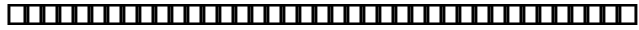


Toward Sharing the Genome

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WHO OWNS THE HUMAN GENOME? A PROFOUND

confusion reigns today over the issue of proprietary rights to human genes, and it is setting the stage for a long-term intellectual-property disaster. The U.S. Patent and Trademark Office, backlogged With tens of thousands of private claims to genetic information, cannot seem to decide Where to draw the line on ownership rights; animosity between government-funded genome; researchers and their industry counterparts continues to mount; and an ominous tangle of lawsuits already looms on the horizon.

And this, as everyone in the field will tell you, is only the beginning of many decades of fast-paced genomic research.

The controversy was simmering just behind the happy facade presented during the White House ceremony in June when President Clinton announced the completion of two working drafts of a human genome map. Despite the grand announcement, there is a startling uncertainty about how to apportion the lucrative information the map contains. For an economic indication of this uncertainty, look no further than the joint statement Clinton and British Prime Minister Tony Blair issued last March. In the statement, Clinton and Blair did nothing more than affirm the widely agreed-upon need to maintain open access to the human genome's raw genetic sequences. Then they watched dumbfounded as a stunning flight of capital bled billions of dollars from the biotech companies involved in the genome field. Some firms, such as Palo Alto, Calif.-based Incyte Genomics, lost nearly one-third of their stock market value in one day.

The irony in Wall Street's jittery response is that firms like Incyte, Millennium Pharmaceuticals, Celera Genomics and Human Genome Sciences--the most vociferous proponents of proprietary rights over human genes--all clamored to explain that they welcomed the Clinton-Blair announcement. Why? Because these companies recognize that some level of open access to the human genome is essential to building a robust industry in the future.

These genomics firms see the tremendous potential of the decoded human genome to medical science. They know, in more detail than most of us, that the diagnostic screening tests and drugs now coming to market offer only a glimmer of the promise ahead. They also understand something else: They have the most to lose if they are shut out from developing these treatments by their competitors' capricious and overly broad intellectual-property claims.

The race to discover and patent human genes is frequently likened to a gold rush, an analogy that captures much of the current frontier flavor. But the savviest players recognize a fundamental difference. Prospectors forever removed the gold when they panned it from rivers and mined it from the earth.

But the information in the human genome is not depleted upon its discovery. The genome is a resource to which biomedical researchers will return again and again to solve the puzzles of human disease; it is a wellspring that will nurture a myriad of overlapping discoveries and inventions for many decades to come. In this sense, the human genome can--and must--support what economists call nonrival consumption: a situation where multiple parties profitably share the same resource.

The problem with the gold rush analogy, then, is that the land claims that helped tame the prospectors' free-for-all were a crude but necessary framework to divide rights to a tangible and decidedly finite resource. By carving up the genome into parcels of exclusive, private real estate, the Patent Office is needlessly replaying this history. Instead, what is called for is an enlightened policy designed to govern the multiple and overlapping uses of the "genome commons": a policy that insures unfettered access to the data and materials that will serve as the building blocks for countless drugs and treatments in the future.

Although the term "commons" traditionally refers to shared property such as a city plaza or communal pastureland, the notion also applies to shared knowledge resources. We would do well to remember the 1799 discovery of the Rosetta stone, the remarkable tablet that offered the same long passage of text sequentially in three ancient languages. The Rosetta stone provided linguists over many ensuing years the seminal key to finally unlock the previously undecipherable hieroglyphics of ancient Egypt. Imagine if someone had proposed to chop the stone tablet into separate proprietary chunks. Such a plan would clearly have diminished, if not destroyed, the central value of the resource.

Sadly though, that is exactly what is happening now with the human genome. Companies must think about their financial bottom line. For today's crop of genomics firms, especially given the absence of clear rules, this means obtaining patents--as many as possible and with the broadest possible claims. The tens of thousands of human gene-related patents pending have polarized an already divisive situation. On the one hand, companies investing millions of research dollars argue that they need to protect their intellectual property. Without patents, they say, the private sector won't ante up the billions of dollars needed to stimulate the rapid development of genome-based healthcare products. On the other hand, the patenting frenzy is kindling understandable fears that only a few corporations will end up controlling a resource of priceless value to humanity. Some, like biologist Jonathan King at MIT, who is circulating a petition to this effect, believe the answer is to prohibit patents on genes.

Between these views is a gray area as big as the Pacific Ocean. As University of Michigan legal scholars Michael Heller and Rebecca Eisenberg explain it, the key question is how far "upstream" or "downstream" proprietary rights ought to be allowed along the path to product development. The problem is that almost any piece of the genome can be seen to have some commercial value. But issuing patents too far upstream could leave the path to drug development looking like a pockmarked road with a nightmare of tollbooths and barricades.

While the specifics can admittedly be confusing, at root there is nothing particularly complicated about the debate over patenting and the human genome.

The key is to treat this as a vital public policy issue rather than a strictly legal or scientific one. The first thing to remember is that the human genome is a precious inheritance of the human species. For this reason alone, it deserves special treatment. Second, the project to decode the human genome has, for more than a decade, been the mission of a publicly funded project that will ultimately cost some \$3 billion. Given this outlay of funds by taxpayers, the public has every right to demand that the genome is used wisely and not simply handed over for private gain. And finally, we must recognize that--with the recent, momentous milestone of a completed working draft of the human genome--the time to act is now. We can save ourselves a lot of bitter litigation, money and acrimony (and speed the next generation of drugs and treatments to market) if we adopt policies that balance the powerful drive of commercial interests with the public interest.

Here are five steps to take immediately:

1. Create the World's First "IP-Free Zone"

THE PUBLICLY FUNDED HUMAN GENOME Project began in 1988 as a grand scientific undertaking to decode all human genes and create a shared resource of knowledge that will be the foundation of 21st-century medicine. It's time to codify that status in law by creating the world's first intellectual-property sanctuary, or "IP-free zone." Specifically, the U.S. government should mandate that the genome's raw sequence data cannot be privately owned.

In a practical sense, we are already well on our way to this goal. Over the past several years, the Human Genome Project's network of laboratories have published on the GenBank Web site (www.ncbi.nlm.nih.gov/Genbank/) a steady stream of decoded nucleotide base pairs within 24 hours of sequencing them. The policy insures that the genome data will be freely available to researchers around the world, and also discourages secrecy or proprietary claims over this valuable raw data.

With the Human Genome Project's laudable commitment to open publication (thereby de facto disqualifying the raw data from patent claims), why bother writing a law? Because the formal establishment of an IP-free zone--a kind of "national park" of genome knowledge--will set a vital precedent that some kinds of precious information resources must be off-limits for private ownership.

As many are coming to realize as we move headlong into the knowledge-based economy, things work best when seminal information assets--particularly those needed by all players in a given high-tech sector to compete--are pooled and shared. This is the idea behind both open-source software and the hardware standards that have come to predominate in many high-tech sectors. These pieces of "infostructure" are what allow different engineers to design distinct machines that all plug into a single type of wall socket or send standardized software files over the Internet. Like public lands or public libraries, pooled knowledge assets must be made freely available and protected within a framework that preserves their integrity. Precisely because the raw sequence of the human genome--the actual string of DNA base pairs themselves--is already widely perceived as deserving of this special status as a category of knowledge, it makes an ideal candidate for the world's first legally mandated IP-free zone.

2. Declare a Moratorium on Gene Patenting

THE U.S. PATENT AND TRADEMARK OFFICE has clearly bungled the issue of gene patenting by years of equivocation and delay. We need a moratorium on gene patenting until we can all agree on sensible rules.

Patents have always represented a compact between an inventor and the public: The inventor gets a 20-year monopoly in order for the public to quickly get the benefit of the new innovation in the marketplace. Issuing broad patents that confer no such clear benefits can, as the Supreme Court noted in the key 1966 case *Brenner v. Manson*, create a "monopoly of knowledge...[that] may confer power to block off whole areas of scientific development, without compensating benefit to the public."

The most urgent task is to clarify that before a gene can be patented, it must be shown capable of providing a benefit to the public--namely by bringing a new product or invention to the marketplace. Within our legal framework, this principle is defined as a patent's "utility."

In a hopeful sign, the director of the Patent Office, Q. Todd Dickinson, has proposed to raise the "utility" bar slightly by adding three words to its guidelines. To win a patent in the human genome field, applicants will have to describe a "substantial, specific and credible" use for their gene. While this represents an important step in the right direction, the Patent Office can and should do more. Although Dickinson may rightly argue that his is not a policymaking body, the Patent Office's role on the front lines requires it to spot emerging problems and report them to Congress or otherwise work to redress them. To stem the continuing confusion in this area, Dickinson needs to take the lead, holding hearings that include all stakeholders and declaring a moratorium on gene patenting until acceptable rules are reached.

3. Institute a Licensing System

THE MOST TROUBLING ASPECT OF THE current spate of gene patenting is the risks that the right afforded by patents "to exclude others" poses to medicine. To avoid the worst potential problems, we need a compulsory licensing system, and Congress should hold hearings as soon as possible to figure out how it should be implemented.

Changing licensing rules would go far to insure that in the future researchers will be guaranteed the right not just to view the genome but also to use the information it contains to develop vital products. Under a compulsory licensing plan, patent holders could still receive compensation, but would no longer retain the right to exclude others from research that could improve public health. Congress needs to spell out new rules in this regard, specifying guidelines for licensing fees and perhaps adopting a sliding scale of payments for public sector vs. commercial research.

Without new licensing rules we risk replaying the sorry history of antitrust actions and patent tangles. A century ago, broad patents tied both the automotive and aviation industries in knots during their first decades. The costly and debilitating tangle of lawsuits only ended with the creation of so-called patent pools that cross-licensed everything and divvied

up the royalties. The patent pools--later used in the semiconductor industry--can successfully end the worst of the wrangling. But they also tend to consolidate entrenched oligopolies and present stiff barriers to entry in the field.

If at all possible, in the case of the human genome we need to try to avoid acrimonious after-the-fact kinds of settlements. A new, transparent licensing system will help companies navigate what's likely to be an unusually complex terrain of patent claims and ensure they have access to what they need to create new drugs.

4. Establish a Zoning Commission

THE MANAGEMENT OF THE HUMAN Genome is a vital matter of public policy. It is not something that should be left to powerful business players, lawyers or scientists to resolve alone. We need a body made up of stakeholders from the public and private sectors, scientists and laypeople alike, to serve as a kind of genomic zoning board.

In the first decade of recombinant DNA research, the National Institutes of Health (NIH) established a body called the Recombinant DNA Advisory Committee (known as "the Rack") to determine policy about what safeguards were needed for certain kinds of previously untried recombinant DNA research. Although the practice of gene patenting also presents many unknowns, there has been little analysis of its economic, social or scientific impact. There isn't even an official body within the NIH to deal with the issue. It is naive to think that a laissez-faire policy can be effective. We badly need a standard-setting group that can help shape policy in this emerging area.

Why think of it as a "zoning board?" Because zoning regulations represent a good example of how community standards can be established and enforced to shape the rules governing private property. We would do well to remember the lesson of Central Park in New York City. At the time it was proposed, the idea of setting aside 700 acres of prime real estate in one of the world's most vibrant cities was controversial to say the least. The land seemed too valuable to turn into a park, but time has shown that, for most Manhattan residents, the value of Central Park far exceeds the monetary worth of the property.

Just as zoning can add value to a community by balancing the needs of the private and public sectors, we need a public policy body tasked with balancing and nurturing the partnerships between the private and public sectors that have brought us to this stage in our understanding of the human genome.

5. Put Public Health First

ULTIMATELY, THE MOST IMPORTANT THING is to remember the overriding public health mission of human genome research--public or private. While it is tempting to try to speed development with patent incentives to private firms and universities, the impulse must be balanced against longer-term concerns for how the ownership rights to genes will ultimately affect the equitable dissemination of health-related products.

The human genome is already raising vexing policy questions about our rights to confidentiality for our genetic health information and protection against genetic discrimination by insurance companies and in the workplace. Just like gene patenting, these kinds of emerging issues will require new solutions and proactive public policy. The time to start is now. As we begin the process of balancing commercial interests and public health, we need to be guided by our sense of fairness, by our democratic values and by established methods of transparency and reporting that will insure our ability to publicly regulate the situation in the future.

President Clinton's joint announcement with Prime Minister Blair in March barely scraped the surface of the vital issue of ownership of the genome and unfortunately did little to stem the continuing uncertainty in the field. But, rhetorically at least, Clinton got it right when he called upon us to "ensure the profits of human genome research are measured not in dollars but in the betterment of human life."