
Biomedicine in the Twentieth Century: Practices, Policies, and Politics

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Genes, Disease, and Patents: Cash and Community in Biomedicine

Daniel J. Kevles

In 1988, in a report on the emerging Human Genome Project, the National Research Council called for keeping open the data the project would generate, declaring that “. . . access to all sequences and material generated by these publicly funded projects should and even must be made freely available.” Shortly thereafter, the National Institutes of Health (NIH), the lead agency in the project, chimed in, holding that the data should be “in the public domain, and redistribution of the data should remain free of royalties.”¹ The admonitions to openness of course expressed the scientific community’s longstanding communitarian norm, part ethical and part practical, that knowledge of nature is to be publicly shared.

But the project had hardly gotten under way before it felt a counter-communitarian jolt toward privatization. The blow came in 1991 from J. Craig Venter, a biologist at the NIH, in Bethesda, Maryland, who proposed the wholesale patenting of human gene fragments called “expressed sequence tags,” or ESTs. Although just 150 to 400 base pairs long, each served to identify the gene of which it was a part. Venter claimed that ESTs would have utility as diagnostic probes for genes, but he also seemed bent on using the fragments to gain control of the intellectual property in the entire gene that the EST identified even though the EST revealed nothing about the gene’s function. Within a year, the number of ESTs covered by the Venter/NIH patent application had multiplied to almost 7,000. A lawyer for the leading biotechnology firm Genentech noted, “If these things are patentable, there’s going to be an enormous cDNA arms race.”²

Much to the relief of most academic scientists and a sizable fraction of the biotechnology industry, the U.S. Patents and Trademarks Office (USPTO) rejected the Venter/NIH application, holding that ESTs were not patentable proxies for entire genes.³ But the episode reveals that, from the beginning, human genomics has been torn between a commitment to communitarianism and an impulse to privatization and cash. Communitarians disparaged the cash impulse as a major and unwelcome departure from a longstanding commitment to cooperativeness in seeking to understand the workings of nature. There is a good deal of truth in the assumption of communitarianism in science, but the assumption is also suffused with a good deal of mythology, a romanticization of scientific practices in the past.

First, then, a few words about past scientific norms and practices in the interest of throwing into perspective the issue of cash and community in contemporary genomics.

Cooperativeness is a cultural value of ancient lineage in science. It was and remains undergirded by the standard of humility before the mysteries of nature to which so many scientists have adhered. The reasoning has gone that nature is infinitely complex, no one scientist can untangle its intricacies, and so all scientists must cooperate in the joint pursuit of understanding. The search for truth thus transcends the individual scientist, the local scientific group, even the national scientific community. Cooperation across national boundaries is one of the fundamental ethics of science. Scientists have often repeated the remark of the British chemist Humphrey Davy, who in 1807 accepted a prize for his research from Napoleon: “If the two countries or governments are at war, the men of science are not—that would indeed be a civil war of the worst sort.”⁴

Through the long nineteenth century, scientific internationalism was reinforced by the increasing integration of the globe that technology was accomplishing via steamships, railroads, telegraphs, telephones. A number of cooperative scientific endeavors emerged in fields such as astronomy, geology, and geodesy. Scientists in these fields were concerned with global tasks—e.g., mapping the heavens and the earth—tasks that

could be efficiently pursued by melding the results of local effort into a cooperative global network.

But competitiveness has also characterized fields that lent themselves to cooperative effort, and it has been perhaps even more manifest in fields that have not—for example, the branches of physics and chemistry that are grounded in the small, individualistic endeavor. More than fifty years ago, the pioneering sociologist of science Robert K. Merton pointed out that at least since the seventeenth century science has been marked by rivalries, some of them ferocious. For example, Galileo attacked competitors for stealing credit for his invention of the military compass and the telescope; and Newton, who was periodically obsessed with getting proper credit, battled with Robert Hooke over priority in optics and celestial mechanics, and waged a sustained war with Leibniz over the invention of the calculus. Merton wrote that priority disputes have not been the exception in science. On the contrary, they “have long been frequent, harsh, and ugly.”⁵

One has to think back only to James D. Watson’s memoir, *The Double Helix*, to be reminded that even without commercial incentives the practice of science could be marked by aggressive secretiveness, competitiveness, and even ruthlessness. In a review of the book the biologist Richard Lewontin wrote, “What every scientist knows, but few will admit, is that the requirement for great success is great ambition. Moreover, the ambition is for personal triumph over other men, not merely over nature. Science is a form of competitive and aggressive activity, a contest of man against man that provides knowledge as a side product.”⁶ Natural competitiveness has also been exacerbated by the exponentially increasing number of players in the game.

Since the late nineteenth century, the longstanding propensity to personal competitiveness was compounded by the increasing utilitarian payoffs of laboratory science. Physics and chemistry fueled what is known as the second industrial revolution that has continued through our own day. In branches of these fields, commercial competition penetrated academic science far more widely than it had hitherto. World War I, World War II, and the Cold War introduced national policies that fostered international rivalry in areas of science related to the technologies of national defense. The close interweaving of science and national security

put many laboratories under the wraps of national security, and it brought many of those that remained open into sharp competition with the West's principal antagonist.⁷

Even so, cooperation continued in high-energy particle physics, the most prestigious and expensive area of that science. Openness in the development of the technologies themselves had helped speed development of accelerators before World War II, and so did a similar policy pursued by the Atomic Energy Commission (AEC) after it.⁸ Unlike participants in human genomics, the early accelerator scientists and engineers thus worked in an environment largely free from patent constraints that greatly speeded accelerator development. Both law and policy have tended to vest in the AEC ownership of patentable inventions made in its laboratories or under its contracts and to make freely available the technologies of particle physics to scientists engaged in basic research.⁹

During the Cold War and since, a similar freedom characterized the exchange of basic data among high-energy physicists. They have achieved a formidable level of integration, now via the Internet, in respect of creating, evaluating, and banking data about the properties of elementary particles. Whence this exemplary cooperation and consensus? The answer, according to a member of a British group: "Particle physics data have no economic or strategic worth."¹⁰

In the life sciences, circumstances contributed to a strong anti-commercial orientation. With some exceptions—for example, hybrid corn—most university research, especially in the basic life sciences, yielded little that was commercializable or patentable, and of that, less that commanded significant, if any, market value. For example, the workhorse of classical genetics was, of course, *Drosophila*. Although fruit fly geneticists developed these creatures into standardized strains at the cost of much time and painstaking effort, no one attempted to profit from them; indeed, fruit fly stocks were freely exchanged among genetics laboratories on an international basis.¹¹ Similarly with bacteriophage in the middle third of the twentieth century, which were also standardized and made widely available among geneticists. Cooperation worked because there was little reason not to cooperate, and many reasons to cooperate, including the prospect of professional rewards. Besides,

most living organisms and their parts were held not to be patentable as a matter of law.¹²

Academic culture's resistance to commercialization was particularly strong in the life sciences related to health and medicine. The University of Toronto scientists who were responsible for the isolation of insulin excluded themselves from shares in revenue from the insulin patent, assigning their rights to the University of Toronto for one dollar each. Ditto for Harry Steenbock, at the University of Wisconsin, who ceded his patent on a process for producing Vitamin D to the institution, which made millions on it until it was declared invalid. In the mid-1930s, Harvard promulgated the explicit policy that innovations in medical research arising from its laboratories must not be patented or, if they were, should be given freely to the public.¹³

Harvard's policy now seems quaint. Molecular biology has been demonstrating for some thirty years that it is highly practical, capable of generating both products and profits. Academic institutions and entrepreneurial faculty, with strong support from the federal government, have used the technologies of recombinant DNA, gene sequencers, and research tools to establish an astonishing fund of new biomedical knowledge. They have also joined with entrepreneurs to establish the modern biotechnology industry and the intellectual property protection on which it is built, including the commercialization of human genes. And they have been assisted by the courts and the USPTO, which have together expanded the scope of patentability to include living organisms and their parts.¹⁴

Commercialization sharply challenged communitarian access to genomic data. If Craig Venter failed at the wholesale patenting of human genes, he sought, successfully, to capitalize on human genomics ultimately through the creation of Celera and fast, shotgun sequencing. Celera's original business plan called for its data to be held as proprietary by the company and released at first only to paying subscribers, while patents would be sought on genes of interest.¹⁵ After the human sequence was completed in 2001 jointly by Celera and the National Human Genome Research Institute at the National Institutes of Health, Celera

allowed academic scientists to download data only on a restricted basis—e.g., requiring that they not be given to anyone else.¹⁶

Other firms in the United States and Europe have managed to achieve exclusive control over genomic databases. Perhaps the best known is the arrangement of DeCode with the Icelandic government: The company enjoys exclusive access for commercial purposes to the national medical database; an agreement it entered into with the government in 1998, for twelve years. The drug firm LaRoche, which financed DeCode, got exclusive rights to develop pharmaceuticals for twelve diseases, in exchange for which it contracted to provide the Icelandic population with any such drugs free of charge.¹⁷

A number of critics both in and out of science have objected strongly to such proprietary arrangements, especially where it involves human genomic sequence data. Many have advanced an ethical argument—that the human genome is humanity's birthright, that it belongs to the human community and ought not to be privatized in any way.¹⁸ That ethical argument has been largely ineffective against the commercial drive, but consequentialist claims arising from the mutual self-interest of most genomic researchers have kept genomic databases largely public.

Several models demonstrated how this could be done. Among them was the *Centre d'études du polymorphisme humain* (CEPH), established in 1984 in France with genetic material from French and American families that was made freely available to scientists constructing a human genetic map.¹⁹ There was also the *Worm Breeder's Gazette*, a record of the worldwide effort to map and sequence and characterize the *C. elegans* genes, including their multiple mutations. The worm breeders shared data, methods, instruments, and stocks, including mutants. Within this community John Sulston began construction of a physical map of the worm's genome, and the community at large linked this map to the genetic map it had been developing collectively.²⁰ The enterprise was characterized by the award of credit within communitarian norms.

The worm model influenced representatives of the multinational human genome enterprise when they met in Bermuda in 1996 to strategize the project scientifically and draw up rules for the treatment of data. Clearly a response to the growing commercialization of the genome, the rules stated that: "all human genomic DNA sequence information,

generated by centers funded for large-scale human sequencing, should be freely available in the public domain in order to encourage research and development and to maximize its benefit to society.”²¹ They urged that all primary genomic sequence data should be in the public domain.

The publicly funded human genome effort, which since the early 1990s has operated on an international scale, has of course undercut privatization by retaining its commitment to openness in its databases. Since the beginning of the sequencing phase of the Human Genome Project, all data generated by participants have been deposited in publicly available databases every twenty-four hours. By 2003, the human genome sequence, essentially complete, was posted on the Internet with no barriers to use, no subscription fees, no obstacles.²² A growing number of journals will not publish genomic articles without proof that the authors have submitted their data electronically to GenBank, in Los Alamos, the central genomic database in the United States. The National Center for Biological Information, which runs GenBank, places no restrictions on reasonable use and distribution of its data.²³

Large, well-established pharmaceutical firms have recognized the value of publicly available databases. Ten of them were instrumental in the establishment of the SNP (for single nucleotide polymorphisms) consortium, in 1999. Far more interested in using genomic data than in generating it, they saw in the consortium a means of reducing costs for the employment of such data and recognized that making it freely available to all would accelerate the growth in the knowledge base and benefit the public good.²⁴

In all, the communitarian commitment in modern life science remains strong and has kept genomic databases widely available.

But despite the ubiquitousness of open genomic data, communitarianism and cash competitiveness remain in conflict in human genomics. The key reason is patents. The Bermuda rules, like CEPH, recommend against patenting human gene sequences. But there is nothing inconsistent with disclosing data and patenting the data if the disclosure occurs after a patent has been filed. And even if academic and biotech scientists submit genomic data to the public databases, they are free to file patents on it first.

What is wrong with patenting human genes? Nothing, many say, adding that much is right with it because it encourages investment and innovation in genomics. But one might counter that patenting human genes is at the least problematic because the practice entails costs to both the enterprise of research and the delivery of medical services.²⁵ In contemporary academic research, the expectation of patentability discourages open discussion of technical detail during the critical R&D phase before patent filing. Then, too, patented genes are research tools, and such tools, according to a decision by a federal court in 2002, are controlled by the patent holder, who may restrict and charge for their use because research even in its most abstract form is part of the “legitimate business” of the university and is not exempt from threats of patent infringement suits.²⁶

A human gene patent establishes what has been called “a chain of dependency” in biomedical research. The chain reaches to efforts to characterize the gene and its functions more fully and to develop diagnostic tests based on it. It thus has a chilling effect on all research that involves the gene.²⁷ One firm patented a gene encoding the CCR5 lymphocyte receptor without any knowledge of its link to HIV infection. When the latter was established by another laboratory, the patent holder declared that it would enforce its patent against anyone making use of the discovery in the development of any pharmaceutical to combat HIV. In 1999, a survey of 74 clinical laboratories revealed that a quarter of them had abandoned a clinical test they had developed because of pending patents and almost half had decided not to develop a clinical test because of the patent.²⁸

In the medical service area, gene patent holders have tended to insist that only they can conduct diagnostic tests using their gene. The practice threatens, among other consequences, to concentrate expertise in only a few centers; to fragment molecular medical services; to elevate the prices consumers pay for diagnostic tests; and to make doctors vulnerable for infringement suits. It also flies in the face of sound medical practice in that it can deny patients access to second and independent diagnostic opinions.

Such threats are not merely hypothetical, as is evident from Myriad Genetics’ management of BRCA1 and BRAC2, the two genes known to

dispose women to breast cancer. Myriad's BRCA1 patent covers the sequence not only as a descriptor of the gene but as the substance in and of itself and its mutant forms; also the uses of the gene as a probe or a primer; and its protein. Myriad's patent claims cover all and any diagnostic method that uses the gene, including those developed by others.²⁹

For various reasons, by the end of the 1990s Myriad held monopoly control through patents and exclusive licenses over the DNA sequence of BRCA1 and BRCA2.³⁰ Myriad demands that all commercial testing for the two genes be done in its laboratory. It will not license the test to anyone, with the result that a woman diagnosed positively by Myriad cannot obtain a second opinion from an independent laboratory.³¹

Myriad has enforced its patent rights against various universities, a hitherto exceptional practice. In 1999, for example, it notified Arupa Ganguly, of the University of Pennsylvania clinical genetics laboratory, that she was infringing the Myriad patents because she had independently developed a test to screen for mutations in the BRCA genes and was charging her patients a fee to undergo the test. Myriad advised the university to halt Ganguly's activities or risk suit. To meet criticism from academic researchers, Myriad negotiated an agreement with the NIH in 2000 whereby NIH-funded researchers would be charged \$1,200 per test instead of the usual \$2,580 so long as the purpose was research. In exchange, Myriad would have access to resulting research data.³²

How should we now think about the evolving conflict between cash and community in human genomics? BRCA1 was identified by Mark Skolnick, of the University of Utah. He had founded Myriad Genetics, and the university granted the fledgling firm an exclusive license on the sequence. Skolnick, contesting the idea that DNA is information, insists that it is a chemical and must be treated as such for patent purposes. He has said, "If you discover a new molecule, whether it's a pharmaceutical or a paint or a dye or a gene, it's a new molecule, you should be protected; . . . genetic patents really follow the model that's been set up in organic chemistry." The USPTO has affirmed that view, saying that if genes are treated as are "other chemicals, progress is promoted because the original inventor has the possibility to recoup research costs, because others are

motivated to invent around the original patent, and because a new chemical is made available as a basis for future research.”³³

The fact of the matter, however, is that no one can invent around a human gene, including the mutated form that causes a disease. Human genes are the only ones we have got and, as such, they are natural monopolies. As a society, we exclude private property rights in some natural monopolies—say, Yellowstone National Park or the Cape Cod Seashore. We allow private property rights in others—say, railroads or the radio spectrum—but we do not permit the property holders to use their rights of ownership absolutely. We regulate the property right.

The time has arguably come to regulate the kind of property right—the intellectual property right—that is represented by a patent in human genes and possibly in human proteins, too. There is ample foundation in the structure of American law for the regulation of patented innovations that are essential to public interests, including health. Congress may grant the federal government “march-in” authority to license a patent to third parties if the patent holder has not made the invention available within a reasonable time or does not reasonably satisfy needs of health or safety.³⁴

The regulation of human-gene patents might take the form of compulsory or voluntary licensing, or patent pools. It might even take the form of denying patentability to human gene sequences, which would then make them available to anyone for research into the gene, the development of diagnostic tests for it, and discovery of its functions and malfunctions, and the creation of pharmaceuticals based on it. This is a position advocated by many scientists, patient groups, and medical practitioners, including the American College of Medical Genetics. The strategy would allow for the patenting of the tests and the drugs while leaving the gene freely available for research.³⁵

Few places are better situated to advance this analysis and suggestion for a modified patent policy on human genes than the National Institutes of Health, the nation’s principal patron and safeguard of biomedical research in the public interest.

Notes

1. Committee on Intellectual Property Rights in Genomic and Protein Research and Innovation, Board on Science, Technology, and Economic Policy, Committee on Science, Technology, and Law, Policy, and Global Affairs, National Research Council, *Reaping the Benefits of Genomic and Proteomic Research: Intellectual Property Rights, Innovation, and Public Health* (Washington, D.C.: National Academies Press, 2005), p. 22. Hereafter, NRC, *Reaping the Benefits*. I am indebted to Bruno Strasser for comments, criticisms, and suggestions.
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3. *Ibid.*, p. 239.
4. Daniel J. Kevles, *The Physicists: The History of a Scientific Community in Modern America* (Cambridge, Massachusetts: Harvard University Press, 1995), p. 141.
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7. Kevles, *The Physicists*, pp. 141, 378-81.
8. Government Accounting Office, *DOE's Physics Accelerators: Their Costs and Benefits* (GAO: RCED-85-96, 1 April 1985), p. 45. A not-for-profit organization, the Research Corporation, obtained rights to the cyclotron from its inventor, the Berkeley physicist Ernest O. Lawrence, on the understanding that his Berkeley Laboratory would continue to be a beneficiary of the Corporation's policy of investing proceeds from its patents in university research. The Corporation hoped that these proceeds would include royalties from licenses to commercial firms using cyclotrons to make radioisotopes for biological and medical applications. No radio-pharmaceutical industry developed before World War II, however, and after the war, owing to inventions made to exploit atomic energy, the cyclotron appeared to have little commercial value. The Research Corporation then wrote all cyclotron laboratories to grant royalty-free use of the machine. J. L. Heilbron and Robert W. Seidel, *Lawrence and His Laboratory* (Berkeley: University of California Press, 1989), pp. 192-93, 196-99.

9. Atomic Energy Act of 1946, Secs. 4, 6; Atomic Energy Act of 1954, Sec. 152. Executive Order 10096, 23 January 1950, gave the government rights to all inventions made by government employees during working hours or while using government facilities. Case law originating in implementation of the Order is reviewed by John O. Tresansky, "Patent Rights in Federal Employee Relations," *Patent and Trademark Society, Journal*, 1985, 67: 451-88.
10. F. D. Gault, "Physics Databases and Their Use," *Computer Physics Communications*, 1981, 22: 125-32.
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13. Daniel J. Kevles, "Principles, Property Rights, and Profits: Historical Reflections on University/Industry Tensions," *Accountability in Research*, 2001, 8: 12-26.
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15. Kevin Davies, *Cracking the Genome: Inside the Race to Unlock Human DNA* (New York: Free Press, 2002), p. 208; NRC, *Reaping the Benefits*, p. 29.
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17. *Ibid.*, p. 85.
18. Lori Andrews, "Genes and Patent Policy: Rethinking Intellectual Property Rights," *Nature Reviews Genetics*, October 2002, 3: 803.
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20. John Sulston and Georgina Ferry, *The Common Thread: A Story of Science, Politics, Ethics and the Human Genome* (New York: Bantam, 2002), pp. 38-55; NRC, *Reaping the Benefits*, pp. 45-46.
21. NRC, *Reaping the Benefits*, p. 46.
22. *Ibid.*
23. *Ibid.*, p. 27. See the statements of policy on sequencing and other data on the National Human Genome Research Institute website: <http://www.genome.gov/>
24. Cassier, "Private Property," pp. 84, 94.
25. Andrews, "Genes and Patent Policy," pp. 803-6.
26. *Madey v. Duke University*, 307 F3d 1351 (Fed. Circuit 2002); NRC, *Reaping the Benefits*, p. 23.

27. Cassier, "Private Property," p. 90.
28. Ibid.; NRC, *Reaping the Benefits*, p. 44.
29. Cassier, "Private Property," pp. 89-90.
30. NRC, *Reaping the Benefits*, p. 52.
31. Cassier, "Private Property," p. 88.
32. NRC, *Reaping the Benefits*, p. 52.
33. Cassier, "Private Property," p. 88.
34. Andrews, "Genes and Patent Policy," p. 806. Andrews notes that "under the Clean Air Act, courts can, when necessary, order compulsory licensing of patents on equipment or technology used in air pollution control on reasonable terms to ensure competition." Ibid.
35. Cassier, "Private Property," pp. 84, 95.