Association for Molecular Pathology
Promoting Clinical Practice, Translational Research, and Education in Molecular Pathology
9650 Rockville Pike, Bethesda, Maryland 20814
Tel: 301-634-7939 ▪ Fax: 301-634-7990 ▪ Email: amp@amp.org ▪ www.amp.org

January 10, 2013

Public Roundtable on Genetic Diagnostic Testing: Written Comments

I. Gene patents cannot be used to prevent physicians from examining their patients' DNA sequences.

In its recent *Mayo v. Prometheus* decision, the Supreme Court reaffirmed the patent ineligibility of natural laws. In *Mayo*, the Court remained true to prior Supreme Court precedents, which render invalid patents that "too broadly preempt the use of a natural law." Such patents, the Court stated, must "also contain other elements or a combination of elements, sometimes referred to as an 'inventive concept' sufficient to ensure that the patent *in practice* (emphasis added) amounts to significantly more than a patent on the natural law itself."

As in Mayo, patents on the *BRCA1* and *BRCA2* gene sequences represent patents on natural laws. The patents at issue have value to Myriad Genetics precisely because in practice they claim relationships between variants in these genes and their biological consequences, namely the inherited predispositions to breast, ovarian and other cancers. These are natural relationships to which the patent holders have added nothing.

II. The informational content of a native gene is not changed during genetic testing.

DNA is a unique and remarkable molecule that is capable of storing vast quantities of information. It is effectively a form of natural software that contains the biological instructions underlying life itself. When one "isolates" DNA one extracts the DNA contained within our 46 chromosomes from the cell. The DNA becomes fragmented, but leaves most individual genes in their native positions, arrangements, and orientations relative to the surrounding DNA on a given chromosome.

After isolation, one uses a formerly patented process, PCR, to make millions of copies of the coding regions of individual genes. This enables the current generation of sequencing instruments to elucidate the linear order of nucleotides that comprise their genetic sequences, allowing physicians to "read" their patients' underlying genetic code.

Throughout the process of genetic testing, this sequence, and therefore the informational content contained within the DNA, remains identical to that of the same gene as it naturally exists in the body. The gene sequence does not and cannot change, for if this fundamental property were altered by removal from the body, it would lose its usefulness for medical testing.

III. Gene patents inhibit the acquisition of new knowledge and represent a barrier to the application of new molecular technologies.

In *Mayo*, the Supreme Court emphasized the long held concern underlying the prohibition against patenting natural laws, natural products and other natural phenomena, i.e., that such patents

would "tie up" natural laws, thereby inhibiting future discovery. In the case of gene patents, such fears are more than justified.

Gene patents prevent the development and application of novel and alternative methods that competition would bring to the testing of patented genes. Such methods may be cheaper, faster and/or more accurate than those used by patent holders or exclusive licensees of patents on underlying genes.

We are now in the midst of a revolution in gene sequencing that is rapidly allowing us to sequence virtually all of a patient's 20,000 – 30,000 genes simultaneously at a cost approaching $1000. As Judge Bryson recognized in his dissent in *Association for Molecular Pathology v. Myriad Genetics*, patents on individual genes potentially represent a substantial impediment to the full realization of the promise of these astounding technologies because of the threat of patent infringement lawsuits. Moreover, current practices with next generation sequencing demand confirmation of putative mutations with Sanger sequencing. Therefore, even if newer technologies are found not to infringe a specific gene patent, the use of older technologies that do infringe is required for completion of the diagnostic analysis.

From a medical standpoint, gene patents have prevented systematic acquisition and publication of data regarding the medical meaning of individual genetic changes that have been identified in patients. Although these are critically important data for research and the care of patients, gene patent holders and exclusive licensees have great incentives to keep such data proprietary. Thus, in the words of the Supreme Court, gene patents unequivocally risk "disproportionately tying up the use of the underlying natural laws, inhibiting their use in the making of further discoveries."

Several years ago, Myriad Genetics began treating data it acquires from patients as proprietary information, refusing to contribute these data to public databases as is the custom in the molecular pathology field. Instead, Myriad has used this information, which is so important to the public health, to solidify its monopoly and to attempt to extend it beyond the life of its patents.

Robert Cook-Deegan described the tactic in an article last fall in the *European Journal of Human Genetics*. Cook-Deegan delineated the commercial advantages conferred on Myriad by its retention of patients' data as trade secrets. Lack of widespread access to these data, which historically would have been broadly disseminated throughout the medical and scientific communities, will impede the ability of physicians and scientists to diagnose, evaluate, and treat breast and ovarian cancer.

IV. Gene patents increase costs of and decrease access to genetic testing.

Gene patents lead to increased test costs and decreased patient access to important genetic testing services. In addition to decreasing innovation in the testing for genetic variants, the lack of competition gene patents engender raises the cost of genetic testing. Plaintiffs in the *Myriad* case could not obtain testing for mutations in *BRCA1* and *BRCA2* because Myriad does not accept their insurance. While some may argue that this is just an "insurance problem," in today's era of rapidly rising healthcare expenditures the costs of genetic testing also matter.

A personal anecdote will bring this point home. My mother was afflicted with idiopathic torsion dystonia, a severe, debilitating inherited neurologic disorder. When I sought to obtain testing the presence of a gene patent left only the patent holder and an exclusive licensee from which I could obtain testing. The patent holder was Massachusetts General Hospital, which had discovered the gene and had retained rights to do the testing. The other was a private company that had obtained an exclusive license to perform testing on the gene. The cost of obtaining the test from Mass General was slightly over

$200.00. The cost of purchasing the test from the company was in the range of $800.00. This substantial difference would have been multiplied several-fold had other family members required testing. I could not test myself without infringing the patent, although it would have been straightforward for me to do so.

V. Insurance reform is unlikely to guarantee that all patients have access to genetic testing of patented genes.

Gene patents "tie up" natural laws, and cannot be 'invented around.' Hence the situation we currently have with *BRCA1* and *BRCA2* – a single provider of testing that sets all the rules. Myriad determines the construct of the test, the methods by which mutations are detected, the order in which mutations are sought, and whether some types of mutations will be detected at all. Myriad establishes the price and the insurance that is acceptable.

The Affordable Care Act was enacted to ensure patient access to essential health care services, including diagnostic testing. Yet, we still have no assurance that all Americans will have access to *BRCA1*, *BRCA2*, and other genetic testing.

VI. Gene patents are not necessary to incentivize the discovery of genetic relationships or to encourage the provision of genetic testing services.

Most genes used in genetic testing have been discovered by academic physicians and scientists, in the normal course of their work. Few who engage in genetic research of this nature have been motivated by the prospect of patents on genes they discover. After all, most inherited diseases are uncommon, meaning that there are relatively few patients to be tested for a given disorder. Thus, gene patents offer the hope of very limited financial rewards to the majority of these investigators. Yet the genes are still discovered!

This is because the traditional academic currencies of publications and research grants, as well as scientific curiosity and dedication to the welfare of our patients, provide ample encouragement for these physicians and scientists to do their work.

Instead of inducing pathologists and geneticists to provide genetic testing, gene patents actually stand in the way of their efforts to do so. Genetic testing can be widely performed using routine, justifiably patented molecular biologic tools and techniques. The costs of developing, validating and providing genetic tests are modest and well within the reach of the typical practitioner when reasonable test volumes and reimbursement that covers costs can be assured. In no way do these tests require the exclusivity conferred by patents to stimulate their delivery to patients. In fact, the opposite is true.

Rather than stimulating the provision of genetic testing, gene patents typically cause multiple providers to discontinue or not engage in offering these vital elements of patient care. In this way, gene patents violate the usual rule that patents advance discovery and provide greater options for consumers and society.

VII. Confirmatory genetic testing does not solve the problems posed by gene patents.

In theory, statutorily guaranteeing confirmatory testing for patented genes could restore our patients' rights to obtain second opinion testing. For example, gene patents abrogate these rights in

women who undergo surgical removal of their breasts or ovaries after they have been told they have mutations in *BRCA1* or *BRCA2*. Superficially, compulsory licensing for second opinion testing seems to be a solution to this problem. However, it is an impractical solution.

Even with compulsory licensing, few providers are likely to engage in testing solely for the purpose of confirming results. Setting up, maintaining, and remaining proficient in genetic testing assays requires deployment of perpetually scarce resources. Therefore, most pathologists and geneticists would be reluctant to provide confirmatory testing for relatively limited numbers of patients, in the face of an uncertain potential for reimbursement.

For example, in the case of confirmations of *BRCA1* and *BRCA2* tests in which mutations were not detected, a provider would need to develop, perform quality control activities for, and offer to patients assays for which Myriad likely charges in the range of $3000.00, with little prospect of being compensated for the testing.

Moreover, even if a small number of providers did choose to engage in confirmatory testing, patients would still be deprived of the right to have the pathologist or geneticist of their choice perform their DNA examination. Further, patent holders could discourage independent confirmatory testing by imposing burdensome documentation requirements on pathologists and genetics who offer this service, or by referring testing to affiliated business units. Finally, the issue of confirmatory testing is in actuality a red herring that primarily serves to distract from the multitude of other problems gene patents cause for patients and providers.

We are optimistic the Supreme Court will settle the gene patent issue on behalf of our patients. However, in light of the preceding, any recommendations by the USPTO for compulsory licensing should not be confined to second opinions, but rather should mandate compulsory licensing of gene patents at reasonable fees for all types of genetic testing.

For the previously stated reasons we urge the USPTO to join us in our efforts to prevent gene patients from interfering with our ability to deliver optimal care to our patients.

***