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Moving Beyond “Isolated” Gene Patents

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On 13 June 2013, the United States Supreme Court handed down its highly anticipated decision in *Association of Molecular Pathology (AMP) v. Myriad Genetics* (1). A unanimous Court held that “genes and the information they encode” are not patent-eligible subject matter “simply because they have been isolated.” Hewing closely to the position of the U.S. Solicitor General, who represents the executive branch of the federal government before the Supreme Court, the Court argued that DNA that has merely been isolated (genomic DNA or gDNA) is a “product of nature,” and not eligible to be patented, whereas DNA with introns removed (complementary DNA or cDNA) is patent-eligible (introns are DNA sequences that do not encode a gene product). The Court also appeared to adopt the Solicitor General's underlying economic logic that drawing the difficult line between what subject matter should and should not be patent-eligible requires respecting the “delicate balance” that patent law strikes between patent claims that create incentives for innovation and claims that block further innovation. Under this “well-established” balancing approach, gDNA claims that cover broad categories of information rather than “the specific chemical composition of a particular molecule” are suspect. Informational content is, however, only one factor in the calculus.

Although the Court indicated that cDNA claims also covered information, it held that the removal of introns makes cDNA molecules patent-eligible. Because intron removal is relatively routine, the Court's decision could be seen as stepping back to some degree from the Court's unanimous but highly controversial opinion last year in *Mayo v. Prometheus* (2). In that case, the Court held that adding scientifically routine activity to a “law of nature” is insufficient for patent eligibility. It unanimously invalidated method claims on measuring a thiopurine metabolite to adjust doses of a thiopurine drug, arguing that the claims in question merely added routine activity to the natural law that individuals metabolize drugs differently.

The Court's analysis does not connect the dots as to why claims to information in the form of cDNA are less problematic than claims to information in the form of gDNA. Nonetheless, as *amicus* briefs from both the Solicitor General and from the renowned geneticist (and co-chair of the President's Council of Advisors on Science and Technology) Eric Lander (3, 4) indicated, claims on cDNA can generally be worked around for research purposes. Additionally, most analysts would agree that the patents most valuable as spurs to innovation are not gDNA patents but those on cDNA or other engineered DNA molecules (4).

The Court's decision clearly weakens the diagnostic service monopoly model of firms such as Myriad Genetics, at least to the degree this model relies on patents. Myriad Genetics offers a genetic test for *BRCA1/2* mutations. The day the opinion was announced, Ambry Genetics, GeneDx, DNATraits, Quest Diagnostics, and Pathway Genomics as well as a number of academic institutions stated that they would begin testing for mutations in the

genes *BRCA1* and *BRCA2*, which increase the risk of breast cancer (5). The Court's opinion not only emboldens competitors that rely on traditional sequencing methods, but also reduces the fear of infringement among those that rely on whole-genome sequencing. Among the new entries are tests not just on *BRCA1/2*, but also multi-gene tests that will now include *BRCA1/2* (6). This could change if Myriad prevails in infringement lawsuits it filed in mid-July.

Firms and university labs are beginning to compete on price. Myriad Genetics and other companies that have relied on gDNA patents for their service monopolies will likely have to compete on other grounds, such as turnaround time, quality of testing, clarity of clinical reports, sales force, and securing payment from insurers.

The quality question is particularly salient. Myriad has performed more than a million tests for *BRCA1/2* during its period of presumed exclusivity since 1998 (7). Even before litigation arose, in November 2004, Myriad had stopped contributing mutation information to public databases. As competitors get into the market place, a key question is whether Myriad and providers with similar business models will maintain their superiority in information regarding mutations. Keeping data proprietary confers an advantage when interpreting the small percentage of BRCA test results whose clinical importance cannot be discerned from public data sources. Patients seeking testing, however, will now have options that include laboratories contributing data to public databases. Two of the competing laboratories, GeneDx and Ambry Genomics, are launching their *BRCA* testing under a “free the data” banner, as an appeal to women and physicians. In the near term, at least, the market will pit Myriad's advantage of having a huge proprietary database built on its period of monopoly against firms promoting medical progress through data access and open science.

More generally, concerns about whole genome sequencing being impeded by gDNA patents are now gone. Dissipating the shadow of patent infringement liability that hung over whole genome sequencing was a significant factor that motivated officials in the U.S. National Institutes of Health and U.S. Office of Science and Technology Policy to persuade the Solicitor General to reject the U.S. Patent and Trademark Office's position allowing claims on “isolated” DNA molecules. In the future, agencies outside the traditional patent community may continue to play a role. For example, the U.S. Department of Health and Human Services, which administers the Affordable Care Act (ACA), Medicare, and Medicaid, may deem it appropriate to invoke the ACA's mandated coverage of *BRCA1/2* testing to increase the public accessibility of mutations information. In other countries with more centralized health insurance systems, purchasers have played a much greater role in determining the terms of access to diagnostic genetic testing (8).

Even within the human diagnostic testing arena, the Court's decision arguably has only a modest practical effect. Many human gDNA patents have already expired or will do so soon. Outside this arena, it is also likely to have only a modest effect. Some analysts have expressed concern about inability to patent prokaryotic DNA, which lack introns, or DNA products based on sequences found in nature. If DNA molecules prove useful as products, however, they will likely not be “merely isolated.” And if such products are indeed merely isolated, then the claims are likely directed broadly at research uses, the very activities the Court was deliberately protecting from patent exclusivity.

An important lingering question involves the opinion's effect on patented molecules other than DNA that have indeed “simply” been isolated from nature. In its *amicus* brief, the Biotechnology Industry Organization (BIO) listed an array of such molecules, many of which have important therapeutic uses (9). These include rapamycin and tacrolimus, naturally produced by bacteria. In each of these cases, however, the patent claims cover the

types of “specific chemical compositions” that the Supreme Court viewed favorably in the *Myriad* case.

Much of the emotional force behind the challenge to the *Myriad* patents emerged from concerns about patient access and control of medical decision-making. Indeed, the case would probably never have arisen had other policy levers – nonexclusive licensing norms for university-generated diagnostic patents and industry traditions of refraining from suing physician-researchers – been used. Moreover, as noted, the most obvious impact of the decision may be increased access, reduced price, and perhaps most importantly, the emergence of multi-gene first-line genetic tests for inherited risk of breast and ovarian cancer—replacing the current multi-step process of testing first for just two genes.

Nonetheless, the Court's opinion views patent-eligibility through the conventional lens of innovation. Indeed, although research and patient access cannot entirely be separated in the case of physician-researchers who also provide clinical care, the opinion makes no mention of patient access, price, or control over medical practice. Whether any of the Supreme Court Justices were influenced by concerns other than innovation is a question we cannot answer. Fortunately, for those preeminently concerned about innovation, the Court's decision should, if read narrowly and through the lens of economic policy, largely preserve innovation incentives.

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