INTEREST OF AMICUS CURIAE[1]

Knowledge Ecology International ("KEI") is an international nonprofit, nongovernmental organization that searches for better outcomes, including new solutions, to the management of knowledge resources. In particular, KEI is focused on the management of these resources in the context of social justice. KEI is drawn to areas where current business models and practices by businesses, governments or other actors fail to adequately address social needs or where there are opportunities for substantial improvements. Among other areas, KEI has expertise in policies of both innovation in, and access to, medicines and medical technologies.

KEI is concerned about the implications of the Federal Circuit decision in the present case because of the far-reaching consequences for the future of patent law, innovation and the affordability of and access to medical technologies. As an advocate of new incentive and financing models for biomedical innovation and the proponent of several mechanisms for stimulating investments and promoting innovation outside of the patent regime, KEI has concerns that the Federal Circuit decision in the present case was incorrectly decided to the lower court's failure to take into account non-patent

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[1] The parties have consented to the filing of this brief. Petitioners have lodged blanket consent to the filing of all *amicus* briefs. Respondent's consent to the filing of this amicus brief has been filed with the Clerk of Court. No counsel representing any party to the case authored this brief in whole or in part and no counsel or party made any monetary contribution to the preparation or submission of the brief.

mechanisms to support and reward investments in the development of new products.

SUMMARY OF THE ARGUMENT

The present case involves the patenting of human genes and isolated DNA. While the Constitution sets forth the rationale for the patent system, that is to promote the progress of science, blocking patents on products of nature have been granted by the United States Patent and Trademark. Human genes represent products of nature and their functions represent laws of nature. Their status as products of nature mean that they cannot be invented around and patents on such products preempt other uses, foreclosing further research and development, thereby hindering the progress of science. This Court has repeatedly rejected products of nature from the scope of patent-eligible subject matter because of their tendency to inhibit their use in making further discoveries and human genes should not be exempted from such exclusions.

Although proponents of liberal standards of patentability argue that patents are necessary to induce investments, such arguments ignore the numerous alternative, non-patent mechanisms that exist to reward investments into research and development. These alternative mechanisms are often used where patents represent and inappropriate or burdensome reward.

By design, gene patents are used to block secondary testing as well as research and

development on diseases or diagnostics related to the patented sequences. The negative impact of patents has been justified on the ground that they are the only instrument that can adequately protect investments in research and development for new medical technologies. This assumption is false and a wide range of public policy instruments that are either currently in use, or have been proposed, to stimulate research and development for new medical products.

As diagnostics and personalized medicine become an increasingly important part of medical treatment, the freedom to undertake research and development on new tools is critical, as are the prices to the end users. If the Federal Circuit decision permitting patents on human genes stands, the proliferation of patents on genes will reduce the pace of research and narrow the direction of innovation which will, in turn, lead to high prices for patented technologies. Ultimately, allowing patents on human genes will negatively impact patients and treatment options, as well as future innovation.

ARGUMENT

I. PATENTING OF GENES IMPEDES THE CONSTITUTIONAL RATIONALE OF THE PATENT SYSTEM TO PROMOTE THE PROGRESS OF SCIENCE AND ALSO HARMS PUBLIC HEALTH.

The Constitution sets the basis for allowing Congress to create laws that permit limited time

monopolies over their inventions. The rationale for permitting such monopolies is to "promote the Progress of Science and useful Arts." U.S. CONST. art. 1, §8, cl. 8. The purpose of a patent, then, is to advance scientific progress; the "embarrassment of an exclusive patent" is justified only because such monopolies serve the "benefit of society." *Graham v. John Deere Co.*, 383 U.S. 1, 7-10 (1966) (*quoting* Thomas Jefferson (internal citations omitted)).

While the Constitution grants Congress the authority to create patent laws, it also sets limits prohibiting the "overreach [of] the restraints imposed by the stated constitutional purposes." *John Deere Co.* at 6. This Court has specifically declared the Constitutional provision to be a "limitation. This qualified authority . . . is limited to the promotion of advances in the useful arts" and discoveries that do not promote the progress of science cannot be permitted. *Id.* It is critical to keep the Constitutional rationale of the patent system in mind and remember the limitations it sets in order to ensure the patent system does not improperly overreach and impede further research and development.

A. Products of Nature, Laws of Nature and Natural Phenomena, Such as the Human Genes, Are Not Patent-Eligible Because They Impede Innovation Rather than Promote It.

This Court, in applying Section 101 of the Patent Act to compositions of matter, has long held

that three specific types of claims are categorically removed from patent eligibility. *Diamond v. Chakrabarty*, 447 U.S. 303, 309 (1980). These claims include "laws of nature, physical phenomena, and abstract ideas." *Id*. *See also Diamond v. Diehr*, 450 U.S. 175, 185 (1981); *Parker v. Flook* , 437 U.S. 584 (1978); *Gottschalk v. Benson*, 409 U.S. 67 (1972) *Funk Bros. Seeds Co. v. Kalo Co.*, 333 U.S. 127 (1948); *O'Reilly v. Morse*, 56 U.S. 112, 121 (1854); *LeRoy v. Tatham*, 55 U.S. 175 (1853). More recently, this Court reaffirmed these "long held" exclusions in *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, 566 U.S. __ , 132 S.Ct. 1289, 1293 (2012) (citations omitted). In eliminating these types of discoveries from patent protection, the Court notes their status as "basic tools of scientific and technological work" and that monopolization of such tools "might tend to impede innovation more than it would tend to promote it." *Id*.

In addition to excluding these broad categories from patentability, this Court has also made specific exclusions. For example, wood pulp and paper pulp were denied patent protection because they were known to be in existence prior to the patent claims. *American Wood Paper Co. v. Fiber Disintegrating Co.*, 90 U.S. 566 (1874). Relying on such jurisprudence, lower federal courts have made similar exclusions from patentability, particularly for materials or objects in merely purified form or that are obtained through extraction without further human processing. Lower courts have excluded from patentability purified uranium, *In re Marden*, 47 F.2d 957 (C.C.P.A. 1931), purified vanadium, *In re*

Marden, 47 F.2d 958 (C.C.P.A. 1931), purified tungsten, *Gen. Elec. Co. v. De Forest Radio Co.*, 28 F.2d 641 (3d Cir. 1928) and vitamin C purified from lemon juice, *In re King*, 107 F.2d 618 (C.C.P.A. 1939). In the aggregate, these cases demonstrate an exclusion of naturally occurring substances from patent eligibility.

The claims-at-issue in the particular case involve purified or isolated DNA. In other words, they represent products that are merely naturally occurring phenomena that have been obtained through extraction and not unlike the long line of cases rejecting such discoveries from patentability. While extraction requires human effort, such as the case with isolated DNA, such effort does not change the characteristic of the claims as non-patentable products of nature. The isolated BRCA genes are not markedly different from those found in nature and therefore not patentable. The limitation contained in the United States' patent system that excludes products of nature from patent protection serves to ensure that the Constitutional rationale for intellectual property is served: to promote the progress of science and the useful arts.

B. Where Patent Protection Improperly Preempts All Other Uses, the Progress of Science is Hindered and the Constitutional Rationale for Patents is Impeded

Preemption plays a critical role in determining whether a patent will promote or hinder the progress

of science. This Court has therefore found that patents may not be granted where the effect of such a monopoly would "remove existent knowledge from the public domain, or to restrict free access to materials already available." *Graham v. John Deere Co.*, 383 U.S. 1, 5-6 (1966). Mere discovery of a naturally occurring substance, therefore, cannot receive patent protection. *Diamond v. Chakrabarty*, 447 U.S. 303, 312-13 (1980). Patented products of nature tend to be impossible to invent around and preempt all other uses. As such, they represents "manifestations of . . . nature, free to all men and reserved exclusively to none." *Id*. at 309 (citing *Funk Bros.*, 333 U.S. 130 (internal quotations omitted)).

In affirming the rejection of laws of nature, natural phenomena and abstract ideas from patentability, this Court has noted that permitting patents on such "basic tools" would run the "danger that the grant of patents that tie up their use will inhibit future innovation premised upon them." *Mayo v. Prometheus*, 566 U.S. __, 132 S.Ct. 1289, 1293 (2012)Where patents "tie up too much future use of laws of nature," monopoly protection cannot be afforded to such objects. *Id*. at 1302.

Monopolies prohibiting all others from creating the same effect or process by any other means discourages scientific progress, contravening the purpose of the patent system. *LeRoy v. Tatham*, 55 U.S. 156, 175 (1853). Preemption remains an important factor in determining the scope of patentability under Section 101 of the Patent Act. *See Bilski v. Kappos*, 130 S.Ct. 3218 (2010).

In the present case, patent protection on the BRCA genes completely forecloses and preempts all other uses, thereby contravening the purpose of the patent system. Patents on human DNA have been called "blocking" patents that represent "unnecessary toll booths on the road to discovery." Alan E. Guttmacher, et. al., *Genomic Medicine—A Primer*, 347 NEW. ENG. J. MED. 1512, 1514 (2002). Human genes, like other products of nature, are extremely difficult, if not impossible, to invent around. *See* Isabelle Huys, et. al., *Legal Uncertainty in the Area of Genetic Diagnostic Testing*, 27 NATURE BIOTECHNOLOGY 903, 907 (2009). Human genes are obvious products of nature, their functions represent laws of nature, and this Court has repeatedly rejected patentability of such objects because of "a concern that patent law not inhibit further discovery by improperly tying up the future use of laws of nature." *Prometheus v. Mayo*, 566 U.S. __, 132 S.Ct. 1289, 1301 (2012). Gene patents thus completely foreclose future research on the effects of the DNA sequences and scientists cannot conduct research on the naturally occurring gene. Patent protection therefore should not extend to isolated DNA.

C. Patenting of Human Genes Harms Genetic Research, Medical Innovations and the Future of Public Health.

The patenting of human genes tends to foreclose future research on the gene and also hinders alternative testing for BRCA mutations.

Scientists and researchers have expressed reluctance to conduct research and development where patents on genes exist because of the fear of possible patent infringement suits. As a result, research on the diseases associated with the genes and development of better diagnostic testing is likely to be forestalled.

Patients will, predictably, face harm as a result of the Federal Circuit ruling. Myriad is currently the sole provider of diagnostic testing for mutations of the BRCA1 and BRCA2 genes and can therefore charge a monopoly price. Some insurance companies do not cover the test and patients must then decide whether to pay the high monopoly price of more than $3,000 or forego the diagnostic. Myriad's monopoly over the genes prevent second opinion testing.

In addition to placing a high price on its diagnostic test, Myriad's exclusive monopoly over the genes prohibits all research on the BRCA1 and BRCA2 genes. Patients are benefited from continued research and development to improve diagnostic testing. In fact, Myriad's test was shown to have a twelve-percent error rate and also failed to identify all known mutations of the gene. *See* Tom Walsh, et. al., *Spectrum of Mutations in BRCA1, BRCA2, CHECK2 and TP53, in Families at High Risk of Breast Cancer*, 295 JAMA 1369, 1386 (2006). As a result, the exclusive monopoly over the BRCA genes prevented patients from accessing more accurate or comprehensive testing.

II. NON-PATENT MECHANISMS CAN AND SHOULD ENCOURAGE PROGRESS WHERE PATENTS ARE AN INAPPROPRIATE, UNNECESSARY, INSUFFICIENT, OR BURDENSOME REWARD

One of the most common justifications for liberal standards on patentability are those that assert, without evidence, that patents are necessary to protect and reward investments in the development of new products. However, this argument fails to take into account the known shortcomings of patents as incentive mechanisms. It also ignores the growing proliferation of alternative, non-patent mechanisms used to stimulate research and development. A wide range of incentives to induce investment into research and development exist or can be implemented as alternatives to exclusive monopoly rights.

In certain areas of innovation, patents do not provide adequate incentives for research or harm future progress. In such cases, other mechanisms to reward innovation may be needed.

In the present case, and as concluded in a report conducted by the Department of Health and Human Services Advisory Committee on Genetics, Health, and Society, gene patents were unnecessary in providing incentives for research and development of clinical testing. Dep't. of Health & Human Services, Sec'y's Advisory Comm. On Genetics, Health and Soc'y, *Gene Patents and Licensing*

Practices and Their Impact on Patient Access to Genetic Tests (Apr. 2010), *available at* http://oba.od.nih.gov/oba/sacghs/reports/SACGHS_patents_report_2010.pdf. In fact, gene patents have harmed patient access to genetic diagnostic testing and have also denied quality assurance of the tests. *Id*. Patents thus represent an inappropriate and burdensome incentive in the context of isolated DNA or human genes and other, more appropriate mechanisms, should be explored.

A wide range of non-patent incentives to promote research and development exist.[2] These mechanisms, used to induce investment into innovation across broad sectors, often take the place of patent incentives. Trade secrets, for example, and while possessing their own shortcomings in terms of limiting access to knowledge, are used to promote investments in medical products, including in particular, developments for medical diagnostic technologies and biotechnology drugs. Iraj Daizadeh, et. al., *A general approach for determining when to patent, publish, or protect information as a trade secret*, 20 NAT. BIOTECH 1053-1054 (2002).

In addition, a wide range of *sui generis* forms of intellectual property exist, often used in parallel to the patent system and implemented where patent protection is unavailable. One commonly used *sui*

[2] *Amicus curiae* does not necessarily endorse the alternative reward mechanisms discussed herein. This listing of alternative mechanisms to induce research and development or reward inventors serves only to illustrate the wise range of alternatives that can be used where patents are not available or represent inappropriate incentives.

generis protection is the application of time limited exclusive rights to rely on clinical test data used to register new drugs or vaccines. Food, Drug and Cosmetics Act, New Drugs, 21 U.S.C. §355. These rights include five years of test data protection for new chemical entity pharmaceutical products, an additional three years of protection where a new indication for an existing product is found, and twelve years for new biologic drugs. *Id*.

Another example of a non-patent reward is the additional five years of market exclusivity granted to encourage research on antibiotic resistance. S.3187, Generating Antibiotic Incentives Now (GAIN), Food & Drug Administration Safety and Innovation Act, 112th Cong., 21 U.S.C. §355(v) (2012). Additional marketing exclusivity is similarly granted for the development of new drug indications for rare, "orphan" diseases or to reward investments in clinical trials for pediatric patents. Internal Revenue Code, Clinical testing expenses for certain drugs for rare diseases or conditions, 26 U.S.C. §45C. with a fifty-percent tax credit.

To stimulate research and development for treatments on rare tropical diseases, Congress created a "Priority Review Voucher" providing for a transferable right to an accelerated consideration of new drug approvals as a reward for registering drugs to treat rare diseases such as cholera or leprosy. Food, Drug and Cosmetic Act, Priority Review to Encourage Treatments for Tropical Diseases, 21 U.S.C. §360n.

In addition to these existing and expanding mechanisms, a new class of rewards to induce investment in medical research and development are under consideration, both international and domestically. This new class involves cash innovation inducement prizes to stimulate investments in the public health and other areas of public and private interests. *See, e.g.*, James Love & Tim Hubbard, *Prizes for Innovation of New Medicines and Vaccines*, 18 ANNALS HEALTH L. 155 (2009); James Love, *The role of Prizes in Developing Low-Cost, Point of Care Rapid Diagnostic Tests and Better Drugs for Tuberculosis*, KNOWLEDGE ECOLOGY INTERNATIONAL (2008), *available at* http://www.keionline.org/misc-docs/Prizes/prize_tb_msf_expert_meeting.pdf; Ron Marchant, *Managing Prize Systems*, 2 KNOWLEDGE ECOLOGY STUDIES (2008); J. G. Morgan, *Inducing Innovation Through Prizes*, 3 INNOVATIONS: TECHNOLOGY, GOVERNANCE, GLOBALIZATION 105 (2008); L. Brunt, et. al., INDUCEMENT PRIZES AND INNOVATION (2008); Bruce G. Charlton, *Mega-Prizes in Medicine: Big Cash Awards May Stimulate Useful and Rapid Therapeutic Innovation*, 68 MEDICAL HYPOTHESES 1-3 (2007); James Love & Tim Hubbard, *The Big Idea: Prizes to Stimulate R&D for New Medicines*, 82 CHI.-KENT L. REV. 1519, 1521-24 (2007); T. Kalil, *Hamilton Project and Brookings Institution, Prizes for Technological Innovation* (2006); Joseph E. Stiglitz, *Scrooge and Intellectual Property Rights: A Medical Prize Fund Could Improve the Financing of Drug Innovations*, 333 BRITISH MEDICAL JOURNAL 129 (2006); Julien Penin, *Patents Versus Ex Post Rewards*, 34 RESEARCH POL'Y

641 (2005); W. A. Masters, *Prizes for Innovation in African Agriculture* (2004), *available at* http://www.eart.columbia.edu/cgsd/prizes; K. Davidian, PRIZES, PRIZE CULTURE AND NASA'S CENTENNIAL CHALLENGES (2004); Burton Weisbrod, *Solving the Drug Dilemma*, WASH. POST at A21 (Aug. 22, 2003); Brian D. Wright, *The Economics of Invention Incentives: Patents, Prizes and Research Contracts*, 73 AM. ECON. REV. 691 (1983).

Domestically, in the 112th Congress, two bills were introduced in the Senate that proposed large cash prizes as an alternative to an exclusive patent monopoly, including S. 1137 and S. 1138. Medical Innovation Prize Fund Act, S.1137, 112th Cong. (2011); Prize Fund for HIV/AIDS Act, S.1138, 112th Cong. (2011). One of these bills would apply to all pharmaceutical drugs, while the other would limit its application to HIV/AIDS drugs.

This approach has been favored by a number of experts and on May 15, 2012, the U.S. Senate Committee on Health, Education, Labor and Pensions (HELP) held a hearing on one of the prize fund bills, S.1138. Nobel Prize winner, Joseph Stiglitz, noted in his testimony at this hearing that the patent system may "have adverse effects on innovation, because the most important input into any research is prior ideas . . . there is a simple way to 'square the circle,' which entails de-linking research and development incentives from drug price . . . It does this through a simple mechanism—prizes." Joseph E. Stiglitz, Testimony to the U.S. Senate HELP Committee, Subcommittee on Primary

Health and Aging, Hearing on the High Cost of High Prices for HIV/AIDS Drugs and the Prize Fund Alternative, *available at* http://www.help.senate.gov/imo/media/doc/Stiglitz.pdf.

In addition to the domestic proposals for prizes, cash inducement funds have gained support in the international community as well. For example, the World Health Organization has called for new proposals to incentivize research and development "addressing the de-linkage of the costs of research and developments and the price of health products and methods for tailoring the optimal mix of incentives to a particular condition or product with the objective of addressing diseases that disproportionate affect developing countries." Global strategy and plan of action on public health, innovation and intellectual property, World Health Assembly 61.21 (2008). Such de-linkage includes the awards of prizes. *Id.* at Annex, element 5.3(a).

Prizes may be particularly relevant in areas where products are not eligible for patents or where it would be inefficient or harmful to permit exclusive monopoly rights to be enforced. Areas where unrestricted access to basic information or discoveries is critical to the progress of science, patents act as a barrier to further innovation and do more harm than good. *See* John Sulston & Georgina Ferry, THE COMMON THREAD (2003); Aaron S. Kesselhein & Jerry Avorn, *University Based Science and Biotechnology Products: Defining the Boundaries of Intellectual Property*, 293 JAMA 850-54 (2005).

In the present case, patents are not an appropriate mechanism for rewarding investments in the isolation of DNA or the identification of genes because of their status as products of nature as well as their effect as a blocking patent. Human genes and other products of nature represent upstream objects and are necessary to future innovation and if patented would have the same clear, adverse effect on innovation that Stiglitz describes. Patents in the area of human genes are burdensome, foreclosing future research and development and preempting all other uses of the gene in direct contradiction to the purposes of the patent system. More viable, alternative reward mechanisms exist and if incentives are necessary, these alternatives should be used to induce investment into research and development in this area instead of patents.

CONCLUSION

The United States patent system operates to provide incentives for research and development, but is not without its limits. Where patents hinder progress rather than promote it, they represent an inappropriate reward. For the reasons stated above, this Court should reverse the decision of the Federal Circuit and rule that human genes are not patentable.

Respectfully submitted,

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