No. 20-

IN THE

Supreme Court of the United States

ARIOSA DIAGNOSTICS, INC., ROCHE SEQUENCING SOLUTIONS, INC., ROCHE MOLECULAR SYSTEMS, INC.,
Petitioners,

v.

ILLUMINA, INC., SEQUENOM, INC.,
Respondents.

ON PETITION FOR A WRIT OF CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

PETITION FOR A WRIT OF CERTIORARI

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QUESTION PRESENTED

Section 101 of Title 35 provides that a patent may be obtained for "any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof." This Court has "long held," however, that Section 101 "'contains an important implicit exception: Laws of nature, natural phenomena, and abstract ideas are not patentable.'" *Association for Molecular Pathology* v. *Myriad Genetics, Inc.*, 569 U.S. 576, 589 (2013) (brackets omitted). The *Myriad* Court applied this rule in holding that "a naturally occurring DNA segment is a product of nature and not patent eligible merely because it has been isolated," and further explained that "separating [a] gene from its surrounding genetic material is not an act of invention." *Id.* at 580, 591.

The question presented is:

Whether a patent that claims nothing more than a method for separating smaller DNA fragments from larger ones, and analyzing the separated DNA for diagnostic purposes, using well-known laboratory techniques is unpatentable under Section 101 and *Myriad*.

CORPORATE DISCLOSURE STATEMENT

Roche Holdings, Inc., Roche Holding Ltd., and Novartis AG directly or indirectly own 10% or more of the stock of Petitioners Roche Molecular Systems, Inc. and Roche Sequencing Solutions, Inc.

Roche Molecular Systems, Inc., Roche Holdings, Inc., Roche Holding Ltd., and Novartis AG directly or indirectly own 10% or more of the stock of Petitioner Ariosa Diagnostics, Inc.

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INTRODUCTION

Seven years ago, this Court held that isolated DNA is not patent eligible under 35 U.S.C. § 101. *Association for Molecular Pathology* v. *Myriad Genetics, Inc.*, 569 U.S. 576, 580 (2013). The *Myriad* Court explained that "a naturally occurring DNA segment is a product of nature and not patent eligible merely because it has been isolated." *Id.* at 580. This principle cannot be evaded by claiming routine and conventional methods to isolate a given DNA segment. As the *Myriad* Court explained, "separating [a] gene from its surrounding genetic material is *not an act of invention*." *Id.* at 591 (emphasis added).

Despite this Court's guidance, a divided panel of the Federal Circuit upheld the patentability of claims for prenatal genetic testing that separate human DNA based on size and, in particular, the patentees' purported finding that a pregnant woman's DNA is typically larger than the fetal DNA circulating in her bloodstream. In so ruling, the Federal Circuit held that separating larger naturally occurring human DNA from smaller naturally occurring human DNA is patentable under Section 101, irrespective of whether the techniques for performing the separation are known and conventional. This holding cannot be reconciled with *Myriad*'s pronouncement that separating DNA "is not an act of invention."

While a method involving *unconventional* steps for separating DNA might plausibly survive Section 101 review, no such method is at issue here. More importantly, the Federal Circuit did not even consider the question. By concluding that the patent at issue was not even "directed to" unpatentable subject matter, the panel majority necessarily held that separation *alone* is

enough to survive Section 101. *See Alice Corp. Pty. Ltd.* v. *CLS Bank Int'l*, 573 U.S. 208, 217-218 (2014) (under Section 101, a court need only consider whether a patent includes an inventive concept if it holds that the asserted claim is directed to unpatentable subject matter).

The Federal Circuit's attempts to distinguish *Myriad* only reinforce the need for this Court's review. The Federal Circuit characterized *Myriad* as applying only to composition claims (*e.g.*, claims to DNA itself), and not the method claims at issue here. But by that logic, the company that was unable to patent isolated breast cancer genes in *Myriad* could have accomplished essentially the same result by patenting conventional acts of isolating those genes. This Court's review is urgently needed to ensure that its holding in *Myriad* that human DNA is not patentable cannot be so easily evaded.

The Federal Circuit next attempted to distinguish *Myriad* by noting that the claims here specify precisely how large the separated DNA fragments must be. But the patents themselves indicate that those size thresholds were generally dictated by fetal and maternal DNA's natural size distributions, which the patentees purported to have discovered in nature. Indeed, the patents claim the very method the patentees used to study and characterize the size distribution of naturally occurring DNA fragments, thereby preventing others from using that method to analyze the natural phenomenon they allegedly discovered. To make matters worse, the specific size thresholds listed in the patents are a product of the off-the-shelf laboratory kits and conventional techniques that the patentees used to separate the DNA, not a product of the patentees' ingenuity.

The Federal Circuit's treatment of *Myriad* creates an end run around this Court's decision, threatening to revive the effective patenting of human DNA without any inquiry into whether the techniques used to separate the DNA were inventive. The implications of such a decision are clear and extend far beyond this case. For the same reasons this Court granted certiorari in *Myriad*, it should do so here and ensure that the mere act of separating human DNA cannot be patented.

Although the Federal Circuit's evasion of *Myriad* alone justifies review, the Federal Circuit's decision also creates significant confusion about when diagnostic claims are patentable. Indeed, it is impossible to square the Federal Circuit's decision here that claims directed to the *separation* of fetal DNA in a maternal blood sample for diagnostic purposes are patentable with its holding in *Ariosa Diagnostics, Inc.* v. *Sequenom, Inc.*, 788 F.3d 1371 (Fed. Cir. 2015), that claims directed to the *amplification* (*i.e.*, selective replication) of fetal DNA in a maternal blood sample for diagnostic purposes are *unpatentable* under Section 101. *Compare* App. 5a-6a, 11a-14a (majority op.), *and* App. 23a-26a (Reyna, J., dissenting), *with* 788 F.3d at 1373-1376.

Similar to its treatment of *Myriad*, the panel majority tried to dodge *Ariosa* by characterizing it as applying only to diagnostic claims, and by classifying the claims at issue here as a "method of preparing" a DNA sample. This is a distinction without difference. The claims here culminate in "analyzing" the human DNA that has been separated, and Respondents have asserted infringement by Petitioners' diagnostic tests. These patents are thus diagnostic method patents, notwithstanding their recitation of "preparation" steps, and should not have been treated differently under Section

101. In fact, diagnostic claims in which DNA is analyzed typically include a step in which the DNA sample is "prepared" as a precursor to analysis, and yet have been declared ineligible for patent protection. In any event, this Court has never endorsed a patent-eligibility test that turns solely on the *label* of the claim at issue as a diagnostic or method of preparation claim, and for good reason—such a test would be easy to manipulate and elevate form over substance.

The decision below thus raises issues of national importance. It creates a back door to the effective patenting of human DNA, presenting serious ethical and scientific issues. It truncates the two-step analysis this Court adopted to prevent inventions directed to natural phenomena and other unpatentable subject matter from being withdrawn from the public domain unless they use unconventional steps that transform the nature of the claim. It creates a roadmap for patent drafters to evade *Myriad* and *Ariosa* by drafting isolated DNA claims as methods for isolating DNA, and by drafting diagnostic claims as "method of preparation" claims. And it exacerbates the continuing confusion regarding the scope and proper application of Section 101 to DNA-based diagnostic patents.

The petition for certiorari should be granted.

OPINIONS BELOW

The modified opinion of the Federal Circuit (App. 1a-37a) is reported at 967 F.3d 1319, and the court's original opinion (App. 39a-69a) is reported at 952 F.3d 1367. The Federal Circuit's orders granting panel rehearing and denying rehearing en banc (App. 89a-92a) are reported at 814 F. App'x 601. Finally, the district court's order granting Petitioners' motion for summary

judgment (App. 71a-88a) is reported at 356 F. Supp. 3d 925.

JURISDICTION

The Federal Circuit entered judgment at the time it issued its modified opinion on August 3, 2020. The court denied Petitioners' timely petition for rehearing en banc on that same date. On March 19, 2020, by general order, this Court extended the time to file this petition to December 31, 2020. The Court has jurisdiction under 28 U.S.C. § 1254(1).

STATUTORY PROVISION INVOLVED

Section 101 of Title 35 of the U.S. Code provides: "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title."

STATEMENT

A. Section 101 Prohibits Patenting Natural Phenomena

For nearly 170 years, this Court has held that "[l]aws of nature, natural phenomena, and abstract ideas are not patentable." *Alice Corp. Pty. Ltd.* v. *CLS Bank Int'l*, 573 U.S. 208, 216 (2014); *see also Le Roy* v. *Tatham*, 55 U.S. (14 How.) 156, 174-175 (1853). These categories of subject matter comprise "the basic tools of scientific and technological work," *Association for Molecular Pathology* v. *Myriad Genetics, Inc.*, 569 U.S. 576, 589 (2013) (internal quotation marks omitted), and "monopolization of those tools through the grant of a patent might tend to impede innovation more than it

would tend to promote it," *Mayo Collaborative Servs.* v. *Prometheus Labs., Inc.*, 566 U.S. 66, 71 (2012).

Under *Alice* and *Mayo*, the patent-eligibility inquiry for a claimed method boils down to a two-step test. At step one, the test asks: Is the patent claim "directed to" unpatentable subject matter, such as a natural phenomenon? *Alice*, 573 U.S. at 217. If so, at step two, the test asks: Does the patent claim include an inventive concept that transforms the claim into a patent-eligible invention? *Id.* at 217-218, 221.

B. Scientists Have Long Relied On DNA Analysis To Screen For Genetic Traits And Disorders

The unique sequence of nucleotides in a gene encodes the instructional information governing cellular function. *Myriad*, 569 U.S. at 580-582. In some instances, alterations in the DNA sequence for a given gene—or extra or missing copies of chromosomes—are linked to certain traits or genetic disorders. Researchers have thus long used DNA analysis to detect or at least predict these traits and disorders, including for prenatal diagnostic purposes. C.A.J.A. 313-314; C.A.J.A. 31 (1:26-34).

It has also been known for nearly a quarter of a century that a pregnant woman's bloodstream contains not only her own DNA, but also small quantities of cell-free DNA—*i.e.*, DNA that circulates freely in the maternal blood—from her unborn child. App. 2a; C.A.J.A. 31 (1:21-25). By analyzing this cell-free fetal DNA in a pregnant woman's blood or plasma, researchers can determine fetal genetic traits without having to take samples from the fetus or placenta.

In 2014, Respondents acquired a patent covering a method for detecting such DNA. Not long after, the

Federal Circuit held that patent unpatentable under Section 101 as directed to a natural phenomenon—*i.e.*, naturally occurring cell-free fetal DNA, which "existed in nature" long before the inventors "found" it. *See Ariosa Diagnostics, Inc.* v. *Sequenom, Inc.*, 788 F.3d 1371, 1376 (Fed. Cir. 2015). This Court later denied certiorari. *See* 136 S. Ct. 2511 (2016).

C. The Prenatal Diagnostics Patents At Issue

The two patents at issue here—U.S. Patent Nos. 9,580,751 ("'751 patent") and 9,738,931 ("'931 patent")[1]—involve similar prenatal diagnostic technology to that at issue in *Ariosa*.

According to the patents, by performing an "examination" of maternal plasma, the inventors purportedly "found" that most fetal DNA is "relatively small" ("approximately 500 base pairs or less") while most maternal DNA is larger ("greater than approximately 500 base pairs"). C.A.J.A. 31 (1:54-67).[2] In particular, the patents state that the inventors found that fetal DNA fragments are "almost completely of sizes smaller than 500 base pairs with around 70% being … smaller than 300 bases." C.A.J.A. 32 (4:50-53).

In making that purported finding, the inventors used conventional methods to remove DNA fragments

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[1] The patents' disclosures are nearly identical. App. 2a (noting that the patents "are related to each other and have largely identical specifications"); *see also* App. 20a n.1 (Reyna, J., dissenting) ("The patents contain nearly identical written descriptions and claims."). For ease of reference, this petition cites only the '751 patent's disclosure unless otherwise noted.

[2] A base pair is a unit of DNA consisting of two nucleobases bound to each other by hydrogen bonds. *See Myriad*, 569 U.S. at 580-581.

larger than approximately 500 base pairs from a maternal blood sample, leaving behind for analysis a sample that "is largely constituted by fetal extracellular DNA." C.A.J.A. 31 (2:1-10). This is the patents' purported invention: analyzing size-separated DNA based on the purported discovery that the DNA's natural characteristics permit such separation. *See* App. 4a.

Claim 1 of the '751 patent is representative and recites a method for analyzing size-separated DNA by "selectively removing the DNA fragments greater than approximately 500 base pairs" from a maternal blood sample, and then "analyzing a genetic locus in the fraction of DNA produced" by such separation. C.A.J.A. 34 (7:54-8:57). Claim 1 of the '931 patent recites a nearly identical method except that it separates DNA fragments based on a 300 base pair cutoff. C.A.J.A. 42 (7:58-8:63). All claims of both patents require that the separated DNA be analyzed, and some claims require analysis for the purpose of detecting a "fetal chromosomal aberration," like aneuploidy or Down's Syndrome. *See* C.A.J.A. 34 (7:54-8:57); C.A.J.A. 35 (9:5-8); C.A.J.A. 42 (8:62-63); C.A.J.A. 43 (9:17-24).

The patents' specifications state that the claimed method was performed using "known methods" and laboratory techniques, as well as commercially available, off-the-shelf kits. C.AJ.A. 31 (2:46-48); C.AJ.A. 32 (3:49-50); C.AJ.A. 33 (5:28-39).

D. Proceedings Below

In 2018, Respondents sued Petitioners for infringement of the patents. The district court granted summary judgment in favor of Petitioners under Section 101.

At step one of the *Alice* test, the district court held that the claims were directed to a natural phenomenon, noting that this conclusion was not altered by the fact that the patents "chang[ed] the ratio of two natural products [*i.e.*, fetal and maternal DNA] in a mixture and analyz[ed] one of those products [*i.e.*, the separated fetal DNA]." App. 79a-84a. At *Alice* step two, the court found that each of the claimed steps is described by the patents as "well-known and conventional." App. 84a-88a. Indeed, the district court noted that the claims at issue were difficult to distinguish from those found unpatentable in *Ariosa*. *See*, *e.g.*, App. 86a ("Here, as in *Ariosa*, the claims extend only to isolation and analysis of a naturally occurring phenomenon and employ routine, well-known laboratory techniques.").

On appeal, a divided panel of the Federal Circuit reversed, holding that the claims survived Section 101 review because they are not directed to a natural law or natural phenomenon. The majority distinguished this Court's ruling in *Myriad* on the ground that the claims there recited *compositions* of isolated DNA, whereas the claims here recite *methods* for isolating DNA. App. 51a.[3] Further, while the panel majority acknowledged that the inventors "discovered" the natural phenomenon that cell-free fetal DNA tends to be smaller than cell-free maternal DNA, the majority nonetheless characterized the claims as "methods of preparing" a DNA sample, which the majority found distinguishable from the diagnostic claims at issue in *Ariosa*. App. 47a, 53a-54a.

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[3] Petitioners cite directly to the panel's original opinion only in summarizing its contents. All other citations are to the opinion as modified on rehearing.

Having found the claims patent eligible at step one, the panel majority did not rule on whether the claimed method includes an inventive concept at step two of the *Alice* test. It thus held that the claims are patent eligible without any inquiry into whether they use unconventional steps that might transform the claims into an inventive application of a natural phenomenon.

Judge Reyna dissented. He disagreed with the majority's attempt to side-step *Myriad*, noting that there is "no principled reason why, under the facts of this case, *Myriad* … should not apply simply because this case presents a method claim and not a composition of matter claim." App. 66a. He explained, moreover, that the majority's characterization of the claims as "'method of preparation' claims" does not render inapplicable *Ariosa*, as a "'method of preparation case' is treated no differently than any other process claim under" the law. App. 59a. Finally, Judge Reyna agreed with the district court that the claims merely recite conventional, well-known laboratory techniques. App. 66a-69a.

In response to Petitioners' petition for rehearing, the panel issued a modified opinion that is nearly identical to its original opinion except that it describes the asserted claims' 300 and 500 base pair thresholds as "human-engineered parameters" and suggests that they show the patents-in-suit are not directed to natural phenomena. App. 11a. Judge Reyna again dissented, noting that "[t]here is nothing in the patent[s] [themselves] 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." App. 29a.

REASONS FOR GRANTING THE PETITION

The Federal Circuit's decision holds that the mere separation of smaller human DNA fragments from larger ones is sufficient to survive a Section 101 challenge, without regard to the inventiveness of techniques used to achieve that separation. That decision should not be permitted to stand. It cannot be reconciled with *Myriad* or prior decisions involving diagnostics, and thus will cause confusion in the courts below over when DNA-related and diagnostic inventions are patentable. It promotes arbitrary distinctions that will lead to artful patent drafting in an effort to exploit the Federal Circuit's holding. And it involves a question of profound national importance regarding the limits on using patents to control the use of human DNA.

I. THE FEDERAL CIRCUIT'S HOLDING THAT MERE SEPARATION OF DNA IS PATENT ELIGIBLE CONFLICTS WITH *MYRIAD* AND WILL CREATE CONFUSION AT ALL LEVELS OF THE PATENT SYSTEM

A. The Federal Circuit's Ruling Cannot Be Squared With *Myriad*

1. In *Association for Molecular Pathology* v. *Myriad Genetics, Inc.*, 569 U.S. 576 (2013), the Court reversed the Federal Circuit's determination that isolated segments of DNA encoding genes associated with an increased risk of breast and ovarian cancer are patent eligible, *id.* at 580. In so ruling, this Court held that "a naturally occurring DNA segment is a product of nature and not patent eligible merely because it has been isolated," even where the isolating step "severs chemical bonds" so as to "create[] a nonnaturally occurring molecule." *Id.* at 580, 593. The Court expressly noted, moreover, that "separating [a] gene from its surrounding genetic material is not an act of invention." *Id.* at 591.

The *Myriad* ruling is consistent with the Court's broader pronouncement that the mere act of changing the concentration of one naturally occurring substance relative to another (*e.g.*, by isolating, multiplying, or aggregating) is generally not patent eligible where the constituent substances are not altered and therefore "serve the ends nature originally provided and act quite independently of any effort of the patentee." *Funk Bros. Seed Co.* v. *Kalo Inoculant Co.*, 333 U.S. 127, 131 (1948). Such claims are directed to the naturally occurring substances themselves.

Here, the claims separate smaller human DNA fragments from larger ones in a maternal blood sample and culminate in the analysis of the separated DNA. It is undisputed that the claimed method does not change the molecular structure or nucleotide sequence of the separated DNA. App. 14a; App. 24a (Reyna, J., dissenting). Under *Myriad*, therefore, the separated DNA fragments are themselves unpatentable. 569 U.S. at 590-594 (isolated DNA is not patentable where inventors do not "create or alter the genetic structure of" the DNA). And methods employing only routine steps to carry out that separation in order to facilitate the analysis of the separated DNA are likewise unpatentable. *Id.* at 591 ("[S]eparating [a] gene from its surrounding genetic material is not an act of invention.").

2. The Federal Circuit attempted to side-step *Myriad* by characterizing it as applying only to *composition* claims, and not *method* claims. App. 14a-15a. To support that distinction, the Federal Circuit quoted dicta in *Myriad* suggesting that, had the patentee "'created an innovative method of manipulating genes … , it could possibly have sought a method patent.'" *Id.* (quoting *Myriad*, 569 U.S. at 595-596).

But *Myriad*'s reach is not so limited. The Court expressly stated that "separating [a] gene from its surrounding genetic material is not an *act* of invention." 569 U.S. at 591 (emphasis added). Moreover, if the Federal Circuit were correct, it would be relatively easy to exercise effective control over human DNA in contravention of this Court's concern about granting "the exclusive right to isolate an individual's … genes." *Id.* at 585. This is because just about any DNA composition claim can be written as a method for isolating the DNA. And such method claims create the same "considerable danger that the grant of patents would tie up the use of such tools and thereby inhibit future innovation" that this Court warned about in *Myriad*. *Id.* at 589 (internal quotation marks omitted).

Further, the Court has never endorsed a patent-eligibility test that turns solely on the label of the claim at issue. To the contrary, the Court has expressly rejected such a test, holding that "the determination of patentable subject matter" should not depend "simply on the draftsman's art." *Parker* v. *Flook*, 437 U.S. 584, 593 (1978); *see also Alice*, 573 U.S. at 226 (holding both computer system and method claims unpatentable under Section 101 because "the system claims are no different from the method claims in substance"); App. 31a (Reyna, J., dissenting). By cabining *Myriad* to reach only composition claims, the Federal Circuit created an end run around *Myriad*'s holding.

Regardless, far from supporting the Federal Circuit's holding in this case, *Myriad*'s dicta demonstrates precisely why that holding is wrong. The dicta suggests that had the patentee in *Myriad* developed an "*innovative*" method for isolating DNA, that method might have been patent eligible. But that is a question for step *two* of the Section 101 analysis. *Alice*, 573 U.S.

at 221 ("At … step two, we must examine the elements of the claim to determine whether it contains an 'inventive concept' sufficient to 'transform' the claimed abstract idea into a patent-eligible application.").

Step two plays an important role in ensuring that a claimed "process has additional features that provide practical assurance that the process is more than a drafting effort designed to monopolize the law of nature itself." *Mayo*, 566 U.S. at 77. If "virtually any step beyond a statement of a law of nature itself should transform an unpatentable law of nature into a potentially patentable application" at step two, then "'the law of nature' exception to § 101 patentability" would become "a dead letter." *Id.* at 89.[4]

Here, the Federal Circuit never truly considered whether the claimed separation is innovative or unconventional because it never reached step two. Had the

[4] To be sure, it is sometimes appropriate to terminate the Section 101 analysis at step one, such as when a claim is directed to a method of treatment. *See, e.g.*, *Vanda Pharm. Inc.* v. *West-Ward Pharm. Int'l Ltd.*, 887 F.3d 1117, 1136 (Fed. Cir. 2018) ("At bottom, the claims here are directed to a specific method of treatment for specific patients using a specific compound at specific doses to achieve a specific outcome" and thus "are patent eligible" at step one); *see also Endo Pharm. Inc.* v. *Teva Pharm. USA, Inc.*, 919 F.3d 1347, 1354 (Fed. Cir. 2019) (citing *Vanda* and upholding under step one "method of treatment including specific steps to adjust or lower the oxymorphone dose for patients with renal impairment"); *Natural Alternatives Int'l, Inc.* v. *Creative Compounds, LLC*, 918 F.3d 1338, 1346 (Fed. Cir. 2019) (citing *Vanda* and upholding at step one claims that "go[] far beyond merely stating a law of nature, and instead set[] forth a particular method of treatment"); *Boehringer Ingelheim Pharm. Inc.* v. *Mylan Pharm. Inc.*, 803 F. App'x 397, 400 (Fed. Cir. 2020) (citing *Vanda* and upholding at step one claims "directed to a method of treating type 2 diabetes mellitus using a DPP-IV inhibitor, such as linagliptin"). But this is the exception, not the rule.

panel majority conducted a full inquiry into whether the patents describe an inventive concept, it almost certainly would have followed the district court and the dissent in concluding they do not. This is because the patents describe the claimed steps as being performed using commercially available tools and kits. C.A.J.A. 31 (2:46-48); C.A.J.A. 32 (3:49-50); C.A.J.A. 33 (5:28-39); *see also* App. 28a-29a (Reyna, J., dissenting) (observing that "the written description identifies the claimed method steps as well-known or performed using commercially available tools or kits" and listing patent citations). The majority itself acknowledged that the patentees "did not invent centrifugation, chromatography, electrophoresis, or nanotechnology," each of which is recited in the claims. App. 16a. Rather, they merely applied conventional tools to naturally occurring materials.

Proof that the panel majority's holding is inconsistent with *Myriad* lies in its logical consequences. Consider an instruction to filter larger material from a sample of pond water before analyzing a microorganism contained therein. The microorganism is a product of nature and would not be patentable merely because it has been separated from other natural material in the pond. *Myriad*, 569 U.S. at 593; *Funk Bros.*, 333 U.S. at 130 ("The qualities of these bacteria, like the heat of the sun, electricity, or the qualities of metals, are part of the storehouse of knowledge of all men."). Yet, under the Federal Circuit's holding, the mere instruction to filter the microorganism from its surroundings would be patent eligible without regard to whether the filtration method is unconventional.

3. Perhaps recognizing the weakness of its first attempt to distinguish *Myriad*, the Federal Circuit's modified opinion also tethers its holding to the claims'

300 and 500 base pair threshold limitations. According to the court, these 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." App. 11a.

This post-hoc justification for the majority's original ruling is unavailing, as it starts from a mistaken premise. The patentees did not "invent" or "engineer" the base pair thresholds. Indeed, the patents themselves refer to the thresholds as "finding[s]," not as engineering choices. App. 4a; *see also* App. 21a.[5] The panel majority seems to implicitly acknowledge this fact at least once, as it notes that the patent "inventors *discovered* that" fetal DNA "has characteristics"—*i.e.*, a size distribution—"that make it distinguishable, and therefore separable, from the maternal DNA." App. 18a (emphasis added). Fetal DNA's size distribution is dictated by *nature*, not by humans.

The Federal Circuit overlooked that *all attributes* of naturally occurring DNA, and not just the *existence* of the DNA, are natural phenomena. In other words, the size distributions of cell-free fetal and maternal DNA—like all of their other attributes—are them-

[5] *See, e.g.*, C.A.J.A. 31 (1:63-2:2) ("Circulatory extracellular fetal DNA in the maternal circulation has thus been *found* to be smaller in size (approximately 500 base pairs or less) than circulatory extracellular maternal DNA (greater than approximately 500 base pairs). This surprising *finding* forms the basis of the present invention … ." (emphases added)), (2:8-14) (similar); C.A.J.A. 32 (4:50-53) (describing results of experiment in which the patentees found 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").

selves natural phenomena. *See, e.g.*, *Flook*, 437 U.S. at 593 n.15 (invention that merely "reveals a relationship that has always existed" is not patentable); *Funk Bros.*, 333 U.S. at 130. If that were not the case, then any manipulation of DNA based on any of its attributes would potentially be patentable, removing large swaths of DNA manipulation techniques from the public domain. App. 36a (Reyna, J., dissenting).

Further, the specific 300 and 500 base pair thresholds recited in the claims are hardly new or inventive. The patents and the record below make clear that those base pair values derive from the fragment sizes used in the off-the-shelf DNA ladders reported in the patents. *See* C.A.J.A. 32 (4:3-9) ("The Gel was cut into pieces corresponding to specific DNA sizes according to the DNA size markers (New England Biolabs, 100 bp ladder and Lamda Hind III digest). *The DNA sizes contained by the specific gel fragments were*: 90-300 bases, *300-500 bases*, 500-1000 bases, 1.0-1.5 kilo bases ('kb'), 1.5-23 kb and >23 kb." (emphases added)).[6] In other words, the 300 and 500 base pair parameters reflect the unremarkable fact that the DNA ladders the inventors used to carry out the claimed size separation employed those thresholds. Thus, even if *someone* could be said to have invented the base pair thresholds at issue, it certainly was not Respondents.

In short, neither the Federal Circuit's attempt to cabin *Myriad* to method claims nor its reliance on the claimed 300 and 500 base pair limitations permitted it to evade *Myriad*'s reach.

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[6] A DNA ladder is a commercially available standard reference containing DNA fragments of a known size. It is used to identify the approximate size of a sample molecule by visual comparison.

B. The Federal Circuit's Holding Will Create Confusion And Conflict

In addition to contravening *Myriad*, the Federal Circuit's ruling creates a significant possibility for confusion in the Federal Circuit, the district courts, and the Patent and Trademark Office. That is because the Federal Circuit has, in previous decisions, applied *Myriad* to hold near-identical sets of patent claims *unpatentable* under Section 101.

1. In *Ariosa*, the Federal Circuit held that claims directed to the "amplification" of cell-free fetal DNA (*i.e.*, the multiplication of the number of fetal DNA molecules using laboratory techniques) in a maternal blood sample in order to analyze such DNA for diagnostic purposes is *not* patent eligible, notwithstanding that the claims included a technique for enriching the blood sample for cell-free fetal DNA. 788 F.3d at 1374-1375. Until the decision on review, *Ariosa* had been consistently followed by the Federal Circuit when addressing similar claims. *See, e.g.*, *Genetic Techs. Ltd.* v. *Merial L.L.C.*, 818 F.3d 1369, 1376 (Fed. Cir. 2016) ("The similarity of claim 1 to the claims evaluated in *Mayo* and *Ariosa* requires the conclusion that claim 1 is directed to a law of nature.").

Indeed, the Federal Circuit's precedent had established a well-defined distinction between diagnostic claims (such as at issue in *Mayo*, *Ariosa*, and here), on the one hand, and method of treatment claims, on the other hand. *See Roche Molecular Sys., Inc.* v. *Cepheid*, 905 F.3d 1363, 1373 n.7 (Fed. Cir. 2018) (noting that the court's precedent "underscore[s] the distinction between method of treatment claims and those in *Mayo*," *i.e.*, claims "directed to a diagnostic method" (alteration in original)). While the Federal Circuit has consistently

held the former unpatentable under Section 101, it has held the latter patentable. App. 9a ("Under *Mayo*, we have consistently held diagnostic claims unpatentable as directed to ineligible subject matter. In contrast, we have held that method of treatment claims are patent-eligible." (citations omitted)). Up until the Federal Circuit's decision here, inventors and others in the patent ecosystem had been able to rely on that bedrock distinction in the otherwise ever-shifting Section 101 landscape.

In its decision below, however, the panel majority departed from Federal Circuit precedent by holding that diagnostic claims that separate fetal DNA in order to analyze it *are* patent eligible. This holding cannot be reconciled with *Ariosa* or its progeny. Just as claims to amplifying and analyzing DNA are unpatentable, so too are claims to separating and analyzing such DNA. The purpose of both laboratory techniques is to isolate DNA for diagnostic purposes, and *Myriad* makes clear that such isolation is not patentable. In fact, if anything, the claims here hew even *closer to nature* than those in *Ariosa* because, while the DNA in that case was artificially multiplied in the laboratory to create new molecules, the separated DNA analyzed here is all initially present in the maternal blood sample itself.

Rather than confronting *Ariosa* and other relevant diagnostic precedent head-on, the Federal Circuit dismissed them because, according to the majority, the claims here are "method of preparation" claims rather than "diagnostic" claims. App. 9a, 13a-14a, 17a-18a. But the court's characterization of the claims at issue as "method of preparation" claims is inapt. Indeed, these claims have all the normal indicia of *diagnostic* claims. Each culminates in an "analysis" step whereby the separated DNA is "analyz[ed]," and some claims recite

analysis for the purpose of detecting a "fetal chromosomal aberration," like aneuploidy or Down's Syndrome. *See* C.A.J.A. 34 (7:54-8:57); C.A.J.A. 35 (9:5-8); C.A.J.A. 42 (8:62-63); C.A.J.A. 43 (9:17-24). The patents' disclosures confirm that the claimed analysis is performed for the purpose of detecting—*i.e.*, diagnosing—chromosomal aberrations. C.A.J.A. 31 (2:10-18) (claimed method "permits the analysis of fetal genetic traits"). Indeed, the patents' Titles and Abstracts refer to the "*detection* of fetal genetic traits," not the preparation of DNA. C.A.J.A. 28 (emphasis added).

Further, as Judge Reyna pointed out in dissent, the panel majority created the "method of preparation" category out of whole cloth, and without providing clear guidance about the boundaries between it and the types of claims found unpatentable in *Ariosa* and *Myriad*. *See* App. 26a. Confirming the artificial nature of the panel majority's reasoning, many of the diagnostic claims that the Federal Circuit has held unpatentable *also* recited method of preparation limitations that—if the panel majority is right—should have survived Section 101 review. The *Ariosa* claims, for example, recited "obtaining a non-cellular fraction of the blood sample" and "amplifying a paternally inherited nucleic acid from the non-cellular fraction." 788 F.3d at 1374; *see also Cepheid*, 905 F.3d at 1371 (reciting method for detecting Mycobacterium tuberculosis in a biological sample that is prepared by first amplifying DNA); *Genetic Techs.*, 818 F.3d at 1374 (requiring "amplifying" DNA prior to "analyzing the non-coding region to detect the allele"). In *Ariosa* and subsequent diagnostic cases, the "preparation" step is mere pre-solution activity—*i.e.*, the prerequisite for creating a sample that can be analyzed for diagnostic purposes. Such conventional "'[pre]-solution activity' is normally not sufficient to

transform an unpatentable law of nature into a patent-eligible application of such a law." *Mayo*, 566 U.S. at 79 (quoting *Flook*, 437 U.S. at 590).

2. As explained, there is no principled basis to distinguish *Ariosa* from this case. Accordingly, lower courts and the Patent Office will inevitably struggle to provide a reasonable explanation for whether a particular claim is a patentable "method of preparation" claim or an unpatentable diagnostic claim.

Natera, Inc. v. *ArcherDX, Inc.*, 2020 WL 6043929 (D. Del. Oct. 13, 2020), is illustrative. There, the district court noted the incongruity in the fact that the panel in this case held the claim to be patent eligible even though "the natural phenomenon of cell-free DNA was simply sorted by size, and then the sorted DNA was analyzed, but the cell-free DNA itself was unchanged." *Id.* at *5. Still, the district court reasoned that because the claims it was reviewing "compare favorably" to those held patentable in the Federal Circuit's decision below, it had to follow the same rule. *See id.* ("It seems to me then that if the claim at issue in *Illumina* was patent eligible, the claim being challenged here today also must be patent eligible."). Finally, the court distinguished *Ariosa* on the same dubious ground as the panel majority—*i.e.*, that *Ariosa* involved a diagnostic claim rather than a "method of preparation" claim. *Id.* at *5-6.

The recent decision in *Abbott Labs.* v. *Grifols Diagnostic Solutions Inc.*, 2020 WL 7042891 (N.D. Ill. Dec. 1, 2020), is to similar effect. It read the decision in this case broadly while upholding a method of replicating HIV DNA at step one of the *Alice* test. *Id.* at *6-7. And, once again, the district court relied on the same thin distinction drawn by the panel majority to distin-

guish *Ariosa*. *Id.* at *6 (asserting that *Ariosa* involved "claims [that] 'were directed to detecting a natural phenomenon *after* a sample had been prepared or extracted'" (quoting App. 13a) (emphasis added)).

If the Court does not step in to correct the Federal Circuit's ruling, these errors will continue to propagate, not only in the courts but also in the Patent Office. *See In re Rudy*, 956 F.3d 1379, 1383 (Fed. Cir. 2020) (Patent Office guidance must follow Federal Circuit "caselaw, and the Supreme Court precedent it is based upon" when articulating how to conduct Section 101 analysis). The result would be even more confusion in an area of the law so unsettled that the Federal Circuit itself has remarked that "district courts might be tempted to opt for an effective coin toss rather than a reasoned analysis when faced with a challenge under § 101." *Realtime Data LLC* v. *Reduxio Sys., Inc.*, __ F. App'x __, 2020 WL 6228818, at *1 (Fed. Cir. Oct. 23, 2020).

II. THE FEDERAL CIRCUIT'S HOLDING RAISES ISSUES OF NATIONAL IMPORTANCE

This case presents a question of profound national importance. The decision below is not only analytically incorrect, it will further complicate this already-complicated area of law and sow confusion by eroding this Court's precedents.

First, as noted, the Federal Circuit's holding brings the law one step closer to effectively permitting the patenting of DNA. If a process for separating DNA from its surroundings is patentable, there is little left of *Myriad*'s holding that the isolated DNA itself is not patentable. Applying the Federal Circuit's rule here to the facts in *Myriad* proves the point.

In *Myriad*, the patent at issue covered the sequenced genes linked to an individual's risk of developing breast and ovarian cancer. 569 U.S. at 582-583. This Court held that "a naturally occurring DNA segment is a product of nature and not patent eligible merely because it has been isolated." *Id.* at 580. Under the Federal Circuit's rule here, however, while one could not receive a patent to the genes sequenced in *Myriad*, one *could* receive a patent covering a method for isolating the genes using off-the-shelf products and conventional laboratory techniques. In essence, then, the Federal Circuit's rule allows private companies that devise such methods to hold broad control over the isolated DNA.

As a practical matter, patents on methods for isolating DNA would result in the very removal from the public domain of "the basic tools of scientific and technological work," *Myriad*, 569 U.S. at 589 (internal quotation marks omitted), that Section 101 is meant to prevent. It is difficult to imagine a more foundational building block for the study of human biology than human DNA.

Second, the Federal Circuit's ruling creates a roadmap for patent drafters to evade *Myriad* and *Ariosa*. In particular, the Federal Circuit's holding will encourage applicants to exploit artificial distinctions between isolated DNA claims and methods for isolating the DNA, as well as between diagnostic claims and "method of preparation" claims. But because preparing a DNA sample to be analyzed is a prerequisite to analyzing the sample, just about *any* diagnostic claim can be rewritten as a "method of preparation" claim. Thus, the Federal Circuit's holding will make patent eligibility impermissibly turn on "the draftsman's art." *Flook*, 437 U.S. at 593.

Notably, that is precisely what happened here. The inventors added the "method of preparation" language recited in the '751 patent claims' preambles during prosecution to overcome a Section 101 rejection. *Compare* C.A.J.A. 339, *with* '751 Patent File History, 09/29/2016 Claim Amendment. Prior to that amendment, the preambles recited "a method for *analyzing*" DNA, consistent with the "analyzing" limitation recited in the bodies of the claims. C.A.J.A. 339 (emphasis added).

Third, the tools that Congress gave the Federal Circuit to help it maintain national uniformity in patent law also amplify the court's errors and inconsistencies. The Federal Circuit's decision is binding on all district courts and the Patent Office. Where, as here, the Federal Circuit deviates from sound practice and this Court's precedents, it is incumbent on the Court to intervene. That is particularly true in a case like this one, where the error is foundational and likely to affect many litigants. This Court has a special responsibility to supervise the Federal Circuit to ensure that its pronouncements remain in line with the general principles articulated by the Court. The new rule applied in this case is incorrect and should be promptly reviewed to contain the harm.

Finally, the confusion caused by the panel majority's departure from *Myriad* and *Ariosa* will only deepen the existing confusion and instability surrounding patent-eligibility law—a doctrine that the Federal Circuit recently characterized as among "the most baffling concepts in all of patent law." *Realtime Data*, 2020 WL 6228818, at *1 (internal quotation marks omitted).

The Federal Circuit itself has openly called for this Court's help in interpreting Section 101. For example,

in *Athena Diagnostics, Inc.* v. *Mayo Collaborative Services, LLC*, 927 F.3d 1333 (Fed. Cir. 2019), *cert. denied*, 140 S. Ct. 855 (2020), the en banc Federal Circuit issued eight separate opinions on its decision to deny en banc review. A majority of the en banc Federal Circuit thought *Mayo* rendered medical diagnostic methods ineligible for patent protection, but the court was splintered, and the broad consensus was that the Federal Circuit needed this Court's assistance to resolve the confusion that Section 101 law has engendered.

Athena was by no means the first case in which the Federal Circuit has expressed confusion and division on patent eligibility or called for this Court's intervention. *See, e.g.*, *Interval Licensing LLC* v. *AOL, Inc.*, 896 F.3d 1335, 1348 (Fed. Cir. 2018) (Plager, J., concurring-in-part and dissenting-in-part) (observing that the "incoherent body of doctrine" surrounding Section 101 "renders it near impossible to know with any certainty whether [an] invention is or is not patent eligible"); *Smart Sys. Innovations, LLC* v. *Chicago Transit Auth.*, 873 F.3d 1364, 1377 (Fed. Cir. 2017) (Linn, J., dissenting-in-part and concurring-in-part) (Section 101 "is indeterminate and often leads to arbitrary results"); *Berkheimer* v. *HP Inc.*, 890 F.3d 1369, 1374 (Fed. Cir. 2018) (Lourie and Newman, JJ., concurring in the denial of rehearing en banc) (Section 101 "law needs clarification by higher authority").

The Federal Circuit's decision below adds to this morass in the DNA diagnostic space. Unless and until the Court addresses this issue, district courts, companies, and the patent bar will have to muddle through difficult questions and conflicting precedent on their own. The last thing Section 101 law needs is the additional confusion and bad outcomes that the Federal Circuit's decision is bound to create.

CONCLUSION

The petition for a writ of certiorari should be granted.

Respectfully submitted.

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