patent-eligible. *See Endo Pharm. Inc. v. Teva Pharm. USA, Inc., 919 F.3d 1347 (Fed. Cir.*

2019); Natural Alternatives Int'l, Inc. v. Creative Compounds, LLC, 918 F.3d 1338 (Fed. Cir. 2019); *Vanda Pharm. Inc. v. West-Ward Pharm. Int'l Ltd.*, 887 F.3d. 1117 (Fed. Cir. 2018). The claims in this case do not fall into either bucket, and we consider the claims under the *Alice/Mayo* test.

Here, it is undisputed that the inventors of the '751 and '931 patents discovered a natural phenomenon. But at step one of the *Alice/Mayo* test, "it is not enough to merely identify a patent-ineligible concept underlying the claim; we must determine whether that patent-ineligible concept is what the claim is 'directed to.'" *Rapid Litig. Mgmt. Ltd. v. CellzDirect, Inc.*, 827 F.3d 1042, 1050 (Fed. Cir. 2016). The focus of the dispute in this case is whether the claims of the '751 and '931 patents are "directed to" the natural phenomenon, *i.e.*, whether they claim the discovered natural phenomenon itself versus eligible subject matter that exploits the discovery of the natural phenomenon.

As an initial matter, there are differences between the district court and the parties about how to articulate the natural phenomenon that the inventors discovered. The district court appeared to find that the relevant natural phenomenon is either the "testable quantity" of fetal DNA or "test results" obtained from that fetal DNA. *Decision*, 356 F. Supp. 3d at 933. Roche's articulation of the natural phenomenon was a moving target throughout its briefing and at oral argument, but appears to be the "size distribution" of fetal to maternal cell-free DNA in a mother's blood reflected in Table 1 of the specification, with a particular focus on the number "500 base pairs" as the critical dividing line between the two. *See* Appellee's Br. 14, 18, 21; Oral Arg. 27:58, 28:35, 29:16. And Illumina asserts more simply that the inventors' discovery was that "fetal cell-free

DNA tends to be shorter than maternal cell-free DNA." Appellant's Br. 24; *see also id.* at 8 ("[I]n a sample of cell-free DNA from a pregnant woman, the DNA that arises from the fetus is smaller on average than the DNA that arises from the mother.").

We take note of Roche's inability—despite its status as the party challenging the validity of the patents—to clearly identify the natural phenomenon that forms the basis of its challenge. But, ultimately, we find that the parties' respective articulations reflect distinctions without differences. For simplicity, we adopt Illumina's articulation of the natural phenomenon, *i.e.*, that cell-free fetal DNA tends to be shorter than cell-free maternal DNA in a mother's bloodstream. We thus turn to the crucial question on which this case depends: whether the claims are "directed to" that natural phenomenon. We conclude that the claims are *not* directed to that natural phenomenon but rather to a patent-eligible method that utilizes it.

The claims in this case are directed to methods for preparing a fraction of cell-free DNA that is enriched in fetal DNA. The methods include specific process steps—size discriminating and selectively removing DNA fragments that are above a specified size threshold—to increase the relative amount of fetal DNA as compared to maternal DNA in the sample. '751 patent col. 7 ll. 63-67. Those process steps change the composition of the mixture, resulting in a DNA fraction that is different from the naturally-occurring fraction in the mother's blood. Thus, the process achieves more than simply observing that fetal DNA is shorter than maternal DNA or detecting the presence of that phenomenon.

The dependent claims further illustrate the concrete nature of the claimed process steps. For example, claims 7-8 of the '751 and claims 8-9 of the '931 patent require that the size discrimination step comprise "centrifugation," and specifically "density gradient centrifugation." '751 patent col. 9 ll. 1-4; '931 patent col. 9 ll. 9-12. Other dependent claims in the '931 patent comprise other discrimination and separation means, such as "high performance liquid chromatography" (claims 4-5), "capillary electrophoresis" (claims 6-7), or "nanotechnological means" (claim 10). These dependent claims are supported by the specification's description of the physical means by which the size discrimination and selective removal step of the claims can be achieved:

> The size separation of the extracellular DNA in said serum or plasma sample can be brought about by a variety of methods, including but not limited to: chromatography or electrophoresis such as chromatography on agarose or polyacrylamide gels, ion-pair reversed-phase high performance liquid chromatography [], capillary electrophoresis in a self-coating, low-viscosity polymer matrix [], selective extraction in microfabricated electrophoresis devices [], microchip electrophoresis on reduced viscosity polymer matrices [], adsorptive membrane chromatography [] and the like; density gradient centrifugation []; and methods utilising [sic] nanotechnological means such as microfabricated entropic trap arrays [] and the like.

'931 patent col. 2 l. 61-col. 3 l. 18 (citations omitted); *see also id.* col. 4 ll. 15-22 ("3. The gel was electrophoresed at 80 Volt for 1 hour. 4. The Gel [sic] was cut into pieces corresponding to specific DNA sizes … ."). As described by the specification, the inventors used these

concrete process steps, not merely to observe the presence of the phenomenon that fetal DNA is shorter than maternal DNA, but rather to exploit that discovery in a method for preparation of a mixture enriched in fetal DNA.

Roche insists that the claims in this case are no more eligible than the claims at issue in *Ariosa*. We disagree. In *Ariosa*, the relevant independent claims were directed to a method "for detecting a paternally inherited nucleic acid" (claims 1 and 24) or a method "for performing a prenatal diagnosis" (claim 25). *See Ariosa*, 788 F.3d at 1373-74. The only operative steps in the claims were "amplifying" (i.e., making more of) the cell-free fetal DNA and then "detecting [it]," "subjecting [it] … to a test," or "performing nucleic acid analysis on [it] to detect [it]." *Id.* We found those claims ineligible because, like the invalid diagnostic claims at issue in *Mayo*, *Athena*, and *Cleveland Clinic*, they were directed to detecting a natural phenomenon. In essence, the inventors in *Ariosa* discovered that cell-free fetal DNA exists, and then obtained patent claims that covered only the knowledge that it exists and a method to see that it exists. Here, in contrast, the claims are directed to more than just the correlation between a DNA fragment's size and its tendency to be either fetal or maternal. And the claims do not merely cover a method for detecting whether a cell-free DNA fragment is fetal or maternal based on its size. Rather the claimed method removes some maternal DNA from the mother's blood to prepare a fraction of cell-free DNA that is enriched in fetal DNA. Thus, the claims in this case are different from the claims that we held invalid in *Ariosa*.

Roche also argues, based on the Supreme Court's decision in Association for *Molecular Pathology v.*

Myriad Genetics, Inc., that "a naturally occurring DNA segment is a product of nature and not patent eligible merely because it has been isolated." 569 U.S. 576, 580 (2013). But the claims here are not directed to the cell-free fetal DNA itself. The Supreme Court in *Myriad* expressly declined to extend its holding to method claims reciting a process used to isolate DNA. *See id.* at 595-96. The Court stated:

> It is important to note what is *not* implicated by this decision. First, there are no method claims before this Court. Had Myriad created an innovative method of manipulating genes while searching for the BRCA1 and BRCA2 genes, it could possibly have sought a method patent. But the processes used by Myriad to isolate DNA … are not at issue in this case.

Id. Thus, in *Myriad*, the claims were ineligible because they covered a gene rather than a process for isolating it. Here, we encounter the opposite situation, *i.e.*, the claims do not cover cell-free fetal DNA itself but rather a process for selective removal of non-fetal DNA to enrich a mixture in fetal DNA. Thus, the Supreme Court's decision in *Myriad* is not on point.

In our view, *CellzDirect*, while not directly on point, is instructive. In *CellzDirect*, the inventors discovered the natural phenomenon "that some fraction of hepatocytes are capable of surviving multiple freeze-thaw cycles." 827 F.3d at 1045. Having made that discovery, they patented an "improved process of preserving hepatocytes," that comprises freezing hepatocytes, thawing the hepatocytes, removing the non-viable hepatocytes, and refreezing the viable hepatocytes. *Id.* We found that their claimed invention was patent-eligible because it was "not simply an observation or

detection of the ability of hepatocytes to survive multiple freeze-thaw cycles. Rather, the claims are directed to a new and useful method of preserving hepatocyte cells." *Id.* at 1048.

The inventors in *CellzDirect* did not invent hepatocytes or impart to hepatocytes an ability to survive cycles of freezing and thawing. *Id.* at 1045. Rather, they discovered that hepatocytes naturally have that ability, and they exploited that phenomenon in a patent-eligible method. So too here, the inventors of the '751 and '931 patents obviously did not invent cell-free fetal DNA or the relative size distribution of fetal and maternal cell-free DNA in maternal blood. And, like in *CellzDirect*, the inventors used their discovery to invent a method of preparing a fraction of DNA that includes physical process steps to selectively remove some maternal DNA in blood to produce a mixture enriched in fetal DNA.

Roche argues that the techniques for size discriminating and selectively removing DNA fragments that are used to practice the invention were well-known and conventional. And we recognize, of course, that the inventors of the '751 and '931 patents did not invent centrifugation, chromatography, electrophoresis, or nanotechnology.[1] But while such considerations may be relevant to the inquiry under *Alice/Mayo* step two, or to other statutory considerations such as obviousness that are not at issue before us in this case, they do not impact the *Alice/Mayo* step one question whether the claims themselves are directed to a natural phenome-

[1] We note, without deciding, that Illumina argues that claim 11 of the '931 patent requires the use of micro-arrays, which it claims was a methodology not previously used with cell-free DNA. Appellant's Br. 40.

non. Again, *CellzDirect* is instructive, where we acknowledged that the inventors had not invented the well-known processes of "freezing" and "thawing," but only in the context of the *Alice/Mayo* step two inquiry. 827 F.3d at 1050-51.

Rather than focusing on what the inventors of the '751 and '931 patents did not invent, we focus our *Alice/Mayo* step one analysis on what the inventors *did* purport to invent and what they claimed in their patents: methods for preparing a fraction of cell-free DNA by the physical process of size discriminating and selectively removing DNA fragments longer than a specified threshold. Those methods are "directed to" more than merely the natural phenomenon that the inventors discovered. Accordingly, we conclude at step one of the *Alice/Mayo* test that the claims are not directed to a patent-ineligible concept, and we need not reach step two of the test.

III

In *Ariosa*, we recognized that the inventors had made a discovery with implications that would allow what had previously been discarded as medical waste to be used as a tool for determining fetal characteristics. 788 F.3d at 1373. We acknowledged the profound impact that the discovery had on the field of prenatal medicine, including that it "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." *Id.* Nevertheless, under guidance from the Supreme Court, we determined that the discovery of that natural phenomenon, no matter how significant it was to the medical field, was not itself patentable, and neither was a method for detecting it. *Id.* at 137980.

The invention in this case is the product of further research on cell-free fetal DNA. This time, the inventors discovered that, not only does the fetal DNA exist in the bloodstream of a pregnant mother, but it has characteristics that make it distinguishable, and therefore separable, from the maternal DNA. Again, regardless how groundbreaking this additional discovery may have been, the inventors were not entitled to patent the natural phenomenon that cell-free fetal DNA tends to be shorter than cell-free maternal DNA. "Groundbreaking, innovative, or even brilliant discovery does not by itself satisfy the § 101 inquiry." *Myriad*, 569 U.S. at 591. Thus, they could not claim a method directed to the natural phenomenon, *e.g.*, a method for determining whether a fragment of cell-free DNA is fetal or maternal based on its length. And they did not attempt to patent such a method.

The inventors here patented methods of preparing a DNA fraction. The claimed methods utilize the natural phenomenon that the inventors discovered by employing physical process steps to selectively remove larger fragments of cell-free DNA and thus enrich a mixture in cell-free fetal DNA. Though we make no comment on whether the claims at issue will pass muster under challenges based on any other portion of the patent statute, under § 101 the claimed methods are patent-eligible subject matter.

CONCLUSION

We conclude that the claims of the '751 and '931 patents are directed to patent-eligible subject matter under 35 U.S.C. § 101. We therefore reverse the district court's grant of summary judgment and remand for further proceedings.

REVERSED AND REMANDED

UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

2019-1419

ILLUMINA, INC., SEQUENOM, INC.,
Plaintiffs-Appellants,
v.

ARIOSA DIAGNOSTICS, INC.,
ROCHE SEQUENCING SOLUTIONS, INC.,
ROCHE MOLECULAR SYSTEMS, INC.,
Defendants-Appellees.

Appeal from the United States District Court
for the Northern District of California in
No. 3:18-cv-02847-SI, Senior Judge Susan Y. Illston.

REYNA, *Circuit Judge*, dissenting.

The Majority holds that the asserted patents are directed to patent-eligible subject matter. I respectfully disagree and dissent. I conclude that the claims are directed to a natural phenomenon. The patents' only claimed advance is the discovery of that natural phenomenon. The claims, the written description, and the legal precedent applicable to this case all support the conclusion that the patents are ineligible.

I. The '751 and '931 Patents[1]

At the time of the invention, skilled artisans knew that cell-free fetal DNA ("cff-DNA") existed, that it could be detected in a sample of a pregnant woman's blood or serum, and that it was useful for reliably analyzing fetal genetic markers (for detecting certain diseases and disorders). '751 patent col. 1 ll. 22-34. But for some genetic markers that are found in the genomes of both the mother and the fetus, skilled artisans faced a problem: the relatively small amount of cff-DNA compared to maternal extracellular DNA in the mother's blood made it difficult to identify and analyze genetic alterations in the fetus. *Id.* at col. 1 ll. 4150.

The patent maintains that the problem was overcome when the inventors made a "surprising" discovery. *Id.* at col. 1 ll. 54-61. The inventors discovered a natural phenomenon: that cff-DNA tends to be shorter than cell-free maternal DNA in a mother's blood. *See id.* at col. 1 ll. 5467; *see also* Maj. Op. at 3-4, 8. The written description explains that the majority of cff-DNA in the mother's blood "has a relatively small size of approximately 500 base pairs or less, whereas the majority of circulatory extracellular maternal DNA in maternal plasma has a size greater than approximately 500 base pairs." *Id.* at col. 1 ll. 54-61. The written description states that "[t]his surprising finding *forms the basis* of the present invention." *Id.* at col. 2 ll. 1-2 (emphasis added).

Other than the surprising discovery, nothing else in the specification or the record before us indicates there

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[1] U.S. Patent Nos. 9,580,751 and 9,738,931. The patents contain nearly identical written descriptions and claims. For economy, this opinion will reference only the '751 patent.

was anything new or useful about the claimed invention. In two examples, the patent describes experiments that illustrate the natural phenomenon and a potential application. *Id.* at col. 3 l. 30-col. 6 l. 46. The results of Example 1, as captured in Table 1, demonstrate that "DNA fragments originating from the fetus were almost completely of sizes smaller than 500 base pairs with around 70% being of fetal origin for sizes smaller than 300 bases." *Id.* at col. 4 l. 50-col. 5 l. 7. The results of Example 2 demonstrate that fetal alleles for "D21S11," a genetic marker found in the human chromosome related to Down Syndrome, could be detected in cell-free DNA samples from which fragments greater than 500 base pairs or 300 base pairs had been removed. Both experiments were conducted using known laboratory techniques and commercially available testing kits. *E.g.*, *id.* at col. 3 ll. 49-50, col. 3 l. 65-col. 4 l. 13, col. 5 ll. 45-50; *see also id.* at col. 2 l. 61-col. 3 l. 18.

The claims recite nearly identical method steps. The method steps of the '751 patent separate DNA fragments greater than or equal to 500 base pairs. The method steps of the '931 patent separate DNA fragments greater than or equal to 300 base pairs.

For example, claim 1 of the '751 patent recites the following method:

> 1. A method for preparing a deoxyribonucleic acid (DNA) fraction from a pregnant human female useful for analyzing a genetic locus involved in a fetal chromosomal aberration, comprising:
>
> > (a) extracting DNA from a substantially cell-free sample of blood plasma or blood serum of a pregnant human female to ob-

> tain extracellular circulatory fetal and maternal DNA fragments;
>
> (b) producing a fraction of the DNA extracted in (a) by:
>
> (i) size discrimination of extracellular circulatory DNA fragments, and
>
> (ii) selectively removing the DNA fragments greater than approximately 500 base pairs,
>
> wherein the DNA fraction after (b) comprises a plurality of genetic loci of the extracellular circulatory fetal and maternal DNA; and
>
> (c) analyzing a genetic locus in the fraction of DNA produced in (b).

Id. at col. 7 ll. 54-67, col. 8 ll. 53-57; *cf.*, '931 patent col. 7 ll. 58-67, col. 8 ll. 57-63 (claim 1).

The dependent claims for each patent add detail such as techniques for conducting each method step and the detection of specific chromosomal aberrations. For example, claim 7 of the '751 patent specifies centrifugation for the size discrimination step and claim 10 specifies for the detection of a fetal chromosomal aberration causing Down Syndrome. '751 patent col. 9 ll. 1-2, 7-8.

II. The Claims Are Not Patent Eligible

The Majority sidesteps well-established precedent by reasoning that the claims in this case belong in a unique "bucket" reserved for patents that claim "a method of preparation."[2] *See* Maj. Op. at 8. By placing

[2] *Cf.*, *Rapid Litig. Mgmt. Ltd. v. CellzDirect, Inc.*, 827 F.3d 1042, 1046 (Fed. Cir. 2016) (reciting in claim 1's preamble "[a] method of producing a desired preparation").

this case in that bucket and not in a "diagnostic case" bucket, the Majority summarily dismisses precedent like *Athena*, *Roche Molecular*, *Cleveland Clinic*, *Genetic Techs.*, *Ariosa*,[3] and others. *Id.* Our precedent, however, does not support the Majority's per se grouping of claims. A "method of preparation case" is treated no differently than any other process claim under our law.

35 U.S.C. § 101 grants patent rights to "[w]hoever invents or discovers any new and useful process[4], machine, manufacture, or composition of matter, or any new and useful improvement thereof." *See Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 569 U.S. 576, 589 (2013). Laws of nature, natural phenomena, and abstract ideas, however, are not patent-eligible subject matter. *Id.*

To determine whether a patent claims a patent-eligible application of a natural phenomenon or impermissibly monopolizes a natural phenomenon, we apply the two-step test set forth by the Supreme Court. *Alice Corp. v. CLS Bank Int'l*, 573 U.S. 208, 217-18 (2014). In the first step, we determine whether the claims at issue are "directed to" a patent-ineligible concept. *Id.* If they are, we consider in the second step whether the additional claim elements—both individually and "as an

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[3] *Athena Diagnostics, Inc. v. Mayo Collaborative Servs., LLC*, 915 F.3d 743 (Fed. Cir. 2019); *Roche Molecular Sys., Inc. v. Cepheid*, 905 F.3d 1363 (Fed. Cir. 2018); *Cleveland Clinic Found. v. True Health Diagnostics LLC*, 859 F.3d 1352 (Fed. Cir. 2017); *Genetic Techs. Ltd. v. Merial L.L.C.*, 818 F.3d 1369 (Fed. Cir. 2016); *Ariosa Diagnostics, Inc. v. Sequenom, Inc.*, 788 F.3d 1371 (Fed. Cir. 2015).

[4] The term "process," as recited in § 101, encompasses all "process, art or method" claims. 35 U.S.C. § 100(b).

ordered combination"—"transform the nature of the claim" into a patent-eligible application. *Id.*

A. The Claims are Directed to a Patent-Ineligible Natural Phenomenon

The claims are directed to a natural phenomenon because the patent's claimed advance is the discovery of that natural phenomenon. The Majority disregards well-established precedent for conducting the *Alice*, step one, "directed to" inquiry by failing to consider the patent's claimed advance.

The Supreme Court first articulated the "directed to" inquiry in *Alice*, 573 U.S. at 217-218. To make that determination, the Court analyzed whether the claims "involved" patent-ineligible subject matter (there, an abstract idea). *Id.* at 218-220 (citing *Gottschalk v. Benson*, 409 U.S. 63, 71-72 (1972), *and Bilski v. Kappos*, 561 U.S. 593, 599 (2010)).

In the three years following *Alice*, this court addressed numerous § 101 cases without articulating a more definite "directed to" inquiry. Instead, we performed step one of the patent-eligibility inquiry by comparing the claims at issue to the claims held eligible or ineligible in earlier Supreme Court and Federal Circuit cases. *See, e.g.*, *In re Smith*, 815 F.3d 816, 818 (Fed. Cir. 2016); *buySAFE, Inc. v. Google, Inc.*, 765 F.3d 1350, 1353 (Fed. Cir. 2014).

Since 2016, in a string of cases reciting process claims, we began conducting the "directed to" inquiry by asking whether the "claimed advance" of the patent "improves upon a technological process or [is] merely an ineligible concept." *Athena*, 915 F.3d at 750 (Lourie, J.); *Genetic Techs.*, 818 F.3d at 1375.

To determine a process's "claimed advance," we review the claims and the written description. *Athena*, 915 F.3d at 750. If a written description highlights the discovery of a natural phenomenon—e.g., by describing the natural phenomenon as the only "surprising" or "unexpected" aspect of the invention or that the invention is "based on the discovery" of a natural law—the natural phenomenon likely constitutes the claimed advance. *See Ariosa*, 788 F.3d at 1376; *Athena*, 915 F.3d at 751; *Cleveland Clinic*, 859 F.3d at 1360-61.

In *Ariosa*, we concluded that the claims were directed to a natural phenomenon based in part on the patent's disclosure that the natural phenomenon was a "surprising and unexpected finding." 788 F.3d at 1376 (citation and quotation omitted). In *Athena*, we concluded that the claimed advance was "only in the discovery of a natural law" based in part on the patent's disclosure that the inventors "surprisingly found" the natural law. 915 F.3d at 751 (citation and quotation omitted). In *Cleveland Clinic*, we concluded that the claims were directed to a natural law relying, in part, on the patent's disclosure that "the inventions are 'based on the discovery'" of the natural law. 859 F.3d at 1360-61 (citation omitted).

Here, the claimed advance is the inventors' "surprising[]" discovery of a natural phenomenon—that cff-DNA tends to be shorter than cell-free maternal DNA in a mother's bloodstream. *See* '751 patent col. 1 ll. 54-61. Like in *Ariosa* and *Athena*, the patent's written description identifies the natural phenomenon as the only "surprising finding." *Id.* at col. 1 l. 54-col. 2 l. 6. And the patent explains that the natural phenomenon "forms the basis of the present invention," like the patent in *Cleveland Clinic*. *Id.* at col. 2 ll. 1-6. It is undisputed that the surprising discovery is a natural phe-

nomenon. *See* Maj. Op. at 3-4, 8. The claimed advance is, therefore, the natural phenomenon.

This conclusion is bolstered by the fact that the claimed method steps begin and end with a naturally occurring substance, as in *Ariosa*. 788 F.3d at 1376. In *Ariosa*, we found ineligible process claims directed to a method of detecting paternally inherited cff-DNA. *Id.* The claimed method steps began with a naturally occurring blood sample and ended with cff-DNA, both naturally occurring substances. *Id.* The inventors did not create or alter any of the genetic information encoded in the cff-DNA in the claimed method steps. *Id.*

Likewise, the claimed method here begins and ends with a naturally occurring substance. The claimed method begins with extracting a sample of blood plasma or serum from a pregnant mother that consists wholly of various naturally occurring substances, including cff-DNA. '751 patent col. 7. ll. 58-61. The claimed method separates those naturally occurring substances by size, leaving a "fraction" of the original sample that is predominantly cff-DNA. *Id.* at col. 7 ll. 63-67, col. 8 ll. 53-55. The claimed method ends with analyzing the components of the "fraction," which contains cff-DNA. *Id.* at col. 8 ll. 56-57. The substances present throughout the process are naturally occurring substances, and the claimed method steps do not alter those substances. The claimed method is therefore directed to a natural phenomenon.

The Majority fails to identify the claimed advance

The Majority's step one analysis ignores the claimed advance inquiry altogether. Contrary to the Majority's conclusion, the claims here are not directed to "a patent-eligible method that utilizes [the natural phenomenon]." Maj. Op. at 8-9. Although the Majority

states that the claims "are directed to methods for preparing a fraction of cell-free DNA that is enriched in fetal DNA" (*id.* at 9), the Majority fails to address with specificity the patent's claimed advance.

Instead, the Majority only seems to suggest that the claimed advance is an improvement in "size discriminat[ion]" and "selective[] remov[al]" techniques. *See id.* at 9-10. The Majority reasons that the inventors used "specific process steps" of "size discriminating and selectively removing DNA fragments that are above a specified size threshold" and that these "concrete process steps … exploit [the natural phenomenon] in a method for preparation of a mixture enriched in fetal DNA." *Id.* at 10-11. But whether the steps are concrete is not the appropriate analysis for determining the claimed advance.

Where a written description identifies a technology as well-known or performed using commercially available tools or kits, that technology cannot logically constitute a claimed *advance*. *Ariosa*, 788 F.3d at 751; *see also Athena*, 915 F.3d at 751 (identifying the claimed "immunological assay techniques [as] known per se in the art" and therefore not the claimed advance); *Cleveland Clinic*, 859 F.3d at 1361 (relying on the patent's disclosure of "commercially available testing kits" for detecting the natural law).

Here, the claimed advance is not an improvement in the underlying DNA-processing technology, as hinted by the Majority. The written description identifies the claimed method steps as well-known or performed using commercially available tools or kits. *See* '751 patent col. 2 l. 49-col. 3 l. 18, col. 3 ll. 49-50, col. 3 l. 65-col. 4 l. 13, col. 5 ll. 45-50. For example, the table below highlights the commercially available tools and kits that are

identified in the written description as used to perform each claimed method step.

Performance of Claimed Method Steps

Claimed Method Step	Commercially Available Tool or Kit
Claim 1(a), "extracting DNA"	QIAgen Maxi kit ('751 patent col. 3 ll. 49-50)
Claim 1(b)(i), "size discrimination" Claim 1(b)(ii), "selectively removing"	Invitrogen 1% agarose gel ('751 patent col. 3 ll. 66-67) New England Biolabs 100 base pair ladder (*id.* at col. 4 ll. 4-5) Lamda Hind III digest ('751 patent col. 4 ll. 5-6) QIAEX Gel Extraction kit (*id.* at col. 4 ll. 10-12)
Step (c), "analyzing a genetic locus"	Applied Biosystems (ABI) 7000 Sequence Detection System ('751 patent col. 4 ll. 14-38) TaqMan System and TaqMan Minor Groove Binder (*id.* at col. 4 ll. 19-38)

The selection of 300 and 500 base pairs resulted from using commercially available DNA size-markers. *See id.* at col. 4 ll. 3-9. The claimed DNA-processing technologies do not, therefore, constitute the claimed advance. *See Cleveland Clinic*, 859 F.3d at 1361.

The Majority relies on *CellzDirect*. *See* Maj. Op. at 1213. But *CellzDirect* is different from this case. In *CellzDirect*, the inventors created a new and useful cryopreservation technique comprising multiple freeze-thaw cycles. 827 F.3d at 1048. The claimed invention went beyond applying a known laboratory technique to a newly discovered natural phenomenon and, instead, created an entirely new laboratory technique. *Id.* Unlike *CellzDirect*, the claimed method steps here are not new nor are the claimed techniques used in a new or unconventional way. The Majority recognizes that the inventors "did not invent centrifugation, chromatography, electrophoresis, or nanotechnology"—the claimed techniques described in the written description. Maj. Op. at 13.

The Majority's remaining reasoning fails

The Majority further reasons that the claimed method steps of size discrimination and selective removal "change the composition of the mixture, resulting in a DNA fraction that is different from the naturally-occurring fraction in the mother's blood." *Id.* at 10. On this basis, the Majority concludes that the claimed method in the patent "achieves more than simply observing that fetal DNA is shorter than maternal DNA, or detecting the presence of that phenomenon." *Id.*

The Majority's reasoning is shortsighted. A process that merely changes the *composition* of a sample of naturally occurring substances, without altering the naturally occurring substances themselves, is not pa-

tent eligible. *See Genetic Techs.*, 818 F.3d at 1374 (using PCR to amplify genomic DNA in a sample before detecting it); *Ariosa*, 788 F.3d at 1373 (using PCR to amplify cff-DNA in a sample before detecting it).

Here, the claimed method steps of size discrimination and selective removal do not alter the naturally occurring substances in the sample of blood plasma or serum from a pregnant mother. *Cf.*, *Myriad*, 569 U.S. at 593 ("Myriad's claims are simply not expressed in terms of chemical composition, nor do they rely in any way on the chemical changes that result from the isolation of a particular section of DNA.").

The Majority attempts to distinguish *Myriad*, reasoning that the claims at issue in *Myriad* were not method claims. Maj. Op. at 12 (citing *Myriad*, 569 U.S. at 595). But I see no principled reason why, under the facts of this case, *Myriad* should or should not apply simply because this case presents a method claim and not a composition of matter claim. Whether the asserted claims recite a composition of matter or a "method of preparation," the purpose of § 101 remains the same, to safeguard against claims that monopolize a law of nature, natural phenomenon, or abstract idea. *See Alice*, 573 U.S. at 216 ("We have described the concern that drives this exclusionary principal as one of preemption.").

Because the patent's claimed advance is the discovery of the natural phenomenon, the claims are directed to a natural phenomenon under the step one inquiry.

B. The Claims Fail to Recite an Inventive Concept

Step two of the *Alice* inquiry is a search for other elements that transform the ineligible claims into significantly more than a patent upon the natural law or

phenomenon. *See Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 566 U.S. 66, 72-73. *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 72.

In step two, we ask: "[w]hat else is there in the claims before us?" *Id.* at 78. This question is a lifeline, one that is limited to "additional features" of the claim that transforms the nature of the claim into a patent-eligible application. *Id.* at 77; *Ariosa*, 788 F.3d at 1377.

For method claims that encompass natural phenomena, the method 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."). We must assess whether the additional features are new and useful within the field generally, not in the context of their particular application to the newly discovered phenomenon. *See Roche Molecular*, 905 F.3d at 1372; *see also Athena*, 915 F.3d at 754.

The method steps under review fail to transform the nature of the claims into patent-eligible applications. The three claimed method steps of (a) extracting DNA, (b) producing a fraction of DNA by size discrimination, and (c) analyzing a genetic locus are not new, either alone or in combination. The written description indicates that the laboratory techniques of the claimed method are commercially available techniques. And the written description explains that step (b)'s producing a fraction by size discrimination "can be brought about by a variety of methods." '751 patent col. 2 ll. 49-51.

For step two purposes, that the size discrimination and selective removal method steps were never before

applied to the newly discovered natural phenomenon does not render those steps new and useful. *See Roche Molecular*, 905 F.3d at 1372; *see also Athena*, 915 F.3d at 754. In *Roche Molecular*, we held that the method claims at issue, which involved PCR amplification of DNA, did not contain an inventive concept notwithstanding that the inventors were the first to use PCR to detect the claimed natural phenomenon. *Id.* We reasoned that the claims did not contain an inventive concept because they did not "disclose any 'new and useful' improvement to PCR protocols or DNA amplification techniques in general." *Id.*; *see also Athena*, 915 F.3d at 754 (noting that "to supply an inventive concept the sequence of claimed steps must do more than adapt a conventional assay to a newly discovered natural law").

Like in *Roche Molecular*, the claimed method steps here do not disclose any new and useful improvement to DNA separation techniques. They do not disclose an unconventional assay to the newly discovered natural phenomenon. Instead, they adapt commercially available DNA separation techniques to the natural phenomenon.

The dependent claims also fail to transform the nature of the claims because they too rely on the same commercially available, routine, and conventional techniques as claim 1, only they provide more specificity on which techniques to use (e.g., '751 patent, claim 7, identifies "density gradient centrifugation" for the claimed size discrimination method).

Simply appending routine, conventional steps to a natural phenomenon, specified at a high level of generality, is not enough to supply an inventive concept. Thus, under step two, the claims of the patent in this

appeal that are directed to patent ineligible subject matter are not transformed and made eligible under *Alice* step two.

III. Preemption

The Supreme Court has made clear that the principle of preemption is the basis for the judicial exceptions to patentability. *Alice*, 573 U.S. at 216-217. 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." 566 U.S. at 86.

Here, the claims are drafted in a manner that tie up future innovation premised upon the natural phenomenon because no skilled artisan would be entitled to rely on the natural phenomenon to isolate cff-DNA. That a skilled artisan could isolate or enrich cff-DNA using some unclaimed technique is not dispositive for preemption. *See Athena Diagnostics, Inc. v. Mayo Collaborative Servs.*, 927 F.3d 1333, 1351 (Fed. Cir. 2019) (Chen, J., concurring with denial of the petition for rehearing en banc) ("That claims 7 and 9 do not preempt all ways of observing the law of nature isn't decisive, as none of the steps recited therein add anything inventive to the claims."). Like in *Athena*, the only claimed advance here is the discovery of the natural phenomenon, and as drafted, these claims significantly preempt use of that natural phenomenon.

I do not doubt that process claims that involve naturally occurring phenomena from beginning to end could be directed to patent eligible subject matter, but this is not such a case.

APPENDIX C

UNITED STATES DISTRICT COURT
NORTHERN DISTRICT OF CALIFORNIA

Case No. 18-cv-02847-SI

ILLUMINA, INC., ET AL.,
Plaintiffs,

v.

ARIOSA DIAGNOSTICS, INC., ET AL.,
Defendants.

Filed March 14, 2019
Re: Dkt. No. 48

ORDER GRANTING DEFENDANTS' MOTION FOR SUMMARY JUDGMENT

On May 15, 2018, plaintiffs Illumina, Inc. and Sequenom, Inc. (collectively "plaintiffs") filed this action against Ariosa Diagnostics, Inc. ("Ariosa"), Roche Sequencing Solutions, Inc., and Roche Molecular Systems, Inc., (collectively "Roche"), alleging infringement of U.S. Patent Nos. 9,580,751 ("the '751 patent") and 9,738,931 ("the '931 patent"). Dkt. No. 1. This case was assigned to this Court on June 6, 2018. Dkt. No. 16.

Roche answered the complaint on July 9, 2018 and counterclaimed against plaintiffs, seeking declaratory judgment of noninfringement and invalidity of both asserted patents. Dkt. No. 21. Ariosa responded to the complaint with substantially the same answer and counterclaims on July 9, 2018. Dkt. No. 25. On August

9, 2018, both defendants modified their responses and submitted amended answers and counterclaims against plaintiffs. Dkt. Nos. 40, 41. Plaintiffs answered the amended counterclaims on August 23, 2018. Dkt. Nos. 46, 47.

On August 31, 2018 all defendants moved for summary judgment, seeking a finding that claims 1, 2, 4, 5, and 9-10 of U.S. Patent No. 9,580,751 and claims 1-2 and 10-14 of U.S. Patent No. 9,738,931 are invalid and unenforceable because they are not drawn to patent-eligible subject matter under 35 U.S.C. §101. Dkt No. 48 at 1:10-14. The parties stipulated to an enlargement of time for plaintiffs to respond, which the Court granted. Dkt. Nos. 51-53. Oral argument was held on December 21, 2018.

I. THE '751 PATENT

Illumina is the exclusive licensee of the '751 patent pursuant to an amended 2014 Pooled Patents Agreement between Illumina and Sequenom. Dkt. No. 1 ¶ 7. The '751 patent is titled "Non-Invasive Detection of Fetal Genetic Traits," and was issued to inventors Sinuhe Hahn, Wolfgang Holzgreve, Bernhard Zimmermann, and Ying Lim on February 28, 2017 and assigned to Sequenom, Inc. U.S. Patent No. 9,580,751. The '751 patent relates to prenatal detection methods performed on a maternal serum or plasma sample from a pregnant female, and the claims specifically focus on procedures to separate fetal and maternal DNA in a maternal blood sample. *See id.* at 7:55-9:8. The basis for the patent is the "surprising finding" that "fetal DNA has a relatively small size of approximately 500 base pairs or less" and separating the smaller fragments "provides a possibility to enrich for fetal DNA

sequences from the vast bulk of circulatory extracellular maternal DNA." *Id.* at 1:56-2:6.

According to the patent, "the presence of circulatory extracellular DNA in the peripheral blood is a well established phenomenon" and it has been shown that "fetal DNA is present in the maternal circulation." *Id.* at 1:22-25. However, it can be difficult to examine the fetal DNA because that "major proportion (generally > 90%) of the extracellular DNA in the maternal circulation is derived from the mother." *Id.* at 1:35-44. Separation by size discrimination from maternal DNA "leads to a fraction which is largely constituted by fetal extracellular DNA" that can then be analyzed for various fetal genetic traits. *Id.* at 2:7-20.

The only independent claim of the '751 patent is as follows:

> 1. A method for preparing a deoxyribonucleic acid (DNA) fraction from a pregnant human female useful for analyzing a genetic locus involved in a fetal chromosomal aberration, comprising:
>
> (a) extracting DNA from a substantially cell-free sample of blood plasma or blood serum of a pregnant human female to obtain extracellular circulatory fetal and maternal DNA fragments;
>
> (b) producing a fraction of the DNA extracted in (a) by:
>
> (i) size discrimination of extracellular circulatory DNA fragments, and
>
> (ii) selectively removing the DNA fragments greater than approximately 500 base pairs,

> wherein the DNA fraction after (b) comprises a plurality of genetic loci of the extracellular circulatory fetal and maternal DNA; and
>
> (c) analyzing a genetic locus in the fraction of DNA produced in (b).

Id. at 7:53-8:56.

II. THE '931 PATENT

Illumina is the exclusive licensee of the '931 patent pursuant to an amended 2014 Pooled Patents Agreement between Illumina and Sequenom. Dkt. No. 1 ¶ 7. Like the '951 patent, the '931 patent is entitled "Non-Invasive Detection of Fetal Genetic Traits," and was issued to inventors Sinuhe Hahn, Wolfgang Holzgreve, Bernhard Zimmermann, and Ying Lim on February 28, 2017 and assigned to Sequenom, Inc. U.S. Patent No. 9,738,931. The '931 patent relates to prenatal detection methods performed on a maternal serum or plasma sample from a pregnant female and the claims specifically focus on procedures to separate fetal DNA from a maternal sample through size discrimination methods. *See id.* at 7:55-9:8. The basis for the patent is the "surprising finding" that "fetal DNA has a relatively small size of approximately 300 base pairs or less" and separating the smaller fragments "provides a possibility to enrich for fetal DNA sequences from the vast bulk of circulatory extracellular maternal DNA." *Id.* at 2:14-18.

The '931 patent has substantially the same specification as the '751 patent discussed above.[1] The only

[1] There is an additional paragraph in the specification of the '931 patent that is not in the specification of the '751 patent. This paragraph merely highlights that a Sequence Listing is included in

significant difference is that the patent specifies and claims an invention that separates fetal DNA that is 300 base pairs or smaller, rather than 500 base pairs in the '751 patent. *Id.* at 7:58- 8:61; '751 patent at 7:54-9:8. The only independent claim of the '931 patent is as follows:

> 1. A method, comprising:
>
> (a) extracting DNA comprising maternal and fetal DNA fragments from a substantially cell-free sample of blood plasma or blood serum of a pregnant human female;
>
> (b) producing a fraction of the DNA extracted in (a) by:
>
> (i) size discrimination of extracellular circulatory fetal and maternal DNA fragments, and
>
> (ii) selectively removing the DNA fragments greater than approximately 300 base pairs,
>
> wherein the DNA fraction after (b) comprises extracellular circulatory fetal and maternal DNA fragments of approximately 300 base pairs and less and a plurality of genetic loci of the extracellular circulatory fetal and maternal DNA fragments; and
>
> (c) analyzing DNA fragments in the fraction of DNA produced in (b).

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the specification. *See id.* at 1:25-30. The Sequence Listing is included in both patents.

LEGAL STANDARD

I. SUMMARY JUDGMENT

Summary judgment is proper if the pleadings, the discovery and disclosure materials on file, and any affidavits show that there is no genuine dispute as to any material fact and that the movant is entitled to judgment as a matter of law. *See* Fed. R. Civ. P. 56(a). The moving party bears the initial burden of demonstrating the absence of a genuine issue of material fact. *Celotex Corp. v. Catrett*, 477 U.S. 317, 323 (1986). The moving party, however, has no burden to produce evidence showing the absence of a genuine issue of material fact. *Id.* at 325. Rather, the burden on the moving party may be discharged by pointing out to the district court that there is an absence of evidence to support the nonmoving party's case. *Id.*

Once the moving party has met its burden, the burden shifts to the non-moving party to "designate 'specific facts showing that there is a genuine issue for trial.'" *Id.* at 324 (quoting then Fed. R. Civ. P. 56(e)). To carry this burden, the non-moving party must "do more than simply show that there is some metaphysical doubt as to the material facts." *Matsushita Elec. Indus. Co., Ltd. v. Zenith Radio Corp.*, 475 U.S. 574, 586 (1986). "The mere existence of a scintilla of evidence ... will be insufficient; there must be evidence on which the jury could reasonably find for the [nonmoving party]." *Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 252 (1986).

In deciding a summary judgment motion, the evidence of the non-movant is to be believed, and all justifiable inferences are to be drawn in his favor. *Id.* at 255. "Credibility determinations, the weighing of the

evidence, and the drawing of legitimate inferences from the facts are jury functions, not those of a judge ... ruling on a motion for summary judgment ... ." *Id.* However, conclusory, speculative testimony in affidavits and moving papers is insufficient to raise genuine issues of fact and defeat summary judgment. *Thornhill Publ'g Co., Inc. v. Gen. Tel. & Elec. Corp.*, 594 F.2d 730, 738 (9th Cir. 1979). The evidence the parties present must be admissible. Fed. R. Civ. P. 56(c)(4).

II. SUBJECT MATTER ELIGIBILITY UNDER § 101

Under Section 101 of Title 35 of the United States Code, the scope of patentable subject matter encompasses "any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof." *Bilski v. Kappos*, 561 U.S. 593, 601 (2010) (quoting 35 U.S.C. § 101). Section 101 "contains an important implicit exception: Laws of nature, natural phenomena, and abstract ideas are not patentable." *Alice Corp. Pty. v. CLS Bank Int'l*, 134 S. Ct. 2347, 2354 (2014) (internal quotations omitted). They are not patent-eligible because "they are the basic tools of scientific and technological work," which are "free to all men and reserved exclusively to none." *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 566 U.S. 66, 70 (2012) (internal quotations omitted). The United States Supreme Court has explained that allowing patents for such purported inventions would "tend to impede innovation more than it would tend to promote it," thereby thwarting the primary objective of patent laws. *Id.* at 71.

In *Alice*, the leading case on patent-eligible subject matter under §101, the Supreme Court refined the "framework for distinguishing patents that claim laws of nature, natural phenomena, and abstract ideas from

those that claim patent-eligible applications of those concepts" originally set forth in *Mayo*. *Alice*, 134 S. Ct. at 2355 (citing *Mayo*, 556 U.S. 66). This analysis proceeds in two steps.

> The first step looks to determine whether claims are directed to a patent-ineligible concept. 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.

Ariosa Diagnostics, Inc. v. Sequenom, Inc., 788 F.3d 1371, 1380 (Fed. Cir. 2015) (internal quotations and citations omitted). When additional elements involve only "well-understood, routine, conventional activity previously engaged in by researchers in the field," the additional elements are insufficient to transform a patent-ineligible concept into a patent-eligible application. *Mayo*, 566 U.S. at 73. "Whether something is well-understood, routine, and conventional to a skilled artisan at the time of the patent is a factual determination." *Berkheimer v. HP Inc.*, 881 F.3d 1360, 1369 (Fed. Cir. 2018). However, summary judgment is appropriate for questions of §101 eligibility where no genuine disputes of fact exist. "When there is no genuine issue of material fact regarding whether the claim element or claimed combination is well-understood, routine, conventional to a skilled artisan in the relevant field, this issue can be decided on summary judgment as a matter of law." *Id.* at 1368. "To the extent that the Court must resolve underlying questions of fact related to eligibility, they must be proven by clear and convincing

evidence." *Broadband iTV, Inc. v. Oceanic Time Warner Cable, LLC*, 135 F. Supp. 3d 1175, 1188 (D. Haw. 2015), *aff'd sub nom. Broadband iTV, Inc. v. Hawaiian Telcom, Inc.*, 669 F. App'x 555 (Fed. Cir. 2016).

DISCUSSION

Defendants seek summary judgment on the grounds that both the '931 and '751 patents claim patent-ineligible subject matter. Defendants assert that both patents are directed toward patent-ineligible subject matter and that there are no additional elements that transform the patents' claims into patent-eligible concepts. *See* Dkt. No. 48. Plaintiffs contest defendants' characterization of its patents, arguing the patents cover a laboratory technique for preparing a new and useful composition of cell-free DNA that is enriched for fetal DNA. *See* Dkt. No. 56.

Whether the patents are directed towards ineligible subject matter and whether there is nonetheless an inventive concept that transforms otherwise unpatentable subject matter are discussed in turn below.

I. DIRECTED TOWARDS A PATENT-INELIGIBLE CONCEPT

Defendants argue that the asserted claims are directed to natural phenomena. Dkt. No. 48 at 7. Specifically, defendants argue that "[t]he claimed method begins with a sample of cell-free DNA and ends with an analysis of it," meaning that it is directed to patent-ineligible subject matter. *Id.* at 8:12-18. Defendants compare this case to both *Genetic Techs. Ltd v. Merial LLC*, 818 F.3d 1369 (Fed. Cir. 2016) and *Ariosa v. Sequenom, Inc.*, 788 F.3d 1371, 1376 (Fed. Cir. 2015). In both cases, the Federal Circuit held the claims were directed to detecting the presence of naturally occurring things or phenomena.

Plaintiffs argue the patent claims are directed to a laboratory method for preparing new and useful DNA fractions that do not exist in nature and are thus not a natural phenomenon. Dkt. No. 56. Plaintiffs argue the patents are directed to a process that yields a non-natural composition of cell-free DNA fragments that is enriched for fetal DNA.

The "'directed to' inquiry applies a stage-one filter to claims, considered in light of the specification, based on whether 'their character as a whole is directed to excluded subject matter.'" *Enfish, LLC v. Microsoft Corp.*, 822 F.3d 1327, 1335 (Fed. Cir. 2016) (quoting *Internet Patents Corp. v. Active Network, Inc.*, 790 F.3d 1343, 1346 (Fed. Cir. 2015)) (citing *Genetic Techs.*, 818 F.3d at 1375 (Fed.Cir.2016)). "The courts have recognized that it is not always easy to determine the boundary between abstraction and patent-eligible subject matter." *Internet Patents*, 790 F.3d at 1347 (Fed. Cir. 2015) (citing recent precedent highlighting patents that attempt to preempt use of the laws of nature or abstract ideas when determining the boundary); *See also Parker v. Flook*, 437 U.S. 584, 589 (1978) ("The line between a patentable 'process' and an unpatentable 'principle' is not always clear.").

Regarding patent-ineligible concepts, the Supreme Court has held that there is a "rule against patents on naturally occurring things ..." *Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 569 U.S. 576, 589 (2013). The Supreme Court ruled that "[l]aws of nature, natural phenomena, and abstract ideas are not patentable." *Id.* at 589 (citing *Mayo*, 132 S. Ct. at 1293) (internal quotations omitted).

During prosecution (application no 13/757, 637) Mathias Ehrich, the Senior Vice President of Research

and Development at Sequenom, Inc. filed a declaration in support of the patent. Dkt. No. 48-3 ("Ex. 2") ¶ 2. He stated that "[t]he claimed methods are not directed to a natural phenomenon—a difference in size of the maternal and fetal DNA in maternal blood plasma do not result in a natural phenomenon." He claimed that "the DNA in maternal blood plasma is not the size discriminated fraction produced by the claimed methods" and that "[t]he fetal and maternal DNA found in nature is structurally different and does not exhibit the discussed new utility." *Id.* ¶ 20. After size discrimination, "the ratio" of fetal DNA to maternal DNA "changes and has a new value that does not exist in nature." *Id.*

> The fetal and maternal DNA in maternal blood plasma were subject to size discrimination based on a chosen fragment length (e.g., less than approximately 500 base pairs) to produce a fraction of the maternal and fetal DNA useful for a specific purpose (e.g., detection of a fetal genetic locus that is present in the maternal DNA and that is related to fetal chromosomal aneuploidy). The size distribution of the DNA from maternal blood plasma substantially changed after this size discrimination was performed: certain DNA fragments mostly of maternal origin were preferentially removed and were no longer present in the sample. The difference in structure is directly related to and demonstrated by the new utility for the altered DNA of maternal blood plasma in the claimed methods: detection of certain fetal genetic loci.

Id.

In sum, plaintiffs contend that changing the concentration of fetal DNA relative to maternal DNA in

the sample creates a "difference in structure" which is not naturally occurring.

The PTO originally rejected plaintiffs' applications stating:

> Nothing is added by identifying the techniques to be used in selecting nucleic acids based on size because such techniques were the well understood, routine and conventional techniques that a scientist would have thought of when instructed to enrich fetal DNA from a cell-free sample of maternal blood plasma or serum.

Id. ¶ 21.

Plaintiffs responded that "it was thought the similarity of the fetal and maternal genomes and the complex mixture of fetal and maternal fragments, in terms of fragment sizes and diversity of sequences exhibited for a given fragment size, were insurmountable" in isolating fetal DNA. *Id.* ¶ 21. However, plaintiffs' representations to the patent office conflate the two prongs of the *Alice* test. Changing the ratio of two natural products in a mixture and analyzing one of those products does not impact whether an invention is directed towards a natural phenomenon.

Here, the Court finds that both the '931 and '751 patents are directed towards patent-ineligible concepts, namely naturally occurring phenomena. Both patents claim results from a test of naturally occurring fetal DNA and do not transform the naturally occurring product into something new. Instead the patents lay claim to test results obtained from the use of fetal DNA. This use alone is insufficient to overcome the "directed to" inquiry.

Plaintiffs cite to *Rapid Litig. Mgmt. Ltd. v. CellzDirect, Inc.*, 827 F.3d 1042 (Fed. Cir. 2016) in support of their argument. There, the Federal Circuit found a technique for cryogenically freezing liver cells called hepatocytes was patentable. The Federal Circuit noted that "the claims are simply not directed to the ability of hepatocytes to survive multiple freeze-thaw cycles. Rather, the claims of [the patent] are directed to a new and useful laboratory technique for preserving hepatocytes." *Id.* at 1048. The court found that the inventors "employed their natural discovery to create a new and improved way of preserving hepatocyte cells for later use." *Id.*

In *CellzDirect*, the inventors created a patent to solve a systemic issue with hepatocytes, namely that "certain factors limit their use: fresh hepatocytes can only be obtained from liver resections or non-transplantable livers or organ donors, and their life space is short." *Id.* at 1045. While prior cryopreservation techniques existed before the invention, "the process could damage the hepatocytes, leading to poor recovery numbers of viable cells." *Id.* In addition, "prior methods were unsuitable for preparing a multi-donor hepatocyte pool..[and]…[r]esearchers desired to pool hepatocytes from various source livers to create a hepatocyte preparation approximating average cell livers. Such pools are useful research tools." *Id.* The inventors discovered that some hepatocytes are capable of surviving multiple freeze-thaw cycles. Armed with this discovery, the inventors then developed an improved process of preserving hepatocytes. This process included subjecting previously frozen and thawed cells to density gradient fractionation, recovering the viable cells, and refreezing the viable cells. *Id.* The

claims specified that the resulting preparation could be thawed and used immediately.

In distinguishing *CellzDirect* from prior precedent, the Federal Circuit noted the difference between the claims in *CellzDirect* and the patent ineligible concepts amounting to nothing more than observing or identifying the ineligible concept in *Ariosa* and *In re BRCA1- & BRCA2-Based Hereditary Cancer Test Patent Litig.*, 774 F.3d 755, 761-62 (Fed. Cir. 2014). The court noted, "although the claims in each of these cases employed method steps, the end result of the process, the essence of the whole, was a patent-ineligible concept." *Id.* *CellzDirect*, however, was the result of a new and useful artisan technique. "The inventors certainly discovered the cells' ability to survive multiple freeze thaw cycles, but that is not where they stopped, nor is that what they patented." 827 F.3d at 1048.

The Court finds the facts at hand more analogous to *Ariosa* than to *CellzDirect*. In *CellzDirect*, the end result was cryogenically *frozen* useful liver cells that did not occur in nature. In *Ariosa*, as is the case here, the claims are directed to a testable quantity of genetic information found in nature. Unlike *CellzDirect*, the end result is naturally occurring. Accordingly, the Court finds plaintiffs' arguments unpersuasive and holds that the patents are directed to patent ineligible concepts.

II. INVENTIVE CONCEPT

Defendants argue the asserted claims do nothing more than list a series of conventional steps to detect and analyze DNA fragments. Defendants argue that nothing in the patent specifications or prosecution history identifies novelty or inventiveness beyond the

natural phenomenon itself. Plaintiffs counter that, analyzing the claims as a whole, the inventors present a novel process that exploits the discovery that in a maternal cell free DNA sample from a pregnant woman, the fetal DNA is on average smaller than the maternal DNA. Plaintiffs argue the composition of DNA presents new and useful utility in allowing for improved detection of fetal genetic traits, such as aneuploidy. Plaintiffs also argue the selection of 300 to 500 base pairs is human ingenuity and scientific judgment. In addition, plaintiffs argue that dependent claims include several laboratory steps that do not occur in nature, including PCR and ligase chain reactions for amplification, as well as the use of chromatography and electrophoresis. *See* Dkt. No. 56.

An inventive concept occurs when the claims are "more than a drafting effort designed to monopolize the [abstract idea]" and "claims may be read to 'improve[ ] an existing technological process.'" *Bascom Glob. Internet Servs., Inc. v. AT&T Mobility LLC*, 827 F.3d 1341, 1351 (Fed. Cir. 2016) (quoting *Alice*, 134 S. Ct. at 2356-57). Moreover, "well-understood, routine, conventional activity … is normally not sufficient to transform an unpatentable law of nature into a patent-eligible application of such a law." *Mayo*, S. Ct. at 1291 (citing *Parker*, 437 U.S. at 590).

"To put the matter more succinctly, [where] the claims inform a relevant audience about certain laws of nature; any additional steps consist of well-understood, routine, conventional activity already engaged in by the scientific community; and those steps, when viewed as a whole, add nothing significant beyond the sum of their parts taken separately," then there is no incentive concept. *Mayo*, 566 U.S. at 79-80.

Plaintiffs rely on *CellzDirect* in support of their argument. 827 F.3d 1042 (Fed. Cir. 2016). There, the court explained that the end result of the patent at issue was not simply an observation or detection of the ability of the liver cells to survive multiple freeze-thaw cycles, but rather a new and useful method of preparing the hepatocyte cells. In so holding, the court distinguished the case from *Myriad* noting that whereas "the processes used by Myriad to isolate DNA were well understood[,]" in *CellzDirect* the "claims [were] directed to a new and useful process of creating [a] pool [of the cells], not to the pool itself." *Id.* at 1049. The court also distinguished the patent from those at issue in *Genetic Techs* and *Ariosa*, noting "[a]lthough the claims in each of these cases employed method steps, the end result of the process, the essence of the whole, was a patent-ineligible concept." *CellzDirect*, 827 F.3d at 1048.

This Court finds the facts at hand far closer to those in *Ariosa* and distinguishable from *CellzDirect*. The invention in *CellzDirect* went beyond applying a known laboratory technique to a newly discovered natural phenomenon, and instead created an entirely new laboratory technique that "is not simply an observation or detection" based on the natural phenomenon. *Id.* Here, as in *Ariosa*, the claims extend only to isolation and analysis of a naturally occurring phenomenon and employ routine, well-known laboratory techniques. *See Roche Molecular Sys., Inc. v. CEPHEID*, 905 F.3d 1363, 1373 (Fed. Cir. 2018) (distinguishing the patent at issue by noting that the patent in *CellzDirect* "went beyond applying a known laboratory technique to a newly discovered natural phenomenon, and instead created an entirely new laboratory technique that is not simply an observation or detection based on natural

phenomenon[,]" while "[i]n contrast the [patent at issue] claims a method of detection based on a natural phenomenon and employs only conventional, well-known laboratory techniques.").

The Court finds that the claims of each patent are not inventive. The independent claims require three phases: extraction, size production, and selective removal. Each of the steps is described as well-known and conventional. *See* Dkt. No. 61. Plaintiffs suggest that the novelty of their invention is in the use of routine and conventional steps to isolate and analyze smaller DNA fragments. However, the Court finds that the 'inventive concept' is the application of the well-known routine and conventional techniques for extraction and removal. For example, the patents require "extracting DNA," "producing a fraction of DNA", and discuss "discrimination" and "removal steps." These broad terms are "well-understood, routine, conventional activities previously known to the industry," particularly given that the claims provide them no more explicit definition. *Broadband iTV, Inc.*, 135 F. Supp. 3d at 1188.

Accordingly, the Court finds that plaintiffs' evidence does not raise genuine issues of material fact sufficient to defeat summary judgment. The "novelty" of an idea is not enough in itself to confer patentability, where the novelty does not exceed the "inventive concept" limitations. *See, e.g., Diamond v. Diehr*, 450 U.S. 175, 188-89 (1981) ("The 'novelty' of any element or steps in a process, or even of the process itself, is of no relevance in determining whether the subject matter of a claim falls within the § 101 categories of possibly patentable subject matter.").

In addition, the Court finds that the dependent claim limitations do not add enough to render the patents eligible. The claimed combination of elements lacks an inventive concept because the combination was well-understood, routine and conventional at the time of invention. *Exergen Corp. v. Kaz USA, Inc.*, 725 F. App'x 959, 974 (Fed. Cir. 2018). Accordingly, the Court GRANTS defendants' motion for summary judgment.

CONCLUSION

For the foregoing reasons and for good cause shown, the Court hereby GRANTS defendants' motion for summary judgment. The parties are directed to file a joint statement identifying the issues which remain to be decided in this case and proposing a schedule for same. ***Such joint statement must be filed no later than January 9, 2019***.

IT IS SO ORDERED.

Dated: December 24, 2018

signature

SUSAN ILLSTON
United States District Judge

APPENDIX D

NOTE: This order is nonprecedential.

UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

2019-1419

ILLUMINA, INC., SEQUENOM, INC.,
Plaintiffs-Appellants,
v.

ARIOSA DIAGNOSTICS, INC.,
ROCHE SEQUENCING SOLUTIONS, INC.,
ROCHE MOLECULAR SYSTEMS, INC.,
Defendants-Appellees.

Appeal from the United States District Court
for the Northern District of California in
No. 3:18-cv-02847-SI, Senior Judge Susan Y. Illston.

ON PETITION FOR PANEL REHEARING

Before LOURIE, MOORE, and REYNA,
Circuit Judges.

PER CURIAM.

ORDER

Appellees Ariosa Diagnostics, Inc., Roche Molecular Systems, Inc. and Roche Sequencing Solutions, Inc. filed a combined petition for panel rehearing and rehearing en banc.

Upon consideration thereof,

IT IS ORDERED THAT:

The petition for panel rehearing is granted to the extent that the previous precedential opinion and judgment issued March 17, 2020, are withdrawn and replaced with the modified precedential opinion and judgment accompanying this order.

FOR THE COURT

August 3, 2020
Date

/s/ Peter R. Marksteiner
Peter R. Marksteiner
Clerk of Court

APPENDIX E

NOTE: This order is nonprecedential.

UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

2019-1419

ILLUMINA, INC., SEQUENOM, INC.,
Plaintiffs-Appellants,
v.

ARIOSA DIAGNOSTICS, INC.,
ROCHE SEQUENCING SOLUTIONS, INC.,
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for the Northern District of California in
No. 3:18-cv-02847-SI, Senior Judge Susan Y. Illston.

ON PETITION FOR REHEARING EN BANC

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

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[*] Circuit Judge Stoll did not participate.

PER CURIAM.

O R D E R

Appellees Ariosa Diagnostics, Inc., Roche Sequencing Solutions, Inc., and Roche Molecular Systems, Inc. filed a combined petition for panel rehearing and rehearing en banc. A response to the petition was invited by the court and filed by appellants Illumina, Inc. and Sequenom, Inc. The petition for rehearing and response were first referred to the panel that heard the appeal, which granted the petition in part as indicated in the accompanying order. Thereafter, the petition was referred to the circuit judges who are in regular active service.

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 September 9, 2020.

FOR THE COURT

August 3, 2020
Date

/s/ Peter R. Marksteiner
Peter R. Marksteiner
Clerk of Court