

**Owning the Code of Life:
Human Gene Patents in America**

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ABSTRACT

In 2013, the United States Supreme Court heard the case of *Association of Molecular Pathology v. Myriad Genetics*. The case asked one question: are human genes patentable? Gene patents became commonplace during the biotechnology revolution of the 1980s, but generated a complex web of moral, legal, and biological questions. While some viewed gene patents as necessary in promoting and sustaining innovation, others felt that owning the code of life was morally and legally misguided. This tension played a central role in the early years of the Human Genome Project, and continued as people experienced the challenging consequences of assigning property rights to our shared biology. Several patients with genetic diseases were forced to navigate limited or expensive testing because of a company's genetic monopoly. Some scientists worried that their research might infringe a patent. When the Supreme Court decided the *Myriad* trial, ruling that unaltered human genes were not patent-eligible, their decision marked a surprising and historic shift in the relationship between patent law and fundamental biology—but questions and uncertainty about a future without gene patents remain.

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Owning the Code of Life: Human Gene Patents in America

In 2005, Runi Limary found a lump in her right breast. Her doctors thought she was surely too young to have cancer¹ – few invasive breast cancers occur in women younger than 45,² and Limary was only 28. But they were wrong.

“There’s always a red flag for being diagnosed at such a young age,” says Limary. She’s sitting by the window in her bright office in Austin, Texas. Two paintings – flowers and a tree – are hung on the pale green wall behind her, next to a bookshelf holding several notebooks and a troll doll with bright orange hair. For eight years, Limary has worked for Austin’s Breast Cancer Resource Center, advising young women facing the same diagnosis she did nearly a decade ago.³

Limary’s “red flag” is the fact that breast cancers in younger women are often linked to genetically inherited mutations. Limary’s medical oncologist urged her patient to get genetic testing for a mutation in the genes most commonly associated with heritable breast cancers—BRCA1 and BRCA2.⁴

Mutations in BRCA genes can be passed through generations, and significantly increase the risk of developing breast cancer, as well as ovarian and prostate cancers⁵. If a genetic test indicates a cancer-causing mutation, patients can choose to take preemptive action to limit their risk. In May 2013, actress Angelina Jolie revealed she had done just this in an Op-Ed in the *New York Times*. After learning she carried a mutated BRCA1 gene, Jolie elected to surgically remove both of her breasts. Jolie had lost her mother to ovarian cancer, and two weeks after her article was published, her maternal aunt died of breast cancer, likely linked to a BRCA mutation that was only discovered at the time of her diagnosis. In her editorial, Jolie revealed the peace of mind she gained from her procedure: “My chances of developing breast cancer have dropped from 87 percent to under 5 percent. I can tell my children that they don’t need to fear they will lose me to breast cancer.”⁶

Such confidence would prove elusive for Runi Limary.

At the time of her diagnosis, Limary's health insurance did not cover the "Comprehensive BRCAAnalysis test" she needed to evaluate her genes. The test, designed by Myriad Genetics, a small company based in Salt Lake City, Utah, cost thousands of dollars.⁷ Unable to afford a genetic evaluation, Limary made the best decision she could. Her cancer was aggressive, and required chemotherapy; she didn't want to risk having radiation as well. She decided to have her breast removed.

But after her surgery, the uncertainty of her situation plagued her. If her genes were cancer-prone, her body was a ticking time bomb. Every time she felt a lump in her other breast, she says, "I just felt as if it was back."

After two years of MRIs and mammograms, Limary switched jobs. Her new health insurance now covered the BRCA test she needed. After all the waiting and wondering, Limary finally got tested. "And that's when it came back with a 'Variant of Uncertain Significance,' " she says.

While Limary's BRCA2 gene appeared normal, her BRCA1 gene had an anomalous pattern. But the test could not determine whether this mutation was linked to a higher cancer risk.⁸ Shocked at this outcome, Limary called Myriad, asking for insight. The company told Limary, who is Asian American, that they had seen her mutation in other women of Asian descent. But, they said, she was only the third person they'd found to have it. Of the other two patients, only one had breast cancer. Ambiguous test results, Limary learned later, were more common for minority women.

Limary had no idea whether or not her mutation put her at a higher risk for cancer. Worse, she soon discovered there was no hope of finding out. She could not get a second opinion: Only Myriad offered the test. In fact, it was illegal for another company to attempt to analyze BRCA genes, because Myriad held a patent not only on the test, but

also on the genes themselves. Once Limary's genes were removed from her body, they were no longer legally hers. They belonged to Myriad Genetics, Inc.

Limary struggled with her decision. With no concrete diagnosis from the test, she had to go with her gut once more. She ultimately decided to remove her other breast as well. "Before I made that decision...that was tough," she says. "And then having the decision made was still hard, because then I had my ovaries to consider."

Ovarian cancer is often hard to detect until it is advanced,⁹ so if Limary knew her BRCA mutation increased her cancer risk, she would have removed her ovaries. But she had no such certainty, and the consequences would be dire. "I just wasn't quite ready for that. Not having any children...I decided to just kind of wait and see," she says. Her doctors don't believe that she has a cancer-causing mutation, but nobody is one hundred percent sure, she says. After receiving her test results, she has approached Myriad representatives at various conferences to ask if they have expanded their testing to accommodate rare mutations like hers. "And they said no," she says. "They actually told me no."

In 2009, two years after receiving her inconclusive test results, Limary joined a large group of physicians, geneticists, nonprofits, and other patients that challenged Myriad's ownership of the BRCA genes. Her experience was a tiny skirmish in what had become a ferocious, high stakes battle with legal, ethical, and biological implications. In the spring of 2013, after a labyrinthine journey through lower courts, the case of whether or not Myriad should be allowed to retain their ownership of human genes came before the justices of the United States Supreme Court. But the question before the Court was bigger than one biotechnology company, and larger still than the doctors, lawyers, professionals and patients who brought their case before the most powerful judges in the nation: Where is the line between biology and business? Should human genes, the code of life, be owned?



When Myriad filed their first gene patent application, they were seeking the protection of a powerful but complicated legal tool. Gene patents generate particular complexities, but even the simplest patent faces a tension between its intended effect – protecting inventors and promoting innovation—and its possible suppression of both competition and progress. This has been a conceptual challenge since the first patents were issued – and patents have played a role in American business for close to the country’s entire history.

On April 10, 1790, President George Washington signed the bill that established the United States’ patent system. For a fee of four to five dollars, the entrepreneurs and inventors of the young nation could now be guaranteed the rights to make, use, and sell their inventions and methods of manufacture (or any improvements to those already in existence).¹⁰

It was decreed that all patents should be stored in a large book in the office of the Secretary of State.¹¹ In 1790, that office belonged to Thomas Jefferson, who was also the patent system’s first administrator and patent examiner—the man responsible for determining which inventions could be protected under the new act.¹²

But despite these duties and his own prowess as an inventor,¹³ Jefferson famously harbored doubts about patenting. He felt that “ideas should freely spread from one to another over the globe, for the moral and mutual instruction of man, and improvement of his condition.” Given this, Jefferson wrote, “Inventions then cannot, in nature, be a subject of property.”

Still, it was Jefferson’s job to approve those patents that met the standards of America’s new law. It was a challenging assignment. In an 1813 letter, he wrote, “I know well the difficulty of drawing a line between the things which are worth to the public the embarrassment of an exclusive patent, and those which are not.”¹⁴ It is a telling statement, recording both Jefferson’s distaste of assigning exclusive rights, and the arduous task of determining what should receive them.

The specific rules that govern whether or not an invention or discovery should gain patent protection, the guidelines that distinguish what is worth that “embarrassment” Jefferson so loathed, are today clustered under Title 35 of the United States Code. Much of Title 35 seems to have fallen straight out of the original Patent Act: patents may be granted to “whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof.”¹⁵ There are multiple types of patents, such as those that cover designs or plant species, but the most common and diverse type of patent issued is the utility patent. It protects any tangible invention, or the process for making such a product.¹⁶

Title 35 contains two specific clarifications of “new and useful” that must be met before a patent can be issued. The first caveat is that a patent has to be sufficiently novel. That means that anything already patented, described, or in any way available to the public can’t receive a patent.¹⁷

The second catch is usually more complex in patent law cases. It’s known as “non-obviousness.” If someone “having ordinary skill in the art to which the claimed invention pertains” could have easily figured out how to come up with the invention on their own – if the new creation is basic enough to be obvious – then it doesn’t deserve a patent either.¹⁸

If a patent application can clear these hurdles, the granted patent will give its bearer specific but limited power. Unlike a copyright, which protects “works of authorship” like novels, music, and other “tangibly expressed” arts, a patent does not actually give its holder the exclusive right to reproduce the invention in question. A patent only grants the right to *prevent*, or as the Code puts it, “exclude,” someone else from “making, using, offering for sale or selling” the invention or, if the patent is for a process, anything made with this process.¹⁹ It’s a crucial distinction. Certain elements of a new patent may already be covered by somebody else’s earlier patent. In this case, a new patent holder could be prevented from producing the invention covered by her own patent – she could only ensure that someone else did not do so.²⁰ This design applies when adjustments or

improvements are made to existing technologies – a process central to the intended role of patent protection.

As the founders intended it, a patent’s true purpose is to encourage development and innovation. If an inventor can be assured that she will have the first right to make money on her invention or discovery, she should be eager to secure such protection. And as soon as she does, her triumph becomes public knowledge: when a patent is granted, it is immediately published where the public can see it. Nobody else will be allowed to make money on that invention or discovery for a set period of time – currently, 20 years.²¹ But they can immediately begin to build on it, perhaps expanding their own skills and knowledge or further improving its functions.

This design takes after the British patent system. In 1790, while upholding a patent on telescope lenses, the Lord Chief Justice of England posited that the business advantage given by a patent is a reward not for creating a useful invention, but for being willing to share that knowledge with the public.²² While patents do allot monopolies, their purpose is to reward open access of knowledge.

In 1790, Jefferson’s patent office granted a grand total of three patents. The next year saw a significant leap, all the way to 33. In 2014, the US Patent and Trademark Office granted over 300,000 patents.²³ Since the year that Washington signed the patent system into law, over nine million American patents have been granted. They cover creations from televisions to electric bicycles to multiple iterations of the cutlery hybrid known as a “spork.”²⁴

And by the year that Rumi Limary was diagnosed with breast cancer, US patents also covered 4,382 human genes.²⁵

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Patenting living organisms, or in the case of genes, portions thereof, has a long history in the United States. In 1873, Louis Pasteur, the same famous scientist who also developed

pasteurization and the first rabies vaccine, was issued a US patent that covered, in part, pure cultures of yeast cells. (The rest of the patent covered methods of using these fungi to make beer.)²⁶ Six years later, the hormone adrenaline, purified from livestock, was patented.²⁷ The early years of the twentieth century saw an explosion of patents on plant species; the Plant Patent Act of 1930 made new varieties of plants created through human interventions such as grafting or planting cuttings patent-eligible.²⁸ (In 1970, the Plant Variety Protection Act would make plants that reproduce on their own – seeds and tubers, for example—eligible for patent-like legal protection as well.)^{29 30}

But compared to other patents, and even those on life, gene patents are uniquely powerful and controversial. A gene is not crafted at a workbench or a lab bench; it is a fundamental unit of life, crafted by nature and evolution. It contains massive amounts of biological information, and transcends both individual humans and individual species.

The word “gene” is colloquially used to refer to some unit of inheritance,³¹ a vessel for carrying a characteristic such as dimples, freckles, or tallness from parent to offspring. This is what Danish botanist Wilhelm Johannsen intended when he coined the term in 1909.³² But as the science has evolved, so has our understanding of what genes are, and what they do. Genes specify far more than “many characteristics” of a living organism – they form the instruction manual that directs the construction of life.

The letters of this manual are written in deoxyribonucleic acid – DNA. The molecule has only four letters—four different chemical “nucleotides” – with which to spell biological directives. These nucleotides pair with one another in a highly specific manner, forming the characteristic helical shape famously described by biologists James Watson and Francis Crick in 1953.³³ Like the 1s and 0s of a computer’s binary code, they can store massive amounts of information. In living organisms, DNA writes instructions for how to produce and arrange the different proteins that build our cells and bodies. Scientifically speaking, a “gene” refers to a specified length of DNA, a sentence of the manual of life that will be read by ribonucleic acid (RNA), which helps convert DNA into proteins. Not all DNA encodes proteins. It can also produce small molecules, or can serve to monitor

the regions that do encode genes. And the majority of our DNA actually has no known function³⁴ – at least, for now.

The entirety of a human’s genetic material, his “genome,” contains over three billion DNA base pairs; this is coiled around 23 pairs of threadlike, microscopic scaffolds called chromosomes. This DNA encodes the directions to make brown eyes or blond hair, skin cells and heart cells, teeth and toenails. It can also contain directions that cause disease—stuttering out repetitions of code that lead to the fatal brain damage of Huntington’s disease, garbling the production of a crucial protein, or switching on the uncontrolled growth of certain cancer cells. Our genes define how we are made; every cell, every fluid, every ounce of our biology is programmed here.

From the perspective of a patent, a gene is both product and process. It is a tangible entity, a specifically ordered string of chemical letters that can be isolated, measured, and adjusted. But it is also an instruction, a code for building part of a human being. The extreme specificity of DNA is reflected in how similar every human’s genetic code is: any two humans have DNA that is around 99.9% identical.³⁵ We share over 98% of our DNA with chimpanzees,³⁶ and around 50% of our genetic code is the same as a banana’s.³⁷ Thus, a gene patent makes it possible for a company to own both a biochemical sample of one human’s cells, and the instructions for life shared by billions of other human beings.

The concept of patenting life has long been controversial, in part because it seems to clash with a longstanding protocol of the US Patent and Trademark Office (USPTO). The USPTO is clear in its guidelines to patent examiners: laws of nature, physical phenomena, and abstract ideas are *not* eligible for patent protection.³⁸ For example, Albert Einstein could discover general relativity, but he couldn’t patent it. A precedent in patent law, held since the 1880s, established the same rule for “products of nature” such as minerals or trees.³⁹ Some select entities seemed to have slipped past this barrier over the years, including Pasteur’s yeast and adrenaline, though both patents also included methods for preparing or purifying such biological materials. Plant species can also

receive intellectual property protection, but they have long obeyed different laws than other patentable entities (and these still remain controversial, eliciting protests over farmers' rights, among other concerns).

But regardless of the Patent Office's stance, the Supreme Court's position on patenting life seemed to be a clear, resounding "no." It was a standpoint reinforced in the 1948 case of *Funk Bros. Seed Co. v. Kalo Inoculant Co.* Kalo held a patent on a combined strain of three different bacteria that could be mixed together and used as a soil inoculant to improve the growth of leguminous plants. The Court ruled that the supposed invention was merely "the discovery of some of the handiwork of nature," in this case, natural characteristics of bacteria that allowed them to exist together in culture and improve plant growth. The Court ruled that such a discovery was not patent-eligible after all, firmly stating, "patents cannot issue for the discovery of the phenomena of nature," and "The qualities of these bacteria, like the heat of the sun, electricity, or the qualities of metals, are part of the storehouse of knowledge of all men. They are manifestations of laws of nature, free to all men and reserved exclusively to none."⁴⁰

This established the environment for biological patents that remained standing in the early days of genetics and biotechnology research. For Runi Limary's genes to end up in Myriad Genetics' hands, a change had to occur.

This shift came in the form of the 1980 Supreme Court case of *Diamond v. Chakrabarty*. In 1972, Ananda Chakrabarty, a microbiologist at General Electric, applied for a patent on a strain of bacteria he had genetically altered to break down crude oil. The patent would apply not only to the method of making the bacteria, but also the bacteria themselves. The Patent Commissioner, Sidney A. Diamond, refused to grant the patent, saying that as living things, the bacteria could not be given patent protection.⁴¹ Chakrabarty appealed his decision, and the case worked its way through the judicial system to the Supreme Court. In a split 5-4 decision, the Court held that genetically engineering an organism was different from discovering a natural mineral. The bacterium

would not have been found as it was in nature, they said, and as such, it was patentable.⁴²

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When the ruling came through, the science to support gene patents was already in place. Through the 1970s, researchers had discovered ways to quickly identify, isolate, and manipulate genetic code. In 1973, biochemists Stanley Cohen and Herbert Boyer produced the first laboratory-manipulated genome, moving genes around in *E. coli* bacteria.⁴⁴ In 1977, British biochemist Frederick Sanger developed a method of quickly “reading” genetic code from DNA samples in the laboratory.^{45 46} These developments set the stage for a revolutionary era in biotechnology; the Supreme Court’s decision in *Diamond v. Chakrabarty* opened the floodgates.

The Supreme Court never changed their minds about whether or not a product of nature should be patented, says Lori Andrews, a professor at the Illinois Institute of Technology’s Kent College of Law. “The test really is, is what you’re proposing to patent markedly different from what occurs in nature...the fact that it’s biological is not the dividing line,” she says.⁴⁷ The genetic material of Chakrabarty’s bacteria had been manipulated, altered; it never occurred in nature. Human genes, in their natural state, were built by evolution, not invention.

But this distinction did not seem to hold up in the USPTO. After *Diamond v. Chakrabarty*, something changed in the Patent Office. “The Patent Office was granting patents on more and more things that, in my mind, should not have been patented,” Andrews says. And soon, courts also seemed to reason that if entire organisms were patent-eligible, so were their genetic components.⁴⁸

When Myriad Genetics was granted their first patent on the BRCA1 gene in 1997, the company was assigned exclusive rights on a functional gene sequence that had not been manipulated by humans in any way.⁴⁹

“Many of us...thought it was totally absurd,” says Jonathan Alan King, a professor of biology at the Massachusetts Institute of Technology. “These people had not invented these genes, these sequences had evolved over millions of years. They’re not the product of human invention or activity, and we thought that it should be disallowed.”

But despite what he remembers as a “robust social movement” against patenting life, King says grassroots campaigns didn’t stand a chance against the well-funded, powerful biotechnology and pharmaceutical industries. “And the patent office just began allowing gene patents,” he says.⁵⁰

Through the mid-1990s, the ranks of genetic patents swelled, growing by over 50 percent every year.⁵¹ And as the impact of these patents in both science and society became clear, the tension that King remembers grew as well.

Many saw gene patents as an essential element of a new, thriving biotechnology industry. In 2000, Q. Todd Dickinson, then the Director of the USPTO, wrote, “Biotechnology is heavily dependent on patent protection to maintain viability.”⁵²

Genetic research could be an expensive, rigorous process; patents provided a way to financially recoup some of that investment. As Ron Rogers, head of Public Relations at Myriad Genetics put it in an e-mail on February 26, 2015: “Strong patent protection is essential to innovation because it allows institutions to publicly disclose their inventions, while guaranteeing a period of reward in return for very significant investments of time and money.”⁵³ To secure some financial return from their research investment, an invention itself – whether it is gene, genetic test, or electric bicycle – can be sold to those interested in using it. The patent holder can also profit from selling a license to allow others to use and sell the gene, test, or bicycle.

But not all scientists agreed that gene patents were beneficial. In fact, protests over these patents and fear of what private ownership of human genes would mean became a central

struggle in the largest genetic research project in history. It thrust the issue of owning the code of life onto the scientific and public stages.



In 1990, a decade after the Supreme Court settled *Diamond v. Chakrabarty*, the Human Genome Project officially began.⁵⁴ The project's goal was to uncover the full code of mankind's genetic material, a daunting task driven primarily by medical interests. Scientists studying the effects of radiation on genetic material – a mission fueled both by the effects of Hiroshima and a burgeoning interest in nuclear energy and weapons⁵⁵ – found they needed a better template to study. Cancer researchers hoped a full genome would finally allow identification of the genes that caused malignancy.⁵⁶

James Watson, half of the team that had presented DNA's structure to the world nearly four decades earlier, was one of the project's largest proponents.⁵⁷ For a very personal reason, he too hoped it would yield medical advancements. His son, Rufus, had been committed to a psychiatric hospital after trying to jump off the World Trade Center, and had subsequently been diagnosed with possible schizophrenia. Watson saw it as "pretty obvious schizophrenia had a genetic cause." If scientists could find the genes associated with the disease, he thought, his son might have a shot at a normal life.⁵⁸

Many viewed the task of elucidating the entire human genome as Herculean, if not impossible. One Nobel laureate claimed that the task of identifying every base would be "like pursuing the holy grail."⁵⁹ Though the first methods and tools necessary to identify human genes, including Sanger's sequencing method, had already been identified, these methods required significant time, money, and effort. When the plans were set for a fifteen-year endeavor in 1990, a paltry 100,000 bases had already been read.⁶⁰

Over the course of the next two decades, however, sequencing efficiency would improve drastically. New measures for reading off bases in bulk would become commonplace; soon, machines and computers joined the fight, rapidly improving the speed of the

search.⁶¹ Over twenty different laboratories, institutions, and government agencies in the USA, Japan, Germany, Britain, France, and China would contribute to the process.⁶²

The Human Genome Project operated under the notion that its benefits would be available for all. After all, the Project was decoding the biology of mankind as a whole. By careful design, it will never be known whose DNA was actually sequenced. A diverse group of volunteers consented to providing blood samples, but the Project managers took five to ten times as many samples as they needed, and removed all labels before selecting which samples they used. None of the volunteers could possibly know if their own DNA was sequenced, or if their sample was discarded.⁶³ The protocol would make the resulting genome completely faceless; it would represent a species. As Watson put it in 1989, the Project's goal was to discover "what being human is."⁶⁴ In late February 1996, fifty researchers met at a genomics strategy conference on the tropical island of Bermuda. They agreed: all DNA sequences longer than 1,000 bases should be made public knowledge, and updated daily – and none of them would be patented.⁶⁵

But not everybody was inclined to adhere to these "Bermuda Principles." On May 12, 1998, at a meeting in Cold Springs Harbor, New York, biochemist and genetics pioneer Craig Venter informed several leaders of the Human Genome Project that they had competition.⁶⁶ At the time, Venter – ambitious, confident, and combative⁶⁷ – was the president and chief scientific officer of a brand new biotechnology company that would soon be named Celera.⁶⁸ Celera hoped to sequence the human genome⁷⁰ – and it intended to make a profit doing so.

It was not the first time that Venter had created a stir among the leaders of the Human Genome Project. While working as a neurobiology researcher for the National Institutes of Health (NIH) in 1991, Venter helped develop a method of sequencing DNA that he felt could speed up the Project significantly.⁷¹

On genes, DNA that contains directions to build proteins is often mixed up with interludes of mysterious non-coding DNA. But as the process of translating DNA's

information into a protein begins, the molecular “reader” – messenger RNA – can selectively inscribe only the regions of DNA that code for amino acids, sequences called “exons.” In the laboratory, scientists can use an enzyme to copy these exons from RNA back into DNA. The new DNA sequences have all intervening “junk” DNA chopped out, and are called “complementary DNA” or “cDNA.”⁷²

Only searching for protein-encoding DNA regions would cut out the work of sequencing nearly 98% of the genome. But Venter and his team also found that small, random sections of cDNA could be used to quickly identify and “tag” portions of DNA. Venter thought that these “expressed sequence tags,” or “ESTs,” would be a quick way to identify unknown genetic code.⁷³

James Watson, heading the Human Genome Project, shot down the idea of using ESTs to proceed with genome sequencing. Venter’s approach would be quicker and less expensive than sequencing the whole human genome, but ESTs would miss the important DNA sequences that code for small, gene-regulating molecules instead of proteins. (Today, scientists believe that non-coding DNA may contain important genetic information, too.) Further, this cheap and easy technique would undercut funding and enthusiasm for sequencing the whole genome. Still, Watson would later say that Venter’s EST sequencing technique was “immensely useful.”⁷⁴

But while Watson felt the technique was useful, he apparently didn’t feel the same about the actual sequence tags. This became clear after the NIH applied for patents on around 2,000 ESTs. The tags didn’t have any known genetic function, but the thinking seemed to be that someday, some function might be discovered, and if the sequences were not patent protected, it could result in a financial loss.⁷⁵

When Watson heard of the NIH applications, he called the plan “sheer lunacy.” Watson continued, “To get a patent, you should have a useful product.”⁷⁶ A strand of DNA didn’t make the cut in Watson’s mind, future potential aside. Maynard Olson, a professor of Genome Sciences and Medicine at the University of Washington and, at the time, an

advisor on the Human Genome Project, also protested, from both a legal and ethical standpoint: “If the law is interpreted to give intellectual property rights for naked DNA sequences, then the law should be changed. It’s like trying to patent the periodic table.”⁷⁷ Other scientists agreed with Watson and Olson, and it seems the USPTO did, too. The Patent Office rejected the NIH’s patent applications more than once, and the NIH gave up in 1994.⁷⁸

Venter later recalled that the public fuss around patenting ESTs gained him both notoriety and several job offers from biotechnology companies. Ultimately, it was biological patents that helped create a position he desired. He accepted an offer from private investors to start a not-for-profit research institute he called The Institute for Genomics Research (TIGR). The deal: Venter’s research would be funded, and the for-profit agency funding him would receive intellectual property rights from his work.⁷⁹

In 1995, Venter and his colleagues at TIGR championed a new DNA sequencing “shortcut,” a technique that blasted several copies of a genome into fragments and quickly pieced them back together.⁸⁰ Three years later, Venter left his not-for-profit position for a new post at Celera. Armed with his methods and an arsenal of rapid new DNA-sequencing machines⁸¹ from his partner, Michael Hunkapiller at Applied Biosystems, Inc.,⁸² Venter was determined to give the slow-moving Human Genome Project a run for its money.

Most of the prominent researchers involved with the project were shocked by Venter’s competition, and several disapproved of the business plan that accompanied it. Celera would upload any discovered sequences after three months, as opposed to twenty-four hours. And while they would upload genetic data, they planned to charge access fees for “user-friendly” ways to interpret this data.⁸³

Ultimately, Craig Venter and Celera didn’t beat the Human Genome Project to their final goal. On April 14, 2003⁸⁴ – under budget and two years ahead of their intended deadline – the allied laboratories and agencies of the Human Genome Project announced that 99%

of the human genome had been sequenced, with 99.99% accuracy.⁸⁵ No known sequencing methods could reveal the remaining 1% of coding genes, so the Project was termed complete. The Project adhered closely to the Bermuda Principles, quickly making all of its genomic data public for free on the Internet.

But this did little to keep private interests out of the human genome.

According to the National Human Genome Research Institute, “[W]e really don’t know how much, if any, of the genome can be used freely for commercial purposes.”⁸⁶ This is because both before and after the project’s completion, private companies have filed numerous patents on human genes.

The Human Genome Project offered an early, public glimpse of the scientific conflicts generated by patents and private ownership of genes. It is an issue that would be revisited later, in the context of a lawsuit that challenged the legality of such ownership altogether.

But at the time the Human Genome Project was completed, a different lawsuit was actually underway – one that made it clear that scientists weren’t the only ones struggling with the impact of gene patents. The private ownership of human genes also confronted patients facing a genetic disorder. One case in particular would become an infamous example of the potential dark side of gene patents in medicine: Canavan disease.

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Andreas was just one year old, but Judith Tsipis knew her son wasn’t developing properly. “We knew that he had some kind of a progressive neurological disease,” says Tsipis, a professor of biology and the Director of the Genetic Counseling Program at Brandeis University. But Andreas’s symptoms were given “all sorts of strange names,” and he was fifteen years old before the correct diagnosis arrived. Andreas had Canavan disease.⁸⁷

Canavan disease results when one inherits two mutated copies of the ASPA gene, one from each parent. The gene normally produces a protein needed to break down an acid; when the gene is broken, the acid builds up in the brain and destroys brain cells. Symptoms of the disease include a lack of head control, developmental delays, loss of muscle control, and as the disease progresses, muscle spasms and seizures. Canavan disease is always fatal, usually by the teenage years.⁸⁸

Like the better-known Tay-Sachs disease, also a progressive, fatal neurological disorder, Canavan is most commonly seen in Ashkenazi Jewish populations.⁸⁹ But Andreas's father was not Ashkenazi, and "Andreas' symptoms were less severe than most kids with Canavan disease," Tsipis says. Both factors probably helped delay Andreas's diagnosis. In fact, when Tsipis and her husband consulted a geneticist before their second pregnancy, they were told that their son's condition was probably not genetically linked.⁹⁰ Any child of two parents who each carry a recessive disease gene has a 25 percent chance of inheriting the disease, but fortunately, Tsipis's second child was born healthy. "We were very lucky, obviously, because we did not know we were gambling," Tsipis says. At the time of Andreas's diagnosis, it was still unclear which gene, and what mutation, was associated with Canavan disease.

In 1987, Daniel and Deborah Greenberg set out to change this. The Greenbergs, a Chicago couple with two Canavan-afflicted children, encouraged a geneticist at the University of Illinois at Chicago to find the cause of the disease that was killing their kids. Dr. Reuben Matalon (also a professor and pediatrician) took on the task with a single-minded frenzy. He even went to the care facility where the Greenberg children lived to draw blood samples himself. By 1988, Dr. Matalon had discovered the enzyme deficiency responsible for Canavan disease.

A year later, Dr. Matalon became Director of Research at Miami Children's Hospital, where he and his team continued to research Canavan disease. In 1990, they developed a prenatal screening test for the disease. But Canavan proved highly challenging to diagnose using samples of amniotic fluid or placenta. Tragically, four children that Dr.

Matalon's test deemed healthy while in the womb were born with Canavan, and Miami Children's Hospital was forced to settle multiple lawsuits over these errors. It became clear that a DNA-based test was needed for Canavan disease.⁹¹

The breakthrough came in 1993, when Dr. Matalon and his team finally isolated and sequenced the gene and mutation associated with Canavan.⁹² Judith Tsipis, along with the National Tay Sachs and Allied Diseases Foundation (NTSAD), the Canavan Foundation, and the Ashkenazi Jewish population, leapt into action.⁹³ Around 13,000 people received screening in the first year alone to see if they carried the disease gene.⁹⁴

In 1998, Andreas Tsipis died at 22 years old. This same year, both the American College of Medical Genetics and the American College of Obstetricians and Gynecologists (ACOG) recommended that parents of Ashkenazi descent be screened for Canavan disease before conceiving.^{95 96}

But within a month of ACOG publishing its guidelines, Judith Tsipis says, laboratories testing for Canavan across the country received letters ordering them to stop, or be sued.

Two days before publishing the sequence of the gene and mutations associated with Canavan disease, Dr. Matalon had filed for patent protection on this discovery. In late 1997, the U.S. Patent office assigned Miami Children's Hospital Research Institute, Inc. the patent rights to the gene, the enzyme it produced, and methods of screening for the mutations associated with Canavan disease. The gene now belonged to Miami Children's Hospital; any laboratory interested in testing for Canavan disease would have to purchase a license from the Hospital, or face a lawsuit for unauthorized use of private property. Additionally, every Canavan test would now incur a royalty of \$12.50 (discounted from an original \$25 or higher) for the Research Institute, and academic laboratories would be limited to 100 Canavan tests a year.⁹⁷

For the parents and organizations that had fought so hard to see the Canavan gene discovered, it was a devastating blow. "Here we were, trying to do something from our

own kids' personal experience, and all of a sudden, it was patented," Tsipis says. It was a particularly horrifying development for the parents who had offered Matalon their children's samples for research. "The people who actually gave samples from which the sequence and the mutation was determined had no knowledge that the outcome of their donating their children's blood and tissue would result in a gene patent that would then limit testing," Tsipis says.

In 2000, Daniel Greenberg, along with parents and organizations in the Canavan community, sued Dr. Matalon and the Miami Children's Hospital Research Institute. Their suit did not actually attack the claims of the patent, but rather the lack of informed consent of the parents donating their children's samples, concealment of intentions, and misappropriation of trade secrets (in this case, a registry of Canavan patients), among other complaints.⁹⁸

The lawsuit was settled after just under three years, out of court.⁹⁹ "To bring a lawsuit against a hospital required enormous resources," says Tsipis. "We didn't have a chance." There is a gag order on the settlement, so it's impossible to know exactly what happened. But the plaintiffs "agreed not to further challenge" the licensing and patent ownership of Miami Children's Hospital, while the hospital would continue charging for licenses and royalties. The only other publicly acknowledged outcome of the settlement was that the hospital would allow license-free use of the gene in Canavan disease research.¹⁰⁰

While the issue of gene patenting was not directly challenged as a result of the Canavan lawsuit, the case "helped put the problems associated with gene patenting on the map," Judith Tsipis says. And one of the lawyers who represented the Canavan families in their fight against Miami Children's Hospital wanted to continue charting the course.

Lori Andrews was the attorney who had watched with dismay two decades before as the USPTO allowed gene patents following *Diamond v. Chakrabarty*. The Canavan case "left a lot of things unsettled," she says, "because that was a pretty unique situation, where the idea for the research was the patient's, where the families gave so much."

Andrews realized that there was a larger legal issue at play here. Canavan was an unusual case, but it wasn't the only gene patent that was causing problems in the clinic. She knew of at least one more – a breast cancer gene patent, one that was limiting patients' access to diagnostic testing.

Andrews saw the “systematic issues” she was concerned about reflected in that patent. “I saw women that were not able to get access to the test because it cost over \$3000 and could have been done for a couple hundred or even under a hundred, if it weren't for the royalty of the patent, because the test itself is not that difficult to do,” she says. She was also worried that even those women who could afford it couldn't get an accurate second opinion.

“So I went to the ACLU [American Civil Liberties Union] and said, ‘You've got to do something about this,’” she says.

When Andrews first made her plea, in the midst of the Canavan case, the ACLU said they couldn't help. No large legal firms wanted to get involved, either, Andrews says, because they all had interests in biotechnology clients. “I had no backup,” she says.

But that was about to change.

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In 1990, the same year that the Human Genome Project kicked off, a young graduate student named Wendy Chung entered a joint MD-PhD program.¹⁰¹ Her plan: to study genetics. “I knew that that was going to be the future of medicine,” she says. Her instincts paid off. The Project, driven in part by the threat of patenting, reached its goals ahead of schedule, and so did Chung.¹⁰² Today, she is a clinical and molecular geneticist at Columbia University Medical Center.¹⁰³

In the clinic, Dr. Chung found that it was often difficult for her patients to get access to genetic testing. There was a range of issues, she says. In some cases, testing wasn't available, because the rights to a gene had been licensed to specific laboratories. In other cases, patients could get a test, but its cost was "exorbitant," as a single laboratory's monopoly on the gene patent eliminated market competition on test prices. Patients who did receive testing faced a new set of problems, as Runi Limary discovered: interpretation of test results could be limited, second opinions were not an option, and there were limited improvements or innovations in test quality.

"So for a variety of reasons, it was extremely frustrating," Dr. Chung says. She saw this challenge for not only patients with hereditary breast cancer, but with many other diagnoses, including Long QT syndrome (a genetic heart condition) and "a variety of neurological conditions."

Dr. Chung went to the National Institutes of Health and testified before Congress about the problem. Neither offered direct assistance, but the American Civil Liberties Union saw the congressional record, and decided they wanted to get involved.

"After they started thinking about exactly what disorders were affected by this, they started thinking about nationally, what would have the most visibility," Dr. Chung says. "And they decided, ultimately, to do breast cancer and Myriad."

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On October 7, 1994, *Science* magazine published a research article entitled "A Strong Candidate for the Breast and Ovarian Cancer Susceptibility Gene BRCA1."¹⁰⁴ The authors were members of Myriad Genetics, a three-year-old biotechnology company created as a spin-off from a laboratory group at the University of Utah's Center for Genetic Epidemiology.¹⁰⁵

Those researchers formed Myriad in the midst of a fierce race to uncover the gene's code. At least six other research groups provided fierce competition, including Mary Claire

King's team at the University of California at Berkeley, which had originally discovered that the gene was located on chromosome 17.¹⁰⁶

Myriad won the race in late 1994, sequencing the gene, which comprised about 80,000 nucleotides of information, buried within the 80 million other nucleotides on chromosome 17.¹⁰⁷ Just under a month before the results were triumphantly published in *Science*, Myriad filed its first patent application on the BRCA gene. By 1998, the company held a total of seven patents that covered the gene, its mutations, and diagnostic tests.¹⁰⁸

The company filed for a patent on the second BRCA gene less than two years after the first. BRCA2 was also about 80,000 nucleotides long, located among the 114 million letters of chromosome 13.¹⁰⁹ The US Patent and Trademark Office granted Myriad two patents on BRCA2, covering the gene's DNA and mutations, plus methods of diagnosing mutations. Their patents also granted them the rights to the BRCA genes' cDNA sequences. The company began offering a total of three tests covering the genes – the Comprehensive BRACAnalysis test that Runi Limary took, plus a multi-site and a single-site mutation test.¹¹⁰

Myriad's approach to licensing its patents was highly restrictive. Myriad sold licenses only to a limited number of laboratories, and allowed these laboratories to perform only a limited number of tests. All complete sequence analyses were performed at Myriad's own labs in Salt Lake City, at a cost of \$2,580 each.¹¹¹ With its patents on the gene and the genetic tests in hand, Myriad moved to prevent other laboratories from infringing their intellectual property.¹¹²

What happened next greatly resembled the story of patent enforcement on Canavan disease. But the response would be very different.

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In the late 1990s, Dr. Harry Ostrer, a clinician and researcher at New York University’s Molecular Genetics Laboratory, received troubling news from the laboratory to which he sent his patients’ samples for genetic screening. The laboratory would no longer accept samples for BRCA testing.¹¹³ Myriad was enforcing the “right to exclude” granted by its new gene patents.

At the time, Dr. Ostrer also oversaw genetic risk programs at two hospitals, and he became keenly aware of two clinical challenges as well: first, many patients without health insurance could not afford Myriad’s test.¹¹⁴ Second, many patients faced the same “variants of unknown significance” as Runi Limary. The predictive power of the genetic test – at both the scientific and clinical level – seemed to be constrained by its patent.

In 2004, Dr. Ostrer went to the Laboratory Director at Myriad Genetics to propose a more efficient, less costly BRCA test that could also help address some of the unknown gene variants.¹¹⁵ “They didn’t want to do it,” says Dr. Ostrer, now a professor of pediatrics and pathology at Albert Einstein College of Medicine. “They had their own model for doing genetic testing, and they weren’t as interested in setting up something different. From a business point of view, their model was obviously very successful.”

But whether or not Myriad’s patents benefited the company financially, they seemed to be having less success in serving the stated purpose of patent protection: promoting new research and innovation. In fact, the patents seemed to be doing just the opposite. Physicians and patients weren’t the only ones who recognized this risk. At least one scientist saw the problem, as well – and he realized that it was bigger than many people thought.



On the banks of New York’s East River, several sleek white buildings form the Weill Cornell Medical Center. On the thirteenth floor of one of those buildings, Christopher Mason’s office provides a view of rooftops and a hazy uptown sky. Mason is a geneticist, a fact expressed in his office decorations. There’s a stuffed chromosome pillow leaning

against the window; the wall displays complex genome maps and an illustration of a Holstein cow and a chicken staring at a cow-patterned egg between them. “I was fascinated by the fact we started as one cell and all the instructions later, become the entire panoply of cells in your body,” Mason says. “And so all you need is time and the right cues, and it’s amazing that it works as well as it does.”¹¹⁶

Mason’s laboratory works to understand how to read the genetic code that controls this process. He observes extreme mutations, and also looks at the evolution of the genome, studying DNA, proteins, RNA and its regulation, and more. “If you add it all up, it sounds like we do everything,” Mason says. “But we kind of do a little bit of everything...because I’m, like, ADHD and barely function as a scientist.” He is presumably joking, but he does seem to be managing several things at once, sometimes pausing our conversation to check up on a grant application or a rescheduled meeting later in the afternoon. His wide range of focuses also helps explain his interest and involvement in law.

As a graduate student at Yale, Mason had stumbled across a 2005 research paper that detailed the breadth of genetic patents and their effect on research. The paper suggested that nearly 20% of human genes were patented.¹¹⁷ Mason had just begun to study human genes associated with autism, combing through them to search for disease-causing mutations. The paper stunned Mason, who remembers thinking, “That means that almost every day, I’m infringing on someone’s patent.” It seemed too weird to be true, he says, but he soon discovered that it was.

This made an impact on Mason, who partnered with a friend in law school to create a course exploring both science and law (“We called it Law and Order, Special Genomics Unit”). He decided to pursue postdoctoral work at Yale, creating himself a position he called the “Visiting Fellow of Genomics, Ethics, and Law.”

In early 2007, California representative Xavier Becerra introduced a bill in Congress that proposed prohibiting patents on nucleotide sequences and their functions.¹¹⁸ Mason

immediately got involved, emailing congressmen and legislative aides. “I thought, ‘Wow, this is great, maybe this will get solved,’ ” he says.

He quickly discovered his mistake. “It’s hard to get the representatives to one, care about it and two, support it,” he said. “And if it’s perceived to hurt business at all, they’re generally very wary about doing anything like that. So it didn’t move that fast.” Becerra’s bill was abandoned and soon died.

But the issue of gene patents continued to plague Mason. He wondered if different parameters could be used to more accurately represent just how many genes in the human body were patented. This was largely a semantic problem. “If you look in the patents, you can define your own language,” he says. “And so a lot of them say, ‘We claim any piece of DNA that has even 65% homology,’ and then down below it defines ‘homology’ as at least 40% the same.” This means that extracting a gene with at least 26% similarity to a patented gene could be considered infringement. Was it possible that the original gene patenting paper that had shocked Mason years before might actually be underestimating the true scope of genetic patents?

To choreograph life at large, genetic code must be highly specific and controlled. But when there are only four letters to work with, it’s impossible not to repeat letters every now and then. Every three nucleotides direct the formation of a single amino acid, the biological bricks used to build proteins. The average human gene needs between 10,000 and 15,000 nucleotides (around 3,000-5,000 amino acids) to encode its specific instructions.¹¹⁹ But when Mason went looking through patents, he found that patent protection was applied to much shorter stretches of DNA. In fact, the magic number seemed to be...15. Not 1500, not 15,000, but 15 individual nucleotides.

Patenting 15 nucleotides of the human genome presents a problem when repetition of these nucleotides occurs in multiple other genes. It’s akin to having legal protection on the letter “s,” when the average word is ten letters long. That means that “sandwiches,” “schoolwork,” “settlement” and “shantytown,” though clearly different in meaning, all

contain the same patent-protected letter. And “sandwiches” is the biggest violator, because it contains that patented portion *twice*. (Nothing says that the words have to *start* with s, either, so “racecourse,” “filibuster,” and “generators” all infringe the imaginary “s” patent as well.)

Using the coding language Perl, Mason went through the National Center for Biotechnology Information’s open database of gene sequences, looking for matches of specific nucleotides. “It only took maybe an hour to write that script,” he says. “Within the language of Perl, it’s an extraordinarily easy thing to do.” In fact, the challenging part of his study was navigating the semantics of the patents, he says, not analyzing the genes themselves.

His results were dumbfounding. When he compared 15-nucleotide sequences covered by gene patents to the genetic code of all human genes in the open database, Mason found at least one patented sequence in 100% of known genes. Every single gene in the human body was at least in part private property. One patent’s claims alone matched a sequence found in over 90% of all human genes. The similarities between all creatures’ DNA complicated matters further: Mason’s study found that a patent applying to cow genes actually contained nucleotide sequences that matched 84% of human genes as well.¹²⁰

It was a shocking discovery. Even patenting the entirety of a single gene could limit research unintentionally. “To think that one gene does one thing—we know it’s not true,” Mason says. One gene can often be linked to a range of functions, and its failure to a range of diseases. A patent on a gene probably restricts research on “five or ten other things,” he says. BRCA1 is a great example; its mutations are implicated in breast cancer, but also prostate cancer, lung cancer, and other cancers as well.¹²¹

The fact that miniscule fractions of genes were protected created the potential for even more indiscriminate limitations. “If I was testing for asthma and those 15 base pairs occurred in the segment that I was testing, then it would infringe the Myriad patent,” says

Lori Andrews. "...So there was actually a lot, lot more at stake than just breast cancer here."

As an academic researcher, Mason says, he felt (and feels) relatively safe from patent infringement lawsuits. He's referring to a widely held notion of a "research exemption" on biological patents. If a researcher violates a patent while working for an academic university, many believe he is protected from the consequences of the infringement.

But, says Mason, "There's no actual law written that says anyone at a university does not have to worry about patent infringements. It's not at all true." The apparent exemption, he says, is more a matter of public relations than law. "If you were suing every university for working on breast cancer, it would look bad, basically."

Myriad's position on the research exemption was somewhat unclear. The company is said to have stated in media interviews that it did not intend to enforce its patents against scientists using the genes for research. But a conflict with the University of Pennsylvania's Genetics Diagnostics Laboratory (GDL) muddled the issue somewhat. The GDL had been performing BRCA1 and BRCA2 testing using their own methods. When Myriad obtained its patents in 1998, the company sent the GDL cease-and-desist orders. At first, the GDL refused to stop testing, saying that because its tests were provided for researchers, it qualified for a research exemption. Myriad disagreed, arguing that this research didn't occur at the GDL itself. The company wrote up a Memorandum of Understanding with the National Cancer Institute, defining "research" in relation to their patents to mean only the grant-supported work of an investigator. Any technical services supporting such research were not permitted. Though Myriad later defended its pro-research stance, noting that it didn't require a license for research and pointing to a large collection of publications involving BRCA genes, the company's actions left many researchers believing that Myriad would use its patents to stifle scientific progress in favor of turning a profit.¹²²

Christopher Mason says that modern technology has advanced a researcher's ability to navigate around a genetic patent. Many patents are written for single isolated, purified genes, he says, and today, sequencing a cell's entire genome has become a more common practice. But even advanced sequencing technology fails to eliminate the risk of gene patent infringement, Mason says, because examining a single gene more closely, or running a common lab procedure that isolates genetic sequences, can immediately violate a gene patent.

Following the failure of the 2007 bill, Mason started talking to lawyers with the ACLU. They realized there might be a second possible route to enacting change: challenge a gene patent itself.

For the next year, Mason discussed genetics with the ACLU. By 2009, the ACLU was ready to launch a court case. And they found several allies ready to join them.

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The ACLU put together a diverse team of plaintiffs willing to take Myriad's patents to court. This included several physicians, including Dr. Wendy Chung, one of the first to join the case. When the ACLU approached Dr. Harry Ostrer, he also swiftly agreed to stand with them. "I wanted to make sure it was a serious lawsuit," he says.

Several patients whose medical decisions had been impacted by the BRCA patents joined the team as well. One of these plaintiffs was Runi Limary. "I was all on board on this," she says. In her declaration to the Court, Limary wrote that if the Myriad patents were no longer a barrier, Dr. Chung had said she would conduct further testing on the meaning of uncertain gene variants, including Limary's own rare mutation.

Dr. Chung, Dr. Ostrer, and Limary united with a handful of other physicians, researchers, geneticists, and patients. The far-reaching implications of genetic patents also garnered support from a diverse group of organizations. The Association of Molecular Pathology served as the lead plaintiff, and was joined by the American College of Medical Genetics,

the American Society for Clinical Pathology, Breast Cancer Action, and more. “It’s really about the principle of persevering public access to information about our genetics,” says Judy Norsigian, who was the Executive Director of Our Bodies Ourselves, a public interest organization that focuses on women’s health, when she joined the case as a plaintiff. “It’s not something that should be controlled by companies.”¹²³ In May 2009, the ACLU and the Public Patent Foundation filed their case against Myriad Genetics, Inc.¹²⁴

“Everyone said, ‘You can’t win,’ ” says Mason, who did not serve as a plaintiff, but submitted a declaration for the proceedings. “ ‘The patents have been around for decades, the whole biotech industry might collapse’ ...we just thought, well, it’d be better if people could just research on other things. There’s other things you can make money on.”



In lower Manhattan, the golden doors of the New York Federal District Court face a tree-lined city park. Through these doors lay the first hurdle for the case that would become *Association of Molecular Pathology et al v. Myriad Genetics, Inc., et al.*

The challenge was highly specific: Myriad’s patents should be ruled invalid, the petitioners argued, because as a product of nature, the BRCA1 and BRCA2 genes could not be considered an “invention.”

Myriad’s position was that the genes were significantly different from their natural form, much like Chakrabarty’s genetically manipulated bacteria had been. In removing a gene from the human body, the defendants argued, they had to sever the chemical bonds that hold DNA and genes together. In isolating this gene, cutting it out of its usual home in the human genome, they said they had significantly changed the natural form of the gene.¹²⁵

The plaintiffs disagreed. Whether or not the gene had been removed from the body didn’t change its function whatsoever; the gene worked exactly as it had evolved to work in

nature. (Mason notes that isolated DNA isn't always a laboratory creation, either; fragments of a baby's DNA can show up in her mother's bloodstream, and transplant patients can express pieces of DNA from their donor's organs.)

The District Court assigned Judge Robert Sweet to the case. It was, as one article puts it, "a remarkable happenstance" that Sweet's clerk just so happened to have a PhD in molecular biology.¹²⁶ When Sweet handed down his decision in March 2010, his ruling shocked the biotechnology industry.

Sweet found all of Myriad's claims to the BRCA genes invalid, ruling that "DNA represents the physical embodiment of biological information," and this could not be considered patentable subject matter. As for the argument that isolating DNA made it a new form, and therefore patent-eligible, Sweet called it a "lawyer's trick."¹²⁷

Myriad appealed the ruling, and the case proceeded to the Court of Appeals for the Federal Circuit in Washington, D.C., which handles all patent appeals from the District Court.

A panel of three judges heard the appeal.¹²⁸ Mason remembers the tension of the process clearly. At one point, he says, Harry Ostrer was the only plaintiff left to testify. "And we're like, 'Don't get sick, don't go on a plane,' " Mason says. "If he had died, we would have thought he was assassinated, unquestionably."

This time, the ruling was different. Two of the three presiding justices decided that isolating DNA did indeed create a new chemical product, and should be legally patent-eligible.¹²⁹

The one dissenting judge, Justice William Bryson, protested that removing a gene from the human body to patent it was "akin to snapping a leaf from a tree."¹³⁰ At one point during the proceedings, Mason says, Bryson forced the Myriad lawyer into saying that by

the current logic, it should be legal to patent an organ, say a kidney, if it was removed from the human body and purified. “Which is crazy, right?” Mason says.

This time, it was the plaintiffs’ turn to appeal – now, to the highest court in the land. The Supreme Court agreed to hear a single question: “Are human genes patentable?”¹³¹ On April 15, 2013, the Court heard oral arguments from both sides. Fifty-nine days later, the nine justices issued their unanimous answer to the question: no.

“A naturally occurring DNA segment is a product of nature and not patent eligible merely because it has been isolated,” wrote Justice Clarence Thomas in the Supreme Court’s decision. Further, the court ruled, “Myriad’s claims are not saved by the fact that isolating DNA from the human genome severs the chemical bonds that bind gene molecules together,” because the patents had nothing to do with the chemical composition of the genes, but rather the “genetic information encoded” within.

However, the Court also determined that cDNA is “not a ‘product of nature,’ so it is patent eligible...Its creation results in an exons-only molecule, which is not naturally occurring.” While the “order of the exons may be dictated by nature,” the decision continued, “the lab technician unquestionably creates something new” when she makes a strand of cDNA.¹³²

Over three decades after *Diamond v. Chakrabarty* opened the door to widespread gene patenting, *Myriad Genetics v. Association of Molecular Pathology* seemed to have forced it mostly shut.

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The decision pleased many of the people who had fought for years to see gene patents overthrown.

“Hopefully this will encourage the patent office to go back to its constitutional foundation, that it’s supposed to promote innovation,” says Lori Andrews, “which I think might get us back to having patents on more tangible things.”

In the months since, the decision has “completely changed the landscape, at least for hereditary cancers,” says Dr. Wendy Chung. The Court’s ruling, Dr. Chung continues, frees researchers to look at the entire genome without worrying about whose patent they might be infringing upon. “So it really enables a whole new way of being able to provide genetic diagnostics to patients.”

“I think we were very successful in accomplishing our goals,” says Dr. Ostrer. Other competitors moved into the market for breast cancer testing, he says, and the cost of such tests dropped “almost three-fold.”

Runi Limary agrees that she’s seen changes in the pricing, and notes that even Myriad is offering a more comprehensive line of testing now. She’s excited to see other companies sharing their research data, too. “Now we have more data, so someone hopefully down the line from now, they’ll have a sample population of the hundreds, not me where I had three. So at least they can make a little bit more educated guess on what body part to remove, and which medicine to take.”

Others are less satisfied with the ruling. Dr. William Noonan, a former physician who is a patent attorney and head of the life sciences group at Klarquist Sparkman, L.L.P., says that legally speaking, DNA should be patentable. Precedents aside, United States patent law “says something is patent eligible if it is a composition of matter,” he says. In his opinion, DNA is still, “except to the most scientifically illiterate person, obviously a composition of matter as intended by the patent statute.”¹³³

On top of this, the Supreme Court’s distinction between isolated DNA and complementary DNA is “incoherent,” says Dan Burk, the Chancellor’s Professor of Law at the University of California, Irvine. Burk says the decision effectively presents “two

different holdings,” the second contradicting the first, he says. Genomic DNA is not patent-eligible, regardless of changes to chemical structure, because their genetic function is the same as native DNA. But cDNA is patent-eligible, regardless of changes to genetic function, because the chemical structures are not completely the same as native DNA. “If a client walks into your office and said, you know, ‘I have a nucleotide I want to patent,’ I really don’t know what you would tell them,” Burk says.¹³⁴

Burk says that it’s now up to the Federal Circuit courts and, “to some extent,” the USPTO, to interpret the meaning of the Supreme Court’s decision. “And my students are thrilled to death, because it’s essentially full employment for patent lawyers for 30 years,” he says.

Dr. Noonan expresses concern that the United States is now falling behind the rest of the world in terms of their patents, especially in terms of biotechnology. It’s a view echoed by Myriad’s Ron Rogers. “The recent U.S. court rulings that have significantly weakened patent protection in the U.S. relative to the rest of the developed world, which puts the U.S. at a real competitive disadvantage on a global scale,” he writes in a February 26 email. “Many industry experts believe that unless there is a fix, the U.S. will fall behind other countries in terms of scientific innovation.”

But others challenge such claims.

“I don’t think it’s that big of a deal, and I think in many ways it’s a good thing,” says Jon Clardy, a professor of Biological Chemistry and Molecular Pharmacology at Harvard University and Harvard Medical School.¹³⁵ Clardy’s research focuses on finding pharmaceutically important molecules in nature.¹³⁶ He says he holds around fifteen patents of his own, some of which are the types of “products of nature” that will be impacted by the Myriad ruling.

But just knowing the structure of a natural compound isn't ultimately very useful, Clardy says. "What I think the science needs to do is shift its attention to function. And that patent decision has exactly that effect...I think it will accelerate future research."

Burk doesn't believe that losing the ability to patent genetic code will be a major loss for the biotechnology industry. "In the sense that [the ruling] creates uncertainty, yes, it's a serious problem for innovation," says Burk. But, he adds, "It's actually not a problem for biotech in the sense of patenting DNA sequences. That's old technology. Nobody cares about that anymore."

But this hasn't always been the case. "I think it's clear that gene patents were critical to the development of the early biotech industry," says Burk. "...If the patent office hadn't made the decision that it made thirty years ago, the biotech industry would look very differently, or we might not have one."

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Some uncertainty remains about what a future without genetic patents will look like for research and development.

Regardless of how it may complicate matters legally, nobody seems concerned that the Supreme Court's stance on cDNA will provide much of a development incentive for cDNA patents. Lori Andrews and Christopher Mason both even tentatively agree that the patent-eligibility of cDNA is probably supported in this case. The Court's job was to determine whether or not isolated genes could be patented as "products of nature," and cDNA does not occur naturally.

However, neither Andrews nor Mason believes that cDNA patents would stand much of a chance in court if someone challenged them on the other requirement of patentability: non-obviousness. "It's completely obvious to take out the non-coding regions and make a cDNA. People do that in high school biology classes," Andrews says. Mason agrees, saying that there is "nothing remotely inventive or really innovative" about cDNA. He is

more concerned that another legal battle may arise over a different type of biological ownership: epigenetics patents.

“Epigenetics” describes any genetic control that exists above the level of a DNA sequence. Epigenetic controls can be chemical modifications of DNA itself, such as DNA methylation, which consists of adding a cluster of one carbon and three hydrogens called a “methyl group” to DNA. This can “shut off” or “silence” a gene, preventing that gene’s instructions from being expressed.¹³⁷ Removing the methyl group will switch the gene back on. A similar control over how genomes are read comes from loosening or tightening DNA on the spools of its chromosomes. Such epigenetic instructions can be altered in response to environmental changes, and passed down through generations, like DNA itself. Epigenetic regulation is crucial for proper development, as it directs cells to use only the specific genetic information they need, allowing for differentiation between skin cells, bone cells, and brain cells.¹³⁸

The possibility of manipulating epigenetic processes within the patent system appeared when the USPTO issued a new set of guidelines for their patent examiners following the Myriad trial. When Mason read these guidelines, “I almost wanted to start getting involved in more litigation because I was so annoyed,” he says. The new guidelines stipulate that if a small chemical change is made to a naturally occurring product and this changes that product’s function, the resulting creation is significantly different from its naturally occurring predecessor, and it is patent-eligible.¹³⁹

Mason fears that this will apply to gene sequences that have been epigenetically modified—for example, by adding a methyl group. “It’s like launching the same problem we had with DNA, now with epigenetics...And that’s my big concern, is that epigenetics assays, tools, methods, will all become kind of under scrutiny, or some may be patented in ways we may not have liked,” he says.

Even so, Mason, like many who were strongly opposed to gene patents like Myriad’s, still sees a role for intellectual property in biotechnology. He sees a particular value in

protecting lab-synthesized genomes, which he calls “the last frontier.” Mason believes that synthetic gene sequences should be issued legal protection – if not a patent, perhaps a copyright like those assigned to authors of other written works. After all, he says, if you synthesize a gene, “You wrote a genomic story, out of the nucleotides of the world.”

Dr. Ostrer, in turn, believes that patents have their specific place in genetic research – just not on the genes themselves. “I think there should be patents for new methods,” he says. He has filed such patents himself, he says, “including ones that involve these genes.”

But Dr. Noonan believes the Supreme Court would be hesitant to support even this type of patent. He invokes the 2011 case of *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, in which the Supreme Court ruled that a method for comparing drug levels in a patient’s blood to alter a diagnosis was not patent eligible.¹⁴⁰ “They made it sound as if, ‘Oh, well, any sort of manipulation of information in a medical context was an unpatentable law of nature, and so therefore, it shouldn’t be patented,” Dr. Noonan says. “The Patent Office has sort of followed through on that with a vengeance, and it has made it very difficult to obtain meaningful patent protection on methods of genetic diagnosis, or epigenetic diagnosis for that matter.” Burk notes that the ruling in the *Mayo v. Prometheus* case was a far more significant blow for intellectual property in medical diagnostics than the *Association of Molecular Pathology v. Myriad* ruling.

Lori Andrews is more of a maximalist. She warns that even innovation in fields such as synthetic biology would require caution. “In the synthetic biology area, we’re going to have to figure out how much I have to change a gene for it to be patented, and what kind of impact this will have on other areas in which the patent office has kind of exceeded its permissible grants of patents,” she says. It’s a once-bitten, twice-shy approach from someone who has watched the full meteoric rise and fall of gene patents.¹⁴¹

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On April 12, 1955, news anchor Edward R. Murrow held a televised interview with Dr. Jonas Salk. Salk’s polio vaccine, which would prove a powerful weapon against one of

the most dangerous childhood diseases in the US, had just been proven safe and effective.^{142 143} Murrow asked Salk: who owned the patent on the new vaccine?

In a halting answer that has since become famous, Salk replied: “Well, the people, I would say. There is no patent...could you patent the sun?”¹⁴⁴

Of course, his answer was somewhat misleading. A vaccination is, from the standpoint of patent law, nothing like the sun. The one was created; the other, omnipresent. There was nothing inherently unpatentable about a vaccine that saved millions of lives. (And the laboratories where the vaccine had been developed did, indeed, look into patent protection; the idea was abandoned because multiple funding parties and the dependence upon the work of others made the patent of “narrow scope” and “doubtful value.”)¹⁴⁵

But perhaps a human gene is, in fact, a bit more like the sun. Like our closest star, our genomes were not invented, but discovered; we are still uncovering genes’ potential and learning their secrets today. The power of genetic material is shared, like sunlight, by every living creature past and present on this Earth, from bacteria to dinosaurs to humans.

And today, because of the efforts of a handful of doctors, lawyers, and patients, and the unanimous decision of nine judges, genes remain a shared good, property of the humans they came from.

Whether or not this is the best decision for science, for law, for finance, or for basic human rights still remains to be seen. But as John Sulston, the head of the Human Genome Project in Britain, said in 2003, science “succeeds only if our handiwork is in the open for all to see and make of it what they will.”¹⁴⁶

And a world where genetic information is free for all is likely one Thomas Jefferson would have appreciated. As Jefferson put it in 1813, sharing an idea was like lighting a candle, and “he who lites his taper at mine, receives light without darkening me.” The sharing of ideas

[S]eems to have been peculiarly and benevolently designed by nature, when she made them, like fire, expansible over all space, without lessening their density at any point, and like the air in which we breathe, move, and have our physical being, incapable of confinement, or exclusive appropriation.^{147 148}

Speaking centuries before science uncovered the chemical letters that write life into being, his words are perhaps all the more poignant when applied to our genes, the physical and intellectual property that gives us the breath, movement and being of which Jefferson spoke. Through them, we gain the ability to discover or invent, patent and share, and chart a future that optimizes progress and collaboration, in science and humanity at large.

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⁶ Jolie, “My Medical Choice.”

⁷ Limary, “Declaration of Runi Limary,” 2.

⁸ *Ibid.*

⁹ “How is Ovarian Cancer Diagnosed?” *National Ovarian Cancer Coalition*.

¹⁰ “The U.S. Patent System Celebrates 212 Years,” *United States Patent and Trademark Office*.

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¹² “The U.S. Patent System Celebrates 212 Years,” *United States Patent and Trademark Office*.

¹³ “Inventors,” *Smithsonian Education*.

¹⁴ “Article 1, Section 8, Clause 8,” *University of Chicago*.

¹⁵ *Inventions Patentable*, §101

¹⁶ “Types of Patents,” *United States Patent and Trademark Office*.

¹⁷ *Inventions Patentable*, §102.

¹⁸ *Inventions Patentable*, §103.

¹⁹ *Inventions Patentable*, §154.

²⁰ Jeffrey Meldman, in discussion with the author (by phone), May 11, 2015.

²¹ *Inventions Patentable*, §154.

²² Hyde, *Common as Air*, 51.

²³ “U.S. Patent Activity,” *United States Patent and Trademark Office*.

²⁴ “USPTO Patent Full-Text and Image Database,” *United States Patent and Trademark Office*.

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- ³⁰ “Plant Variety Protection Office,” *United States Department of Agriculture*.
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- ³³ Watson and Crick, “A Structure for Deoxyribose Nucleic Acid,” 737-738.
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- ³⁵ “Genetics versus Genomics,” *University of Miami Health System*.
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- ⁴⁷ Lori Andrews, in discussion with the author (by phone), January 22, 2015.
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- ⁶⁷ *Ibid.*, 96.
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