Appeal No. 2017-2508

United States Court of Appeals

for the

Federal Circuit

ATHENA DIAGNOSTICS, INC., OXFORD UNIVERSITY INNOVATION LTD., MAX-PLANCK-GESELLSCHAFT ZUR FORDERUNG DER WISSENSCHAFTEN E.V.,

Plaintiffs-Appellants,

– v. –

MAYO COLLABORATIVE SERVICES, LLC,
dba Mayo Medical Laboratories, MAYO CLINIC,

Defendants-Appellees.

ON APPEAL FROM THE UNITED STATES DISTRICT COURT FOR THE DISTRICT OF MASSACHUSETTS IN CASE NO. 1:15-CV-40075-IT
HONORABLE INDIRA TALWANI, UNITED STATES DISTRICT JUDGE

BRIEF FOR *AMICUS CURIAE* ARUP LABORATORIES, INC. IN SUPPORT OF DEFENDANTS-APPELLEES

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February 6, 2018

CERTIFICATE OF INTEREST

Pursuant to Federal Circuit Rule 47.4, counsel for *amicus curiae* ARUP Laboratories, Inc. certifies the following:

1. The full name of every party or *amicus* represented by one or more of the undersigned counsel is:

   ARUP Laboratories, Inc.

2. The name of the real party in interest (if the party in the caption is not the real party in interest) represented by one or more of the undersigned counsel is:

   Not applicable.

3. All parent corporations and any publicly held companies that own 10 percent or more of the stock of the party or *amicus* represented by one or more of the undersigned counsel are:

   The University of Utah is the sole member of ARUP Laboratories, Inc.

4. The names of all law firms and the partners or associates that appeared for the party or *amicus* now represented by one or more of the undersigned counsel in the trial court or agency or are expected to appear in this court are:

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5. The title and number of any case known to counsel to be pending in this or any other court or agency that will directly affect or be directly affected by this court's decision in the pending appeal.

None.

February 6, 2018

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INTEREST OF AMICUS CURIAE[1]

Amicus ARUP Laboratories, Inc. ("ARUP") is a nationally renowned medical reference laboratory. ARUP is an enterprise of the University of Utah and its Department of Pathology. Offering highly complex and unique lab tests, ARUP provides screening services, as well as molecular and genetic assays with accompanying consultative support. ARUP's tests cover numerous medical fields including allergy and immunology, chemistry, cytogenetics, endocrinology, fetal risk assessment, genetics, hematology, hepatitis and HIV, infectious diseases, neurology, oncology, and pathology. ARUP processes nearly 50,000 tissue and fluid specimens every day. Medical directors and genetic counselors are on staff at ARUP and provide consultation and result interpretation. ARUP's clients include more than half of the nation's university teaching hospitals and children's hospitals,

[1] Pursuant to Fed. R. App. P. 29(a)(4)(E), counsel for *amicus* ARUP represents that it authored this brief in its entirety and that none of the parties or their counsel, nor any other person or entity other than *amicus* or its counsel, made a monetary contribution intended to fund the preparation or submission of this brief. Pursuant to Federal Rule of Appellate Procedure 29(a)(2), all parties have consented to the filing of this brief.

as well as regional hospital networks, multihospital groups, major commercial laboratories, group purchasing organizations, military and government facilities, and major clinics. ARUP has active research programs through which it develops cutting-edge and life-saving assays and diagnostic techniques.

ARUP has an interest in a patent system that functions properly to ensure access to naturally-occurring phenomena. ARUP previously supported the Mayo Clinic in *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, 566 U.S. 66 (2012), which set precedent directly implicated here. Over the last several years, the *Prometheus* decision and subsequent precedent have helped ARUP improve patient services by enabling ARUP to conduct additional tests based on natural phenomena, while reducing the threat of patent infringement litigation. ARUP's research activities, as well as diagnostic services offered to hospitals, physicians, and managed-care organizations across the country, depend on this type of scientific knowledge.

INTRODUCTION

Nearly six years ago, the Supreme Court held ineligible for patent protection under Section 101 of the Patent Act claims that "simply tell doctors to gather data from which they may draw an inference in light of the correlations," then "inform a relevant audience about certain laws of nature," all while applying "well-understood, routine, conventional activity already engaged in by the scientific community." *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 566 U.S. 66, 79-80 (2012). Since that decision, "[c]ourts have nearly universally found 'diagnostic' method claims—those that only include steps for diagnosing a disease or identifying a characteristic in a patient—to be patent ineligible." Geoff Biegler, Megan Chacon, & Dalia Kothari, Fish & Richardson, *Life Sciences Patent Eligibility "101": Mayo at Five* 1 (2017), *available at* https://www.fr.com/wp-content/uploads/2017/09/Life-Science-Patent-Eligibility-101.pdf.

Athena's patent claims here are precisely the type of claims that the Supreme Court addressed: a conventional testing mechanism applied to a natural phenomenon. The correlation

described in the patents at issue in this case is a scientific fact—a law of nature—regarding the detection of naturally-occurring autoantibodies in the human body. The patents assert exclusive rights over the process of detecting this natural correlation using a conventional labeling procedure. Athena's patent is not directed to new and unique medicines, reagents, or testing equipment. Instead, it is directed to the basic concepts of immunoprecipitating and monitoring for a well-known radioactive label.

The district court properly found this subject matter to be patent-ineligible. Doctors and laboratories test patients' blood and routinely evaluate the laws of nature in providing health care. But if claims like this one are sustained, such tests may be blocked by patents on the law of nature on which they are based. *Mayo* warned that laws of nature should not be removed from the public sphere by virtue of the "draftsman's art" in crafting patent claims. 566 U.S. at 72. That warning applies here, and the district court was correct to rule these claims invalid.

Extending protection would impede the progress of research by allowing Athena to own a basic law of nature concerning the

human body's natural production of autoantibodies in response to the disease myasthenia gravis. Athena's patent and others like it allow no room to design around, imitate, or improve upon the so-called "invention" of a law of nature. Such powerful rights lead to the monopolization of tools essential to patient care—increasing prices while decreasing efficiency and quality. Such powerful effects should not be conferred upon claims on laws of nature.

By contrast, invalidating the claims and reaffirming the principles set forth in *Mayo* does not disrupt or impede scientific research. When patent protection is properly denied to claims on laws of nature, patients are able to more quickly, and more cost-effectively, receive more accurate diagnoses of their medical conditions. Affirming the district court will simply affirm the now well-settled distinction between natural phenomena and human-made inventions—a balance that Congress enacted, and that reflects the Constitution and has served the patent system and the progress of science very well.

ARGUMENT

I. THE ATHENA PATENT IMPROPERLY REMOVES A NATURAL PHENOMENON FROM THE PUBLIC DOMAIN

A. Patentable Subject Matter Does Not Include Laws Of Nature, Natural Phenomena, Or Abstract Ideas

Section 101 of the Patent Act provides: "Whoever invents or discovers any new and useful ... composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title." 35 U.S.C. § 101. A bedrock principle of United States patent law is that: "Excluded from such patent protection are laws of nature, natural phenomena, and abstract ideas." *Diamond v. Diehr*, 450 U.S. 175, 185 (1981) (citations omitted). Accordingly:

> [A] new mineral discovered in the earth or a new plant found in the wild is not patentable subject matter. Likewise, Einstein could not patent his celebrated law that $E=mc^2$; nor could Newton have patented the law of gravity. Such discoveries are "manifestations of . . . nature, free to all men and reserved exclusively to none."

Diamond v. Chakrabarty, 447 U.S. 303, 309 (1980) (*quoting Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127, 130 (1948)); *see also Parker v. Flook*, 437 U.S. 584, 593 n.15 (1978) ("[R]ecognition

of a theretofore existing phenomenon or relationship carries with it no rights to exclude others from its enjoyment.") (quoting Peter D. Rosenberg, *Patent Law Fundamentals*, § 4, p. 13 (1975)); *Gottschalk v. Benson*, 409 U.S. 63, 67 (1972) ("Phenomena of nature, though just discovered, mental processes, and abstract intellectual concepts are not patentable, as they are the basic tools of scientific and technological work.").

"Groundbreaking, innovative, or even brilliant discovery does not by itself satisfy the § 101 inquiry." *Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 569 U.S. 576, 591 (2013). Rather, the Supreme Court has now established a two-step eligibility inquiry. *See, e.g., FairWarning IP, LLC v. Iatric Sys., Inc.*, 839 F.3d 1089, 1093 (Fed. Cir. 2016). The inquiry's first step requires a court to "determine whether the claims at issue are directed to a patent-ineligible concept." *Alice Corp. v. CLS Bank Intern.*, 134 S. Ct. 2347, 2355 (2014). When it is "undisputed" that researchers have uncovered only information that "existed in nature before [they] found them," *Myriad*, 569 U.S. at 590, then the core subject covers only a natural phenomenon. In that

instance, the court must then, under the second step, "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." *Alice Corp.*, 134 S. Ct. at 2357 (quoting *Mayo*, 566 U.S. at 72-73, 79-80). This inventive concept must do more than simply recite "well-understood, routine, conventional activity." *Mayo*, 566 U.S. at 79-80.

B. The Athena Patent Claims Nothing More Than A Natural Phenomenon

Athena does not dispute here that its asserted claims do nothing more than combine the application of well-known scientific techniques to the detection of a naturally-occurring phenomenon. Rather, the face of the patent itself concedes that the diagnostic process employs "immunological assay techniques known per se in the art." ('820 patent at 3:33-35.) The specification further states: "Iodination and immunoprecipitation are standard techniques in the art, the details of which may be found in references (4 and 6)." ('820 patent at 4:10-12.) This Court has held that: "For process claims that encompass natural phenomenon, the process steps are the additional features that

must be new and useful." *See, e.g., Ariosa Diagnostics, Inc. v. Sequenom, Inc.*, 788 F.3d 1371, 1377 (Fed. Cir. 2015) (citing *Parker*, 437 U.S. at 591). Here, the mere combination of undisputed "standard techniques" with Athena's "discovery" that autoantibodies to a muscle-specific kinase (MuSK) protein naturally occur in mysathenia gravis patients should not qualify under *Mayo* for a patent monopoly.

Athena attempts to distinguish its patent claims by arguing that, because the labeled MuSK or antigenic MuSK fragment specified for the claimed methods does not occur in nature, they should not be considered "natural occurrences." (Opening Br. at 30 (citing *Myriad Genetics*, 569 U.S. at 594-95).) But the addition of a conventional label to man-made MuSK or an antigenic MuSK fragment merely makes it detectable; it does not, and indeed *must not*, change the fundamental property of the recognition and binding relationship between MuSK and MuSK antibodies. Without that specific binding relationship—whether MuSK is labeled or not—the claimed methods would not work. Furthermore, this antibody/antigen interaction is central to the

natural phenomenon being exploited by the conventional methods of the claim. For Athena's methods to work, the labeled MuSK or labeled fragment must *not* be "markedly different" from naturally-occurring MuSK. *See Myriad Genetics*, 569 U.S. at 590-91 (describing a laboratory made bacterium as having "markedly different characteristics from any found in nature"). Thus, the conventional labeling does not remove the subject matter of the claims from the realm of natural phenomena.

II. ALLOWING ATHENA'S CLAIMS WOULD UPSET THE PATENT BALANCE CAREFULLY STRUCK BY CONGRESS AND THIS COURT AND WOULD HARM LIFE SCIENCES RESEARCH AND PATIENT CARE

The Constitution requires that patents "promote the Progress of Science and useful Arts." U.S. Const. art. I, § 8, cl. 8. Fulfilling this constitutional purpose requires a balance between rewarding existing research and ensuring that other research may go forward freely in the future. Patents fundamentally balance free competition against government-granted exclusive rights. "The Patent Clause itself reflects a balance between the need to encourage innovation and the avoidance of monopolies which stifle competition without any concomitant advance in the 'Progress of

Science and useful Arts.'" *Eldred v. Ashcroft*, 537 U.S. 186, 215 (2003) (quoting *Bonito Boats, Inc. v. Thunder Craft Boats, Inc.*, 489 U.S. 141, 146 (1989).

The key to this balance is the recognition that there are interests in promoting innovation on both sides of any patent. As this Court stated in a different context in *Bonito Boats*, "[f]rom their inception, the federal patent laws have embodied a careful balance between the need to promote innovation and the recognition that imitation and refinement through imitation are both necessary to invention itself and the very lifeblood of a competitive economy." 489 U.S. at 146.

Allowing a patentee to remove a natural phenomenon from the public domain would thwart this constitutional purpose by impeding rather than promoting the progress of biomedical research and medical treatments. Without access to testing and observing natural phenomena, medical researchers cannot build upon the discoveries of others and doctors cannot treat their patients.

Allowing claims such as the ones at issue here would block medical information based on natural, biochemical relationships from appropriate further scientific use. This impediment is especially acute with respect to the information being tested in patients' blood. Disallowing claims such as those being asserted by Athena, by contrast, will cause little harm to scientific progress because a wide range of other appropriate claims would remain available to researchers like Respondent.

A. Allowing The Athena Patent To Stand Would Impede Future Biomedical Research And Treatment That Depends Upon Common Access To Natural Phenomena

Science has always proceeded in an incremental fashion as one discovery builds upon another. Experts in the scientific method have accordingly noted that scientific progress requires that research results be open for all to "use, attempt to replicate, and evaluate." U.S. Nat'l Research Council Comm. on Intellectual Prop. Rights in the Knowledge-Based Econ., *A Patent System for the 21st Century* 26 (Stephen A. Merrill, Richard C. Levin, & Mark B. Myers eds., 2004) (citing Robert K. Merton, *The Sociology of Science: Theoretical and Empirical Investigations* (1973)),

available at https://www.nap.edu/read/10976. This aspect of scientific progress would be impeded if patents could extend to natural phenomena. The United Kingdom Council of the Royal Society has drawn a parallel implication:

> [P]ure knowledge about the physical world should not be patentable under any circumstances. That it should be freely available to all is one of the fundamental principles of the culture of science. Only by having knowledge unencumbered by property rights can the scientific community disseminate information and take science forward.

Royal Soc'y Working Grp. on Intellectual Prop., *Keeping Science Open: The Effects of Intellectual Property Policing on the Conduct of Science* 8 (Apr. 2003), *available at* https://royalsociety.org/~/media/Royal_Society_Content/policy/publications/2003/9845.pdf.

Whatever the effect of the scope of patentability on scientific research in the past, however, these principles are critically important to the next generation of biomedical research. For example, the valuable nature of the information contained within the genetic code presented unique incentives to try to own natural phenomena—at least until the Supreme Court rejected the premise. *See Ass'n for Molecular Pathology v. Myriad Genetics,*

Inc., 569 U.S. 576, 596 (2013) ("We merely hold that genes and the information they encode are not patent eligible under § 101 simply because they have been isolated from the surrounding genetic material.")

Likewise, valuable blood-testing and related treatment of patients would be discouraged by allowing patent claims such as Athena's covering the most basic of medical practices—testing for specific autoantibodies—to be applied to newly discovered natural phenomena and diagnostic correlations.

ARUP itself publishes natural phenomena that its scientists discover in the course of their research and clinical testing.[2] These publications provide to the public domain information about the association of natural phenomena with a variety of diseases and disorders—associations that existed in nature but required the effort and creativity of ARUP scientists and others to find.

[2] *See, e.g.*, Marta Frigeni et al., *Functional and Molecular Studies in Primary Carnitine Deficiency*, 38 HUM. MUTATION 1684 (2017); Mark M. Kushnir et al., *LC-MS/MS Measurement of Parathyroid Hormone-Related Peptide*, 62 CLINICAL CHEMISTRY 218 (2016); Bucky K. Lozier et al., *Detection of Acetylcholine Receptor Modulating Antibodies by Flow Cytometry*, 143 AM. J. OF CLINICAL PATHOLOGY 186 (2015).

These discoveries allow for inventions to be created and for doctors to treat patients more effectively. Similarly, the tests that laboratories like ARUP run on patient samples measure the amount of drugs or biomarkers, or the presence of genetic conditions, in the body, all of which are natural phenomena. These associations, conditions, or relationships would exist in the patients whether or not the measurements took place.

In contrast, if claims like those asserted by Athena were allowed to stand, all such naturally occurring biochemical relationships would be subject to ownership rights on the part of the person who discovers them. For instance, if the effect of a drug in the body creates condition "X," the person who discovers this relationship might seek a patent covering all measurement of condition "X" or all evaluation of condition "X" by a doctor treating a patient. This is not a human-made invention, but a scientific discovery—and a patent to such a discovery would remove from the "storehouse of knowledge" that should be free for all to use. Patents that claim the underlying natural phenomena and biochemical relationships will greatly impede medical research

that builds upon the discovery of scientific facts.

For these reasons, there are special dangers in allowing only one laboratory or entity exclusive rights to the results of a natural phenomenon in the human body. Science will advance more rapidly, with greater benefits to patients, if laboratories may both compete and collaborate with one another through common access to laws of nature.

B. Rule 12 Invalidation Of Athena's Patent Neither Eliminates Incentives To Invest In Research Nor Disrupts The Patent System

Prior to *Mayo* and *Myriad,* the state of the law with respect to ownership of biochemical relationships was relatively unsettled. This resulted in a well-documented "land-grab" mentality, in which patent attorneys sought patents at the outer boundaries of the line between human invention and natural phenomena. This was not surprising, for without guidance about the scope of valid versus invalid subject matter, patent attorneys were obliged to seek the broadest possible claims for their clients. *See Solomon v. Kimberly-Clark Corp.*, 216 F.3d 1372, 1382 (Fed. Cir. 2000) ("A [patent] attorney's professional responsibility is to assist his or her

client in defining her invention to obtain, if possible, a valid patent with maximum coverage.").

But *Mayo* and *Myriad* have conclusively answered the question of patentability of naturally-occurring biological phenomena. Since these decisions, the U.S. Patent and Trademark Office and the courts have applied them carefully. Patent rejections citing these cases now hover above 10% of all rejections per year. James Cosgrove, *Evaluating the Lasting Impact of Mayo/Myriad*, JURISTAT BLOG (Sept. 6, 2017), https://blog.juristat.com/2017/9/6/evaluating-the-lasting-impact-of-mayomyriad. And courts increasingly have begun to hear and decide early subject-matter-ineligibility motions to dismiss. *See* Stephen A. Marshall, *The* Alice-*Effect: An Empirical Study of Section 101 Motion Practice*, FISH & RICHARDSON BLOG (Mar. 9, 2016), https://www.fr.com/fish-litigation/the-alice-effect-an-empirical-study-of-section-101-motion-practice/.

In this milieu, early motions to dismiss premised on subject-matter ineligibility have become commonplace, and have often been affirmed. Just last year, this Court addressed a diagnostic

patent related to detecting biomarkers and correlating them with cardiovascular health. *See Cleveland Clinic Found. v. True Health Diagnostics LLC*, 859 F.3d 1352 (Fed. Cir. 2017). This Court summarily rejected petitioner's procedural objection—that the district court had invalidated the patent too early—as unpersuasive. *Id.* at 1360. Collecting cases, this Court explained:

> [W]e have repeatedly affirmed § 101 rejections at the motion to dismiss stage, before claim construction or significant discovery has commenced. . . . In any event, Cleveland Clinic provided no proposed construction of any terms or proposed expert testimony that would change the § 101 analysis. Accordingly, it was appropriate for the district court to determine that the testing patents were ineligible under § 101 at the motion to dismiss stage.

Id. (citations omitted). The same reasoning applies here. Moreover, the issuance of such early dismissals reduces litigation costs and the burden on the courts, the parties, and all third parties—including diagnostic laboratories and patients themselves—otherwise subject to an improper monopoly.

Far from harming innovation, these increased Patent Office rejections and early-stage ineligibility dismissals have benefited it. Although naturally occurring phenomena are unprotectable,

nothing impedes the protection of new *applications* of laws of nature, such as development of new drugs, new methods of treatment, new molecular reagents, or new instruments that utilize a law of nature. Thus, the scope of patentable subject matter still may legitimately extend to innovative tests, or to inventive pharmaceutical compositions, or to new and useful therapies, or to any number of inventions in technology that researchers have yet to imagine, which add human invention to a natural phenomenon.

As Justice Breyer pointed out in dissent from dismissal in *Laboratory Corporation of America Holdings v. Metabolite Laboratories, Inc.*, 548 U.S. 124 (2006) ("*LabCorp*"), the justification for the longstanding principle of denying patentability to a natural phenomenon is that too much patent protection can impede scientific progress, and that fundamental scientific principles are "part of the storehouse of knowledge" available to all. *Id.* at 127-28 (Breyer, J., dissenting from dismissal of writ as improvidently granted) (quoting *Funk Bros.,* 333 U.S. at 130). The Supreme Court's recent reiteration of the

limitations on naturally occurring biological phenomena have enabled ARUP to invest in a wider range of tests knowing that the courts have ruled that natural phenomena cannot be patented and removed from the public domain—thereby removing potential litigation threats. This has allowed ARUP to offer higher-quality patient care. Across the United States, as ARUP has experienced, competition has increased as more diagnostic companies and laboratories can likewise offer the same tests. In a nation where increasing health care costs are a persistent concern, the newfound certainty surrounding the freedom to test certain biological phenomena has provided a bright spot for ARUP's provision of cost-effective patient care.

CONCLUSION

For all these reasons and those set forth in Mayo's brief, the Court should affirm the judgment.

Dated: February 6, 2018

Respectfully submitted,

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CERTIFICATE OF SERVICE

I hereby certify that on February 6, 2018, I filed the foregoing Brief Of Amicus Curiae ARUP Laboratories, Inc. In Support Of Defendant-Appellee with the Clerk of the Court by using the CM/ECF system. All participants in the case are registered CM/ECF users, and service will be accomplished by the CM/ECF system.

/s/ *Kathleen M. Sullivan*
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CERTIFICATE OF COMPLIANCE

This brief complies with the type-volume limitation of Fed. R. App. P. 29(a)(5) because it contains 3,439 words, excluding the exempted portions.

This brief complies with the typeface and type style requirements of Federal Rules of Appellate Procedure 32(a)(5) and 32(a)(6) because it has been prepared in a proportionally spaced typeface using Microsoft Office Word 2013 in 14-point Century Schoolbook font.

Dated: February 6, 2018

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