organizations challenging some of Myriad Genetics’ patents covering the BRCA1 and BRCA2 genes and their use in screening for elevated risks of breast and ovarian cancer. On March 29, in a startling decision, a federal district court judge invalidated many of Myriad’s patent claims,1 reigniting a long-simmering debate about the patentability of genes.

The Patent Act permits exclusive control for a limited time (currently 20 years) of any “process, machine, manufacture, or composition of matter,” and since its inception, the U.S. Patent and Trademark Office (USPTO) has granted patents on new pharmaceuticals and medical devices. However, as recently as the 1970s, the view among many medical researchers and legal scholars, as well as members of the USPTO, was that DNA sequences were not patentable, primarily because DNA is a naturally occurring substance rather than a human invention. This perception changed in 1980 with the Supreme Court’s landmark ruling in *Diamond v. Chakrabarty*,2 which involved a dispute over the patentability of a microbe that dissolves oil and that had been specially constructed to include a DNA plasmid. The Court held that although the Patent Act did not authorize ownership of laws of nature, “products of nature,” or physical phenomena, “anything under the sun made by man” was patentable, including the human-made bacterium at issue in the case.

After the decision, gene patents — specifically, patents on “isolated DNA” — soon became commonplace. USPTO examiners justified this extension of patent protection on the grounds that the patented genes and DNA sequences had been purified (and therefore transformed) from their natural form through the application of artificial tools. By the 1990s, technological advances in DNA-sequencing strategies began enabling scientists to discover and isolate new genes at a rapid rate. Ultimately, thousands of patents were awarded on different parts of the human genome sequence; reportedly, about 20% of human gene DNA sequences are currently patented.

Myriad was founded in 1991 by Walter Gilbert, who won a Nobel Prize for his work in nucleic acid sequencing, and Mark Skolnick, a geneticist who had spent his career working on the familial characteristics of cancer.

**Gene Patenting — Is the Pendulum Swinging Back?**

Aaron S. Kesselheim, M.D., J.D., and Michelle M. Mello, J.D., Ph.D.

Are human genes and the process of comparing DNA sequences patentable? These questions were raised by a group of researchers, pathologists, patients with cancer, and medical professional
In 1994, building on publicly funded research on the hereditary predisposition to breast cancer that had been conducted in several countries throughout the 1980s and using about $22 million in private venture capital, Myriad’s team won a race with several other groups to identify the nucleotide sequences composing the BRCA1 gene (see timeline). Myriad’s team included collaborators from the University of Utah, the National Institute of Environmental Health Sciences, McGill University, and Eli Lilly and was also supported by grants from the National Institutes of Health and the National Cancer Institute of Canada. A year later, Myriad filed for a patent on the BRCA2 gene, although it may not have been the first to identify its sequence. Myriad’s patents, the earliest of which expire in 2014 and 2015, cover isolated gene sequences, as well as methods of “analyzing” and “comparing” the gene sequences to determine whether the mutations conferring an increased risk of breast or ovarian cancer are present. Myriad launched its combined genetic test, BRACAnalysis, in November 1996. In 2009, the test accounted for most of the company’s $326 million in annual revenue from molecular diagnostics.

Though the BRCA tests are of undeniable public health importance, questions arose about the appropriateness of the underlying patents. In 2004, the European Patent Office rejected some of Myriad’s patent claims and limited others because they did not meet its legal standard of inventiveness. In the United States, legal scholars argued that the Patent Act does not apply to naturally occurring gene sequences, even in their “isolated” form, contending that Congress’s constitutional power to grant patents was intended for inventions in the limited sense of human, physical creations. Similarly, Supreme Court precedent suggested that natural products and naturally occurring properties of living things are legally distinguishable from goods manufactured using substantial ingenuity. From this perspective, DNA sequences are discovered,
not invented, and are therefore quite different from genetically engineered products such as those in the Chakrabarty case.

Physician groups have voiced concern about the impact that Myriad’s patents have on the use of the genetic test in patient care. The BRACAnalysis test, which was initially priced at approximately $1,600, had nearly doubled in cost, to $3,150, by 2009, which may be prohibitively expensive for some patients.

Though Myriad reports that insurance covers more than 90% of the cost of 90% of the tests it performs, the number of tests that are forgone because of cost or lack of coverage is unknown. The DNA patents prohibit other entrepreneurs from selling less expensive tests based on the same genes, even if the test technologies are different. Physicians also noted that the patents prevented other genetic tests with greater sensitivity or specificity from being commercialized. Physician-researchers objected that although Myriad allowed free use of its test in research, it barred investigators from telling women the results, compromising their ethical obligations to their patient-subjects. Myriad and its supporters responded that gene patents are crucial to attracting private capital investment and stimulating research and development in fields such as personalized medicine.

In invalidating Myriad’s patents on the DNA sequences, U.S. District Court Judge Robert Sweet cited the Supreme Court’s prior rulings that patentable products must have “markedly different characteristics” from what is found in nature. Purification alone, he held, does not change the essential characteristic of DNA — its nucleotide sequence. Indeed, the ability to reliably detect mutations depends on this essential characteristic’s remaining unchanged.

Judge Sweet also rejected Myriad’s patent claims relating to the use of these DNA sequences in evaluating a patient’s susceptibility to cancer. Building on the principles outlined in a 2008 federal appeals court decision, In re Bilski, he found these claims to be inappropriate subject matter for a process patent because they related to “abstract mental processes” of “analyzing” or “comparing” and did not involve a transformative step in which matter was turned into a different state or thing. That is, the patented method consisted only of comparing the nucleotide sequence in a test sample to the reference sequence.

The Bilski case has been argued before the Supreme Court and is currently under consideration; a decision that a transformation is not required for patentability could undermine Judge Sweet’s holding on Myriad’s process patents. Even murkier, however, is the fate of his decision about patents on the DNA sequences themselves. Although well-grounded in legislative history and Supreme Court precedent, flies in the face of years of decision making by the USPTO and is headed next to the Court of Appeals for the Federal Circuit, which is known for its friendliness to patent seekers.

How will the decision against Myriad Genetics, if upheld, affect biotechnology research and development? Judge Sweet was careful to limit his holding to the patentability of isolated DNA sequences, as distinct from other compounds, writing that they are unique as “a physical embodiment of information.” The decision thus will affect only a narrow segment of the biotechnology industry — but it may do so deeply. Genes themselves will be off-limits for patents, and in conjunction with Bilski, it is difficult to see how any tests that consist of comparing gene sequences will be patentable either, because they do not involve a transformative step. Therefore, companies whose focus is the discovery of new genes and the development of tests that compare DNA sequences would enter a new commercial landscape. Such tests could still be marketed but could face competition much sooner than they have in the past.

At the same time, research into aspects of our genome will remain an important avenue for public research funds, as it was in the discovery of the BRCA genes, and having fewer competing intellectual property claims at the basic-science level may enhance the prospects for parties interested in building therapeutics based on this information. How any changes may affect innovation is unclear at this point, but potential competitors for BRCA testing will almost certainly wait for the outcome of the appeal. If the Myriad decision is upheld, we will have seen the pendulum on the legal status of DNA patents swing back from the lack of restraint that has characterized the past two decades.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

From the Division of Pharmacoepidemiology and Pharmacoeconomics, Brigham and Women’s Hospital and Harvard Medical School (A.S.K.); and the Department of Health Care Policy and Management, Harvard School of Public Health (M.M.M.) — both in Boston.
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5. In re Bilski, 545 F.3d 943 (Fed. Cir. 2008).