No. 09-490

In The
Supreme Court of the United States

MAYO COLLABORATIVE SERVICES
(D/B/A MAYO MEDICAL LABORATORIES)
AND MAYO CLINIC ROCHESTER,

Petitioners,

v.

PROMETHEUS LABORATORIES, INC.,

Respondent.

On Petition For Writ Of Certiorari To The United States Court Of Appeals For The Federal Circuit

BRIEF OF *AMICI CURIAE* THE AMERICAN COLLEGE OF MEDICAL GENETICS, THE AMERICAN SOCIETY OF HUMAN GENETICS, THE ASSOCIATION OF PROFESSORS OF HUMAN AND MEDICAL GENETICS, THE ASSOCIATION FOR MOLECULAR PATHOLOGY, AND THE COLLEGE OF AMERICAN PATHOLOGISTS IN SUPPORT OF PETITIONERS

KATHERINE J. STRANDBURG
Professor of Law
NEW YORK UNIVERSITY SCHOOL OF LAW
40 Washington Square South
New York, NY 10012
(212) 998-6269

COCKLE LAW BRIEF PRINTING CO. (800) 225-6964
OR CALL COLLECT (402) 342-2831

Blank Page

TABLE OF CONTENTS

TABLE OF AUTHORITIES

TABLE OF AUTHORITIES – Continued

Blank Page

INTEREST OF THE *AMICI CURIAE*

Amici curiae The American College of Medical Genetics, The American Society for Human Genetics, The Association of Professors of Human and Medical Genetics, The Association for Molecular Pathology, and The College of American Pathologists respectfully submit this brief in support of petitioners Mayo Collaborative Services (d/b/a Mayo Medical Laboratories) and Mayo Clinic Rochester (collectively "Mayo") encouraging the grant of a writ of *certiorari* to review the judgment of the United States Court of Appeals for the Federal Circuit, because that judgment stems from an interpretation of patentable subject matter that is inconsistent with this Court's precedent and with public policy regarding both innovation and health care.[1]

Amici are associations of physicians, medical educators, and other providers of healthcare-related services. *Amici* are greatly concerned with the potential impact of the Federal Circuit's decision to allow patenting of claims to natural phenomena such as the correlations covered by Prometheus's patents. Such

---

[1] The parties have consented to the filing of this brief. Counsel of record for all parties received notice at least 10 days prior to the due date of the *amici curiae*'s intention to file this brief. No counsel for a party authored this brief in whole or in part, and no counsel or party made a monetary contribution intended to fund the preparation or submission of this brief. No person other than *amici curiae* and their members or their counsel made a monetary contribution to its preparation or submission.

patents have great potential to impede the practice of medicine and raise the costs of medical treatment.

The American College of Medical Genetics (ACMG) is a private, non-profit, voluntary organization of clinical and laboratory geneticists. The Fellows of the ACMG are doctoral level medical geneticists and other physicians involved in the practice of medical genetics. With more than 1,300 members, the ACMG's mission is to improve health through the practice of Medical Genetics. In order to fulfill this mission, the ACMG strives to: 1) define and promote excellence in medical genetics practice and the integration of translational research into practice; 2) promote and provide medical genetics education; 3) increase access to medical genetics services and integrate genetics into patient care; and 4) advocate for and represent providers of medical genetics services and their patients. The position of the ACMG is that observations of naturally occurring correlations should not, in and of themselves, be patentable.

The American Society of Human Genetics (ASHG), founded in 1948, is the primary professional membership organization for human genetics specialists worldwide. It is a private, non-profit organization. The Society's nearly 8,000 members include researchers, academicians, clinicians, laboratory practice professionals, genetic counselors, nurses, and others who have a special interest in the field of human genetics. ASHG serves research scientists, health professionals, and the public by providing forums to: 1) share research results at annual meetings and in *The*

American Journal of Human Genetics; 2) advance genetic research by advocating for research support; 3) enhance genetics education by preparing future professionals and informing the public; and 4) promote genetic services and support responsible social and scientific policies.

The Association of Professors of Human and Medical Genetics (APHMG) is a non-profit organization that promotes human and medical genetics educational programs in North American medical and graduate schools. Currently, more than 90 medical and graduate schools are members. The APHMG represents the faculty that teach human and medical genetics to virtually all medical students in North America. As educators, they teach medical students to think about, diagnose and treat genetic diseases. It is the APHMG's position that all physicians must be free to think broadly, creatively, analytically and without fear that they risk infringing a patent merely by *thinking* about the relationship between certain treatments and their potential metabolic and clinical sequelae.

The Association for Molecular Pathology (AMP) is an international medical professional association representing approximately 1,600 physicians, doctoral scientists, and medical technologists who perform laboratory testing based on knowledge derived from molecular biology, genetics and genomics. The AMP is dedicated to the development and implementation of molecular diagnostic testing, which includes genetic testing in all of its definitions, in a

manner consistent with the highest standards established by CLIA, CAP, the ACMG and the FDA. AMP members practice their specialty in widely diverse settings, including academic medical centers, independent medical laboratories, community hospitals, federal and state health laboratories and the *in vitro* diagnostic industry, and are involved in every aspect of molecular diagnostic testing. AMP provides national leadership for the advancement of safe and effective practice and education for molecular diagnostic testing.

The College of American Pathologists (CAP) is the world's largest medical society, composed exclusively of pathologists, with nearly 17,000 members. Pathologists are physicians who examine tissues, blood, and other body fluids for the purposes of medical diagnosis and patient care. Through its accreditation and proficiency testing programs, the CAP is also a leader in assuring the quality of laboratory testing. More than 6,000 laboratories are accredited by the CAP and approximately 23,000 laboratories are enrolled in the College's proficiency testing programs.

SUMMARY OF ARGUMENT

New drugs and new tools for diagnosing illness and monitoring treatment are critical to the advancement of medicine. *Amici* medical associations do not dispute that patents on healthcare-related technologies

can enhance the provision of high-quality and cost-effective medical care. The patents at issue in this case, however, do not claim innovative drugs or diagnostic tools. Instead, these patents grant exclusive rights over the mere recognition that there is a natural statistical correlation between certain metabolite levels in the body, as measured by well-known means, and the potential toxicity and effectiveness of a well-known drug. Anyone who tests the metabolite level after the drug is administered and thus is "warned" that it might be advisable to adjust the dosage is an infringer.

If these claims to the body's natural responses to illness and medical treatment are permitted to stand, there will be an unlimited potential for exclusive rights in the use of scientific data that is critical to and must be widely available for providing sound medical care. Patent licenses increasingly will be required for physicians even to consider newly discovered implications of well-established diagnostic tests, and laboratories will risk indirect infringement merely by educating doctors about those implications. It is hard to imagine how the medical diagnostic community will continue to serve the goal of quality patient care and how physicians will continue to practice medicine in an ethical and effective manner under such a regime.

Moreover, the claims at issue are not directed to patentable subject matter. These claims run afoul of this Court's longstanding prohibition on the patenting of "laws of nature, natural phenomena, [or] abstract

ideas," under Section 101 of the Patent Act. *Diamond v. Diehr*, 450 U.S. 175, 185 (1981) (citing *Parker v. Flook*, 437 U.S. 584, 593 (1978) and *Gottschalk v. Benson*, 409 U.S. 63, 67 (1972)). As the district court recognized, the claims "wholly preempt" the natural relationship between the levels of the metabolites 6-TG and 6-MMP in the human body and the likelihood of therapeutic efficacy and toxicity of thiopurine drugs. *Prometheus Labs., Inc. v. Mayo Collaborative Servs.*, No. 04-CV-1200, 2008 WL 878910 at *10 (S.D. Cal. Mar. 28, 2008), citing *Benson*, 409 U.S. 71-72.

The Federal Circuit erred in finding that Prometheus's claims encompass patentable subject matter. It applied a "machine or transformation of matter" test developed in *In re Bilski*, 545 F.3d 943 (Fed. Cir. 2008), which is currently under review by this Court. *Bilski v. Kappos*, 129 S. Ct. 2735 (2009) (granting *certiorari*). Whatever this Court decides about the applicability of that test in *Bilski*'s business method context, the test is clearly inapposite for determining whether a patent claim preempts a natural phenomenon or scientific principle. Whether a natural phenomenon involves a "transformation of matter" cannot determine its eligibility for patenting, or virtually every natural phenomenon could be patentable.

The patentability of claims like those at issue here is an issue of great consequence for the future of health care in the United States. This Court's ruling in *Bilski* is unlikely to resolve the distinct and significant questions about the patentability of

natural phenomena presented in this case. A grant of *certiorari* would be both appropriate and timely.

ARGUMENT

I. Health Care Policy is Best Served by This Court's Well-Established Limits on Patentable Subject Matter, Which Preclude Patents Claiming Observations of Natural Phenomena

The scope of patentable subject matter established by Congress in the Patent Act,[2] although quite broad, does not extend to scientific facts or observations of natural phenomena. *Diamond v. Diehr*, 450 U.S. 175, 185 (1981) (citing *Parker v. Flook*, 437 U.S. 584, 593 (1978) and *Gottschalk v. Benson*, 409 U.S. 63, 67 (1972)). The patents at issue here give Prometheus exclusive private ownership not of a new drug, a new diagnostic test, or even a new method of diagnosing a particular disease. Rather, the patents at issue improperly award Prometheus exclusive ownership of the mere *observation* of a naturally-occurring phenomenon: the correlation between the levels of certain metabolites produced naturally in the human body in response to administration of certain doses of thiopurine drugs and the efficacy and toxicity of those drugs.

[2] 35 U.S.C. § 101.

The potential ramifications of the Federal Circuit's ruling that such claims are patentable are profound and sobering. By observing a previously unknown correlation between obesity and illness, for example, a researcher could obtain a patent on the process of having a patient step on a scale and then thinking about whether to recommend that the patient diet to lose weight. Any entity that made or sold scales and dared to mention that correlation in a brochure might then be liable for intentionally inducing infringement. An observation that some patients tend to run a fever if given too much of a particular drug could lead to a patent on taking a patient's temperature and considering whether to raise or lower the dosage. Patients, physicians and fever thermometer manufacturers might directly or indirectly infringe because the thermometer reading "warned" that it might be advisable to adjust the dosage.

Such results are unthinkable, yet they are eminently plausible extensions of the Federal Circuit's ruling that the claims in this case constitute patentable subject matter. *Amici* medical associations recognize that healthcare-related patents can enhance the provision of high-quality and cost-effective medical care. The financial incentive that patents offer supports the expensive and uncertain research required to identify, test and gain approval for new pharmaceuticals, medical devices, diagnostic testing kits and other products. In this respect, the patent

system has served patients and the medical profession well.

Patents on scientific observations underlying medical care, however, do not have these salutary effects. Such patents raise ethical concerns for physicians, threaten to stifle innovation and raise the costs of medical treatment, and erode the quality of patient care by limiting the knowledge physicians may use to diagnose and treat their patients.

A. Patents on Scientific Observations Raise Ethical Concerns for Physicians

Physicians have longstanding ethical obligations to advance and share useful medical knowledge with patients and other physicians. Principle V of the AMA's Principles of Medical Ethics states, "[a] physician shall continue to study, apply, and advance scientific knowledge," and "make relevant information available to patients, colleagues, and the public. . . ."[3] Opinion 9.08 of the Code of Medical Ethics of the AMA elaborates upon this basic principle:

> Physicians have an obligation to share their knowledge and skills and to report the results of clinical and laboratory research. . . . The intentional withholding of new medical

[3] Available at http://www.ama-assn.org/ama/pub/physician-resources/medical-ethics/code-medical-ethics/principles-medical-ethics.shtml (last visited November 19, 2009).

> knowledge, skills, and techniques from colleagues for reasons of personal gain is detrimental to the medical profession and to society and is to be condemned.[4]

Discovery of a basic scientific principle that could be useful to others in devising medical applications or to physicians in reaching diagnoses and treating patients is a quintessential example of the kind of medical knowledge that physicians are obliged freely to share.[5] To interpret the patent laws to make scientific observations eligible for patent protection threatens to undermine, rather than promote, the ethical practice of medicine.

Indeed, physicians have an ethical obligation to consider the most up-to-date scientific information available when treating their patients. Measurements and observations such as those at issue here are part of the broader clinical evaluation that physicians must undertake when treating patients. It is part of the practice of medicine – indeed, it is essential to meet appropriate medical standards of care – for physicians to monitor metabolite levels and

---

[4] Available at http://www.ama-assn.org/ama/pub/physician-resources/medical-ethics/code-medical-ethics/opinion908.shtml (last visited November 19, 2009).

[5] A similar argument was made in the *amicus* brief of the American Medical Association, The American College of Medical Genetics, The American Society of Human Genetics, The Association of Professors of Human and Medical Genetics, and Mayo Clinic in Support of Respondents before this Court in *Bilski*. *Amicus* brief in *Bilski v. Kappos*, No. 08-964, filed Oct. 2, 2009.

to use those levels, along with other laboratory and clinical parameters, to guide dosage adjustments and, thereby, to provide necessary and appropriate medical care for their patients.

B. Patents on Scientific Observations Threaten to Stifle Innovation, Including the Development of Personalized Medicine, and to Increase Health Care Costs Significantly

Basic scientific facts "are part of the storehouse of knowledge of all men." *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127, 130 (1948). Ensuring wide dissemination and free access to such facts is essential to scientific progress. Ready access to basic facts, such as a relationship between levels of drug metabolites and the drug's efficacy and toxicity, is essential to medical research. These patentees are neither the first nor the last to consider the implications of these particular metabolite levels for human health. Pet. 4. Disclosure of the correlations between these metabolites and drug efficacy and toxicity creates incentives for laboratories, such as Mayo, to compete to develop fast and inexpensive ways of testing for the metabolites and for researchers, such as Dr. El-Azhary, to study similar correlations. Pet. 7. However, a patent that covers a mere "warning" to a physician that he or she might want to adjust the dosage of the associated drug will "shut[] the door" to the development or use of such new tests, and discourage further research and

development. *O'Reilly v. Morse*, 56 U.S. 62, 113 (1853).

Patents on scientific observations, such as the statistical correlations involved here, would stifle rather than incentivize developments in medicine, including those in personalized medicine. Such patents, which do not cover inventive diagnostic tests but instead seek to preempt the scientific observations underlying proper diagnosis, threaten to slow the development of diagnostic testing and undermine competition to provide inexpensive and high quality testing, leading inevitably to higher-priced medical treatment.

Moreover, there is no need for patents to incentivize physicians to study the kinds of clinical correlations at issue in this case. Indeed, a recent report by the Secretary's Advisory Committee on Genetics, Health, and Society found that patents "do not serve as powerful incentives for either genetics research in the diagnostic arena or the development of genetic tests."[6] On the contrary, when knowledge of such correlations is freely available there is enormous incentive for physicians to *make use of them* to provide necessary and appropriate care for their patients.

---

[6] Secretary's Advisory Committee on Genetics, Health, and Society, *Public Consultation Draft Report on Gene Patents and Licensing Practices and Their Impact on Patient Access to Genetic Tests* at 110 (March 9, 2009), available at http://oba.od.nih.gov/oba/SACGHS/SACGHS%20Patents%20Consultation%20Draft%203%209%202009.pdf (last visited November 24, 2009).

C. Patents on Scientific Observations Erode Doctors' Ability to Provide Quality Patient Care

Quality patient care demands that a physician consider test results in light of, among other things, current medical knowledge. Prometheus argued below that a doctor infringes by thinking about the correlation between dosage efficacy and toxicity after receiving results of a metabolite test *even if the test was ordered for a reason other than a desire to adjust dosage in light of the limits set out in the patent claims*. Pet. 8. There can be no design around a scientific fact. A physician who learns – from the medical literature, colleagues, continuing medical education or elsewhere – of the statistical correlation between metabolite levels and drug efficacy and toxicity cannot – and should not – put that knowledge out of mind.

If the claims at issue here were properly patentable, a laboratory might induce infringement simply by informing a doctor of the correlation in conjunction with delivery of test results or perhaps even by publishing articles or brochures discussing the correlation. Indeed, confronting very similar facts in *Metabolite Labs. Inc. v. Lab. Corp. of Am. Holdings*, 370 F.3d 1354 (Fed. Cir. 2004), the Federal Circuit found that the defendant laboratory had induced infringement through the publication of medical articles. *Id.* at 1365. If patent licenses are required for physicians merely to *consider* newly discovered implications of well-established diagnostic

tests and if laboratories become indirect infringers merely by educating doctors about those implications, it is hard to imagine how medical diagnostics will continue to serve the goal of quality patient care.

II. Because the Claims Asserted in this Case Impermissibly Preempt Natural Phenomena, the Ruling Below is Inconsistent with this Court's Precedent

Essentially, the claims at issue here seek to patent the statistical observation that some doses of thiopurine drugs tend to be too high for some patients and some tend to be too low. These claims run afoul of time-honored prohibitions on patenting "laws of nature, natural phenomena, [or] abstract ideas," *Diamond v. Diehr*, 450 U.S. 175, 185 (1981) (citing *Parker v. Flook*, 437 U.S. 584, 593 (1978) and *Gottschalk v. Benson*, 409 U.S. 63, 67 (1972)), because they "wholly preempt" the natural relationship between the level of the metabolites 6-TG and 6-MMP in the human body and the likelihood of therapeutic efficacy and toxicity of thiopurine drugs. *Prometheus*, 2008 WL 878910 at *10, citing *Benson*, 409 U.S. at 71-72.

The argument that the observed correlations between metabolite level and drug toxicity and efficacy are patentable because the metabolites are by-products of a synthetic drug is inconsistent with precedent and would lead to absurd results. In patent law, "natural" means "nature's handiwork" as

generally juxtaposed with the products of human agency and ingenuity. *Diamond v. Chakrabarty*, 447 U.S. 303, 310 (1980); *Flook*, 437 U.S. at 591-94. Thiopurine drugs are man-made compositions of matter, undeniably patentable under Section 101. A natural response to a man-made invention, however, has never been patentable. In *Funk Brothers*, for example, the patentee combined laboratory cultures of selected bacteria to form an "inoculant" that assisted nitrogen fixation in plants. *Funk Bros.*, 333 U.S. at 129. Despite the human effort required to select, culture and combine the bacteria, this Court found the mixture unpatentable because the mutual non-inhibition of nitrogen fixing properties was a natural response to being combined. Though the combination was artificial, the bacteria "serve[d] the ends nature originally provided and act[ed] quite independently of any effort of the patentee." *Id.* at 131.

This distinction between a man-made product and its natural behavior has long been recognized. In *O'Reilly v. Morse*, for example, this Court discussed the English case, *Neilson v. Harford*, 151 E.R. 1266 (1841), and distinguished between the unpatentable "principle that hot air will promote the ignition of fuel better than cold" and the patentable invention of a mechanical apparatus for supplying hot air. *O'Reilly*, 56 U.S. at 114-16. Any invention involving igniting fuel in a furnace is in some sense synthetic, yet that fact would not have rendered patentable a claim to the principle of using hot air to aid ignition. Nor did

the fact that printing characters at a distance is a human endeavor save a claim to the basic scientific concept of using "the motive power of the electric or galvanic current" to make such characters. *Id.* at 119.

The district court in this case correctly concluded that "the relevant inquiry is whether the correlations are 'man-made,' not whether a man-made drug was used to produce the correlation." *Prometheus*, 2008 WL 878910 at *9. The claimed correlations between drug metabolite levels and drug toxicity and efficacy are natural phenomena. Nothing in the claims purports to affect the way in which a patient's body responds to the administration of the medications: the phenomena are merely observed.

Because the claimed statistical correlations are natural phenomena, they are unpatentable, since they wholly preempt every substantial use of those correlations. The claims cover every instance in which anyone considers whether to adjust thiopurine drug dosage in light of the metabolite level measurements. *Id.* at *10.

The Federal Circuit fails to undertake this fundamental "natural phenomena" inquiry and instead applies its inapposite "machine or transformation of matter" test, *Prometheus*, 581 F.3d at 1346, which may be relevant to determining whether a patent claims merely an abstract idea, *Bilski*, 545 F.3d at 961, but is not useful in determining whether a claim preempts a natural phenomenon. Photosynthesis, the freezing of water into ice and its

evaporation into steam, the rusting of iron – all involve transformations of matter, but are unpatentable unless they are part of an invention that does not preempt the phenomenon.

This Court should clarify that, whatever the applicability of the machine or transformation of matter test in determining the patentability of claims to business methods or similar processes, *Bilski*, 545 F.3d at 962, the Federal Circuit erred in employing it as the "definitive test" for patentable subject matter where the issue is whether a claim preempts a natural phenomenon. *Prometheus*, 581 F.3d at 1342.

III. The Issue Raised in this Case is of Great Importance and is Unlikely to be Resolved by this Court in *Bilski*

As argued throughout this brief, the potential for patents that preempt natural phenomena to interfere with the ethical and effective practice of medicine and with the improvement of health care through advances in diagnostic testing is a very serious matter. Exclusive rights to fundamental information about scientific correlations are liable to raise the cost of medical care prohibitively without compensating benefits to medical research. As health care professionals, we believe that patients are served best by the free and broad dissemination of scientific information that is relevant to providing better and more personalized health care treatments. If this Court lets the Federal Circuit's ruling stand, patients,

physicians and laboratory service providers will become entangled in a growing thicket of patents on basic diagnostic information to the detriment of the nation's health.

This Court granted *certiorari* to address this issue in *Lab. Corp. v. Metabolite*, though *certiorari* was later dismissed as improvidently granted because the patentable subject matter issue was not properly considered by the lower courts. *Lab. Corp. of Am. Holdings v. Metabolite Labs., Inc.*, 548 U.S. 124, 133 (2006) (Breyer, J., dissenting). Here, in contrast, this Court has the benefit of full exploration of the issue in a considered district court opinion and a Federal Circuit opinion, which was informed by extensive briefing by both parties and numerous *amici*.

In *Bilski*, this Court is currently reviewing the Federal Circuit's "machine or transformation of matter" test for patentable subject matter. This Court's opinion in that case will no doubt be relevant to patentable subject matter disputes concerning diagnostic tests and procedures. Nonetheless, we believe that the patent claims at issue in this case raise important questions concerning the patentability of natural phenomena and scientific correlations that have not been aired in *Bilski* because of its focus on the appropriate standard of patentability for business methods and similar processes. We thus contend that this case warrants the separate attention of this Court.

CONCLUSION

For the foregoing reasons, the petition for writ of *certiorari* should be granted. At a minimum, however, we support the Petitioner's request for remand for reconsideration in light of this Court's decision in *Bilski*.

Respectfully submitted,

KATHERINE J. STRANDBURG
Professor of Law
NEW YORK UNIVERSITY SCHOOL OF LAW
40 Washington Square South
New York, NY 10012
(212) 998-6269

Blank Page