No. 20-892

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

REPLY BRIEF FOR PETITIONERS

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TABLE OF CONTENTS

TABLE OF AUTHORITIES

CASES

STATUTORY PROVISIONS

This Court has held that "separating [a] gene from its surrounding genetic material is not an act of invention" under 35 U.S.C. § 101. *Association for Molecular Pathology* v. *Myriad Genetics, Inc.*, 569 U.S. 576, 591 (2013). The panel majority, however, came to the opposite conclusion. It held that a patent claim that involves separating larger naturally-occurring human DNA from smaller naturally-occurring human DNA is patentable under Section 101—without any consideration of whether the patented method itself provides an *innovative* process for achieving that result (i.e., an inventive concept).

Respondents' only argument for why the panel majority's ruling does not violate *Myriad* is that this case involves method claims and *Myriad* did not. But *Myriad* explained that the patentee "could possibly have sought a method patent" only if the patentee had "created an *innovative method* of manipulating genes." 569 U.S. at 595-596 (emphasis added). And Respondents' insistence that the claims here are directed to eligible subject matter because they involve a "process" cannot be reconciled with *Alice* v. *Corp. Pty. Ltd.* v. *CLS Bank Int'l*, 573 U.S. 208, 216 (2014), which not only established the governing framework but applied it to invalidate a claim to a process—the same kind of claim at issue here.

Myriad further held that the central idea of the patents in this case—separating human DNA from surrounding genetic material—is "not an act of invention." *Myriad*, 569 U.S. at 591. But here, the panel majority did not even consider whether the patented method was innovative and, if anything, reinforced the district court's conclusion that it was not. *See* Pet. 15. Respondents' vague warning that reversing the panel majority's ruling would "cast a cloud of uncertainty" over

patents on "purifying water" and "cleaning air" (Opp. 17) rings hollow. If such patents described an *innovative* way of purifying or cleaning, Section 101 would pose no obstacle. To the contrary, it is the panel majority's holding—that a process for separating one naturally occurring substance from another is patentable *without any consideration of whether the process is innovative*—that wreaks havoc on existing doctrine.

The petition for a writ of certiorari should be granted.

ARGUMENT

I. THE FEDERAL CIRCUIT'S RULING CANNOT BE SQUARED WITH *MYRIAD* OR EXISTING SECTION 101 DOCTRINE MORE BROADLY

As Petitioners have explained, the panel majority's ruling conflicts with *Myriad* and *Ariosa Diagnostics, Inc* v. *Sequenom, Inc*, 788 F.3d 1371 (Fed. Cir. 2015). Pet. 12-22. Respondents have no persuasive response.[1]

A. Respondents' sole argument regarding *Myriad* is that *Myriad* involved composition claims (i.e., claims to isolated DNA itself) rather than, like here, methods of separating and analyzing DNA. Opp. 7, 13-14. But this rigid distinction between composition and method claims makes little sense (Pet. 13), and this Court has already held in *Alice* and other cases that Section 101 applies to method claims, *Alice*, 573 U.S. at 217.

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[1] Respondents incorrectly allege that Petitioners' Federal Circuit brief "recognized that neither [*Myriad* or *Ariosa*] was directly on point." Opp. 12. Respondents do not cite any such statement about *Myriad*. Moreover, Respondents rely on Petitioners' statement that *Ariosa* "*closely resembles*" this case (*id.* (emphasis added))—hardly a concession that *Ariosa* was not on point.

Indeed, almost any DNA composition claim could be rewritten to be a method for isolating that DNA. For example, the composition claims for the breast cancer genes at issue in *Myriad* easily could have been rewritten to cover a generic two-step process: (1) separating the breast cancer genes from other genetic material and (2) analyzing the breast cancer genes. This method claim would grant the same effective control over the relevant genes as the composition claim invalidated by this Court and thus would raise the same concerns about "inhibit[ing] future innovation" that the *Myriad* Court warned against. Pet. 13. Respondents have no answer.

As discussed above, moreover, *Myriad* indicated that an "innovative" method for isolating DNA might have been patent eligible. 569 U.S. at 595-596. That standard is not met here. *Myriad* was clear that the mere act of separating DNA from genetic material (which is essentially all that is claimed here) is not an "act of invention" sufficient to justify patent eligibility under Section 101. *Id.* at 591. In any event, the panel majority here did not even consider whether Respondents' techniques for separating smaller DNA from larger DNA fragments were innovative because it did not reach step two of the *Alice* test. Pet. 13-14. Again, Respondents have no answer.

B. Unable to distinguish *Myriad*, Respondents urge this Court to ignore it and instead apply the "settled two-part test" laid out in *Alice*. Opp. 7. But *both* cases apply here. *Myriad* informs the *Alice* step-one analysis—a patent is necessarily directed to unpatentable subject matter (i.e., a law of nature) if it merely claims separating a gene from its genetic material. *See Myriad*, 568 U.S. at 591 (describing patents at issue as "f[alling] squarely within the law of nature exception").

In other words, Respondents are simply wrong that this case involves the "factbound" application of the *Alice* standard. Opp. 15. To the contrary, the panel majority ignored the important legal principle outlined in *Myriad* and did so in a way that will have serious ramifications—making it easier to patent human DNA and generally allowing clever drafters to evade the substantive limits on patentability set forth in *Myriad*. Pet. 22-25.

Respondents also argue that it is overly simplistic to describe the patents as directed to the idea of separating smaller DNA fragments from larger ones. Opp. 9-10. Rather, Respondents assert, the patents claim the "selective removal of longer DNA from a maternal sample to enrich the fraction in [smaller] fetal DNA, for use in fetal genetic testing." *Id.* But that is simply another way of saying the smaller fragments of DNA are separated. *See Mayo Collaborative Servs.* v. *Prometheus Labs., Inc.*, 566 U.S. 66, 77-78 (2012) ("If a law of nature is not patentable, then neither is a process reciting a law of nature, unless that 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.").

To the extent Respondents are suggesting that limiting the patents to the specific context of genetic testing somehow alters the analysis, they are wrong. As the *Mayo* Court explained, Einstein could not patent $E=mc^2$ simply by claiming a process by which he told "linear accelerator operators" to apply it, "[n]or could Archimedes have secured a patent for his famous principle of flotation" by claiming a process by which he told "boat builders" to apply the principle. *Mayo*, 566 U.S. at 78.

Respondents relatedly assert that the patents are not directed to a natural law because they specify two different size thresholds that should be used as part of the separation process—500 base pairs and 300 base pairs. Opp. 10. But as Petitioners have pointed out (and Respondents ignore), the patents themselves state that the 500 and 300 base pair thresholds reflect the naturally occurring size of fetal DNA and the use of conventional techniques to separate it. Pet 16-17. For example, both patents explain that on average, the inventors "found" fetal DNA "to be smaller in size (approximately 500 base pairs or less)" than "maternal DNA (greater than approximately 500 base pairs)"—a "finding that forms the basis of the" invention claimed in the patents. *See Id.* 16 n.5. In one experiment, moreover, the patentees found that "DNA fragments originating from the fetus were almost completely of sizes smaller than 500 base pairs with around 70% being … sizes smaller than 300 bases." *Id.*

While Respondents point out (at 10-11) that the size of fetal DNA fragments may vary somewhat from woman to woman, this is a red herring. The question is not whether separating DNA at the 500/300 base pair thresholds will achieve some desired (but unclaimed) level of enrichment of fetal DNA for all people; the question is whether the size distribution of DNA existed in nature before it was described in the patents (and under *Alice* Step two, whether the inventors added anything inventive to it). *See Mayo*, 566 U.S. at 77 ("[A] patent that simply describes [a naturally occurring] relation[ship] sets forth a natural law."); *Parker* v. *Flook*, 437 U.S. 584, 593 n.5 (1978) (invention that merely "reveals a relationship that has always existed" is not patentable). The patents themselves admit that the 500/300 base-pair thresholds did in fact exist in nature.

See Pet. 16-17. Indeed, the patents report that the claimed methods were used to study that natural distribution. *Id.* In addition, Respondents tellingly do not dispute that the 300/500 base pair thresholds were in use before the patents issued, as those values derive from the fragment sizes used in off-the-shelf DNA kits. *Id.* 17.

Respondents also contend that even if the patents are directed to a law of nature at *Alice* step one, they describe an inventive concept at *Alice* step two because the 500/300 base pair limitation does not preempt the basic principle that fetal DNA tends to be smaller than maternal DNA. Opp. 11-12. Respondents' *Alice* step two argument is not only wrong but reinforces the need for review. The panel majority's decision in this case conflicts with *Myriad* and other Section 101 precedent precisely because it held that the separation of smaller fetal DNA from larger maternal DNA survived Section 101 review at *Alice* step one *without considering* whether the process claimed was innovative or nonconventional under *Alice* step two.

Had the panel majority reached the issue, it almost certainly would have joined the district court and dissent in concluding that the patents do not claim an inventive concept because the patents merely apply conventional tools to naturally occurring materials. Pet. 14-15. It is also troubling that Petitioners were granted *multiple* patents claiming different size thresholds. This means that (if the panel majority's logic is upheld) Petitioners could have sought dozens of other patents, each claiming a different threshold—effectively preempting all efforts to separate DNA based on the naturally occurring size distribution of fetal DNA. Indeed, the panel majority's step-one-focused reasoning would allow for patents that undisputedly preempt

basic building blocks of scientific knowledge to survive Section 101 review, as preemption is only an issue at *Alice* step two.

Finally, Respondents contend that an altered version of Petitioners' hypothetical about filtering pondwater to study a microorganism would survive Section 101 review. *Compare* Pet. 15 *with* Opp. 16-17. But Respondents' modified hypothetical—using "an approximately 5-micron diameter filter on water from a specific kind of brackish pond to enrich the proportion of a particular microorganism"—suffers from the same flaws as the patents here. The use of a specific filter size that reflects the average size of the microorganism to be filtered adds nothing inventive to the law of nature at issue—the discovery of the size of the microorganism itself, which is akin to the discovery of the 500/300 base-pair thresholds here. Nor is there anything inventive about looking for "a particular microorganism" in a "brackish pond" where those are known facts—just as the presence of cell-free DNA in maternal blood was already known here (App. 2a). If such a claim were to be patent eligible, it would have to be because, under *Alice* step two, it includes an inventive concept beyond that natural law. But that second-step inquiry into the existence of an inventive concept is exactly what the Federal Circuit failed to perform here.

Step two of the *Alice* test also refutes Respondents' warning that application of the *Myriad* principle will "cast a cloud of uncertainty over" patents on processes like purifying water or cleaning air. Opp. 17. If those processes include an inventive concept under *Alice* step two that goes beyond an underlying law of nature, Section 101 poses no obstacle. This Court created a two-step test for a reason and should not allow the Federal Circuit to collapse the framework it created.

C. In addition to conflicting with this Court's guidance, the panel majority's decision creates incoherence in the Federal Circuit's own jurisprudence. Respondents argue that the Federal Circuit's decision in *Ariosa* v. *Sequenom*, is distinguishable, adopting the panel majority's explanation without further analysis. Opp. 14. As the Petition explained, however, the distinctions drawn by the panel majority make little sense because (1) the "method of preparation" category was created out of whole cloth, and (2) the "enrichment" of the sample in *Ariosa* through selectively copying DNA to create new molecules in the laboratory was, if any, further from nature than the "enrichment" here through mere separation of DNA already present in a blood sample. Pet. 19-21. Tellingly, Respondents do not even attempt to address Petitioners' arguments.[2]

Respondents also contend that "even if there were tension" between the panel majority's ruling and *Ariosa*, "that would not warrant this Court's review." Opp. 14. Respondents, however, never explain why this is so. To the contrary, resolving a conflict between this case and *Ariosa* would serve the important purpose of eliminating confusion in the Federal Circuit, the district courts, and the Patent and Trademark Office.

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[2] Respondents do argue (at 13-14) that this case resembles *Rapid Litigation Management Ltd.* v. *CellzDirect, Inc.*, 827 F.3d 1042 (Fed. Cir. 2016). But the panel majority itself recognized that *CellzDirect* is "not directly on point." Pet. App. 15a. This is because *CellzDirect* involved a patent claiming a "new and useful cryopreservation technique"—rather than the patents here, which merely "apply[] a known laboratory technique to a newly discovered natural phenomenon." *Id.* 30a (Reyna, J., dissenting); *see also* Pet. C.A. Br. 27-30. And regardless of any similarity to *CellzDirect*, the Federal Circuit's decision in this case still conflicts with *Ariosa*, which is more directly on point.

Pet. 18, 21-22. Because the Federal Circuit is the only appellate court that resolves patent law issues and it has declined to grant en banc review in this case, this confusion will linger unless and until this Court acts. Respondents do not deny that the Federal Circuit itself has expressed its confusion and called for this Court's help. *Id.* 24-25.

D. Finally, Respondents repeatedly suggest that because the patents ostensibly claim a "process," they necessarily survive review under Section 101. Opp. 4, 7, 8-9, 11, 12, 16, 18. They cite no authority in support of such a rule and for good reason: This Court has held for nearly 170 years that an invention is not patentable if it claims a "law of nature, natural phenomena, [or] abstract idea[]." Pet. 5. There is no exception to that longstanding rule for inventions that can be described as a "process."[3] Indeed, Respondents acknowledge that the two-step analysis laid out in *Alice* is the "settled legal test" under Section 101. Opp. 15; *see also id.* 5 (*Alice* is the "well-settled test" for Section 101), *id.* 7 (*Alice* provides the "settled two-part test"). More accurately, it *was* the settled test until the panel majority's ruling in this case.

II. THIS CASE PRESENTS AN EXCELLENT VEHICLE TO RESOLVE THE QUESTION PRESENTED

This case provides a strong, straightforward vehicle to reaffirm *Myriad*'s holding that the mere act of separating a gene from surrounding genetic material is not patentable under Section 101. First, the issue is

[3] The only cases Respondents cite (at 8-9) are not even patent cases. *See Virginia Uranium, Inc.* v. *Warren*, 139 S. Ct. 1894, 1900 (2019) (preemption); *Merritt* v. *Welsh*, 104 U.S. 694, 696 (1881) (sugar import duties).

cleanly presented because the Federal Circuit's decision rested solely on its conclusion that the patents-in-suit are not directed to a law of nature—the Federal Circuit did not identify any alternative grounds that would support its holding. Second, the opinion below is published and provides a detailed (although erroneous) analysis to support its holding. If this case is allowed to stand, subsequent decisions will likely be unpublished and will contain less reasoning for this Court to review.

Respondents identify three purported reasons why this case is a poor vehicle, none of which is persuasive. First, Respondents argue that even if the panel majority's decision is reversed, they might prevail on remand under *Alice* step two. Opp. 18. This misses the point. The primary reason for this Court to grant review is that the Federal Circuit truncated the analysis *at step one* and created an end-run around *Myriad*'s holding as a matter of law. The hypothetical possibility that Respondents could prevail at step two on remand—although unlikely—does nothing to detract from the importance of reversing the legal error that is currently binding precedent in the appellate court with exclusive national jurisdiction over patent law matters.

Second, and relatedly, Respondents assert that applying the proper *Myriad*/*Alice* standard would not resolve whether all of the *dependent* claims are invalid. Opp. 19. But the panel majority did not suggest that a different analysis would apply to the dependent claims; rather, in a short footnote, the majority "note[d], without deciding" that Respondents had "*argue[d]*" that one dependent claim employed a novel methodology. Pet. App. 16a n.1 (emphasis added). Notably, the district court held—and Judge Reyna would have held—that all the asserted claims (including the dependent claims) were invalid under Section 101. *Id.* 88a (district

court); *id.* 35a (Reyna, J., dissenting). Regardless, the primary reason for this Court to review is to fix the legal error at *Alice* step one—there is no need for this Court to make a ruling on the patentability of the dependent claims.

Finally, Respondents argue it would "depart from … ordinary practice" to take this case up because it arose in an interlocutory, summary judgment posture. Opp. 17-18. This ignores that each of the Court's last three Section 101 rulings also arose in a summary judgment posture. *See Alice*, 573 U.S. at 214; *Mayo*, 566 U.S. at 76; *Myriad*, 569 U.S. at 586. If anything, this Court's "ordinary practice" in the Section 101 context is to *grant* review of summary judgment rulings.

CONCLUSION

The petition for a writ of certiorari should be granted.

Respectfully submitted.

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