



## Lock Up the Genome, Lock Down Research?

Researchers say that gene patents impede data sharing and innovation; patent lawyers say there's no evidence for this

"Your Genes Have Been Freed." declared a website banner posted on 13 June by Ambry Genetics, a small California firm that analyzes DNA. Earlier that day, the U.S. Supreme Court ruled that raw human DNA is not patentable. Ambry cheered the decision because it wiped out some intellectual property claims on genes "owned" by other firms. Now it seemed that anyone could roam the human genome and use any genes—without a license from the owner.

Ambry and another small company—Gene By Gene, based in Houston, Texas—immediately began to offer to test U.S. clients for two gene variants linked to breast and ovarian cancer, *BRCA1* and *BRCA2*. Prior to the court's ruling, those sequences had been the exclusive property of Myriad Genetics in Salt Lake City. Myriad was the first to isolate the genes, won U.S. patents on them in the mid-1990s, and launched and fiercely defended a *BRCA* testing monopoly that charges more than \$3000 per test. Last year alone, Myriad earned close to \$500 million. Myriad's business, however, was built on the view that naturally occurring DNA can be patented. The company lost that argument in a lengthy legal battle—*Association for Molecular Pathology v. Myriad*—that went all the way to the Supreme Court (*Science*, 21 June, p. 1387).

Many academics and clinicians submitted court briefs opposing Myriad, arguing that no company should have so much control over human genetic information. Even Francis Collins, director of the U.S. National Institutes of Health (NIH), said he liked the court's ruling because it would benefit research.

Myriad is already engaged in a fresh court battle in Utah with Ambry and Gene By Gene. But the Myriad ruling has rekindled debate over just how the U.S. patent system—and gene patenting in particular—affects the conduct of science. The combatants agree that, in principle, the U.S. patent system is intended to encourage the free flow of new knowledge so that society can benefit. In exchange for revealing the details of discoveries so that others can build on them, inventors get patents that give them the right to charge fees to users for up to 20 years—and to go to court if they think someone is infringing.

In practice, however, critics say the system can work against innovators. Instead of promoting the sharing of ideas, it is often used to dam up knowledge. A handful of recent studies, for instance, have concluded that gene-related intellectual property has created a legal thicket that stymies biomedical science and locks away data that could improve clinical tests. Similar, but more muted, complaints have emerged in other fields, from computer science to engineering. That's far from the innovation and sharing that the patent system is supposed to encourage, critics add.

On the other side, champions of the patent system, including many lawyers and a former patent court chief judge who spoke with *Science*, say such attacks are unsupported by the evidence. Claims by gene patent critics, they argue, are based on emotion. "The idea that scientific researchers are being sued or threatened with lawsuits [for doing research] is a fiction," says Paul Michel, former chief judge of the U.S. Court of Appeals for the Federal Circuit, the top patent review body

ILLUSTRATION: DAVID PLUNKERT

below the Supreme Court. “I don’t know where this myth comes from.”

Some researchers, meanwhile, are working to sidestep patent battles by making sure that gene sequences and other kinds of data are quickly entered into public databases, where they are free to all.

### Skeptics and believers

Bio-patent critics include some high-profile advocates. One is Nobel laureate Joseph Stiglitz, an economist at Columbia University. At its heart, the former Clinton administration official wrote in a 14 July *New York Times* editorial blog, the *BRCA* conflict is about whether patients must pay steep fees to access life-saving technologies and clinicians must get licenses to do research. The fees that Myriad charges for its tests are a reward for invention, he noted. But the price isn’t worth it, he argued, because “the two genes would likely have been isolated . . . soon anyway, as part of the global Human Genome Project.” And as part of that publicly funded effort, the sequences would have been entered into a free database.

Stiglitz was retained as an expert by the groups that sued Myriad in the Supreme Court, and he is consulting for Ambry Genetics and Gene By Gene in the ongoing Utah case. (He has donated his fees from these cases to charity.) In a statement filed with the Utah court, Stiglitz argues that DNA patents “impede the dissemination of information.” In general, economists argue that the “transaction costs” of acquiring privately held data—such as signing an agreement to use a patented gene—discourage use. Recent studies that Stiglitz cited examined whether research papers cited proprietary genes less often than those that were “free.” A 2013 study by economist Heidi Williams at the Massachusetts Institute of Technology in Cambridge found that protected DNA was cited 20% to 30% less, and that genes in the private database of the biotech firm Celera Genetics were 20% to 30% less likely to be used in clinical tests than free genes.

Ambry Genetics and Gene By Gene also submitted a statement to the Utah court by geneticist and bioethicist Mildred Cho of Stanford University in Palo Alto, California. She wrote that her own NIH-funded research had concluded that patents on clinical genetic tests “inhibit scientific research.” A 2001 telephone survey of U.S. lab directors working on gene tests, for instance, found that 53% reported deciding not to develop a new clinical genetic test because of a gene patent or license; two-thirds believed that “gene patents resulted in a decreased ability to do research.” Such data have helped persuade Stiglitz that patents and other property claims on genes have done harm by “discouraging further innovation” or even “not allowing any usage of the scientific information at all.”

A case in point, critics say, is Myriad’s refusal to make public data on potentially harmful *BRCA* variations that it has discovered through its exclusive control of DNA used in gene testing. The company argues that U.S. law requires it to protect patient privacy and control how test results are used. Spokesman Ronald Rogers points out that Myriad has collaborated with dozens of “non-commercial, academic” research labs. But it doesn’t put data in public repositories, which he says don’t guarantee privacy or the quality of clinical interpretation.

In contrast, Gene By Gene Chief Scientific Officer David Mittelman says that his company is “a big fan” of making public

the new gene variants it discovers and is ready to launch an initiative promoting this cause, at [freemygenes.org](http://freemygenes.org).

Defenders of the patent system argue that all the attacks on gene patents add up to a weak indictment. They say that although researchers may perceive otherwise, there’s no direct evidence that intellectual property owners have impeded anyone from doing research. Michel, for instance, says companies rarely sue scientists; one reason is that it would guarantee bad press but be unlikely to win a big settlement.

Still, to clarify matters, Michel and others would like Congress to enact a law saying that a researcher who uses patented material for science—and not for commerce—is protected from infringement lawsuits. Other nations have such “research exemptions,” and U.S. case law has recognized this rule as a practical matter. But Congress has balked at enshrining it in a statute.

### Removing fences

While experts debate the effects of patent law, some researchers are taking direct action to liberate genetic data. To prevent patenting or other limitations—as well as improve standards—they’re scooping up any gene variants they can get from clinics and patients and dumping them into a public database. The repository, known as ClinVar, is maintained by NIH’s National Center for Biotechnology Information. In time, leaders say that they should be able to compile a list of all known human gene variants (such as those for *BRCA1* and *BRCA2*) and their health effects, edited to remove personal information.

Geneticist Heidi Rehm at the Brigham and Women’s Hospital in Boston is a key ClinVar contributor. She heads the Laboratory for Molecular Medicine, which provides gene tests and analysis to clinics in the Partners HealthCare network in Boston, affiliated with Harvard Medical School. The lab has already donated about 7000 variants for 155 genes. In all, 56 groups have signed up to collaborate. But several large gene-testers have not, Rehm says. One of them is Myriad.

“There’s no doubt in my mind that lack of data sharing is harmful to patients,” Rehm says. The lack of a universal data bank of gene variants, for instance, could slow the development of more accurate gene tests. When Rehm’s lab recently worked with two others to see just how well their different genetic tests matched when used on the same genes,

they found “a 20% discrepancy,” she says, suggesting the results “can’t all be right.” Public data could help find and resolve such discrepancies, and ultimately improve health care.

To speed that outcome, the International Collaboration for Clinical Genomics—which includes early ClinVar submitters—met last month at NIH to work out plans for curating information, protecting privacy, and granting database access. NIH has awarded three lead institutions, including Rehm’s, nearly \$25 million over the next 4 years to get the project under way. The aim is to set high standards for data collection and annotation. In addition, it could make some private gene variant collections, like Myriad’s, redundant.

In the meantime, court battles over patented genes continue as judges digest the implications of the Myriad decision. Last month, the Utah court heard arguments on Myriad’s request for an injunction to stop its rivals in California and Texas from offering *BRCA* tests. A decision was pending at press time. It’s not likely to be the last word, and the legal battle could rumble on for months—or years. —ELIOT MARSHALL

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—JOSEPH STIGLITZ,  
COLUMBIA UNIVERSITY