Public Versus Private Ownership of Scientific Discovery: Legal and Economic Analyses of the Implications of Human Gene Patents

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Introduction: Patents, Genomics, and Academic Medicine

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This issue of *Academic Medicine* presents a collection of original scholarly articles and commentaries on the legal and economic rationales supporting—and opposing—patents on human gene sequences. In this introduction, we review the concerns that led us to invite these analyses from authors who are each distinguished in their respective professions of the law, economics, medicine, research, and education. We then provide an overview of their arguments and related themes.

BACKGROUND

U.S. patent law is rooted in Article I, Section 8, of the Constitution, which gives Congress the power to "promote the progress of science and useful arts by securing for limited times to authors and inventors the exclusive right to their respective writings and discoveries." The intent of the language was to incite creative work that could be further developed and applied to the benefit of society. The patenting process itself involves a tradeoff: in return for a time-delimited period of exclusive right to benefit from the commercial exploitation of an invention, the inventor must publish (in the patent claim) a full description of the invention and at least one reduction of the invention to practical use. It is thus argued that the patent system serves as a strong inducement to innovation by requiring inventors to make their discoveries and inventions public, rather than sequestering them in the form of trade secrets.

The patent system has worked well for more than 200 years to foster innovation and its commercial development, in large part because Congress and the courts have continuously revised and reinterpreted the system to improve its responsiveness to changing circumstances.[1] During the past decade a series of judicial holdings have raised strong concerns about whether certain aspects of patent law interpretation and application might be socially dysfunctional and in need of re-examination and modification. These concerns have emerged from the biomedical, business, economics, and legal communities, and most recently from the Congress, and have focussed especially upon the way in which patent law has been interpreted and applied to human gene sequences and to business methods encoded within computer software or other media.[2] In aggregate, the questions raised have been directed at each one of the patentability criteria specified in U.S. patent law. Specifically, are patents being issued on claims to inventions/discoveries that

- do not (or should not) constitute "patentable subject matter"?

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- do not meet the criteria of novelty, non-obviousness, or utility?
- do not meet the written description and enablement criteria?

In biomedicine, an additional concern has been raised about the patenting of human gene sequences containing mutations that have been shown to have a probabilistic correlation with susceptibility to disease. At the time the patent is claimed, nothing more may be known about the gene than an estimated strength of association as typically determined from kindred studies. The question is, are such patents being issued and enforced in a manner that restricts both medical research and practice in a way that is without precedent and has troublesome implications for the futures of both?

More broadly speaking, these various concerns ask whether patent law and practice are being used to permit the privatization of scientific information that is too far "upstream" in the development pathway, and therefore distant from practical products. Such fundamental information has traditionally been deposited in the public domain freely and without restriction of its accessibility or use. Given the rush by universities and industry to patent human (and non-human) genes and gene fragments during the past decade, and the evidence of an emerging, similar rush to patent human protein structures determined from proteomics research, this question is nowhere more salient than in biomedicine.

These concerns must be considered in a context mindful that strong intellectual property protections play a critical role in public health, as the nation relies almost entirely on the private sector to accomplish development, testing, and production of new therapeutics, vaccines, medical devices, and related products. The biotechnology industry remains particularly vulnerable to the sensitivity of its capital and equity markets to perceptions of patent policy, as most recently evidenced in a single-day collapse in the biotechnology equity markets following a brief U.S.–British communiqué related to the international Human Genome Project.[3]

During the past few years, the Association of American Medical Colleges (AAMC) has become progressively more engaged with these issues, in particular with trying to understand their effects on biomedical research and the practice of medicine. Although the Association has adopted no formal position on the matter of human gene patenting per se, it has strongly supported recent actions of the National Institutes of Health (NIH) to facilitate access to biomedical "research tools" and to strengthen the utility criterion of the patent law. The AAMC has also worked closely with the American College of Medical Genetics and the Association of Molecular Pathologists to raise concerns about restrictions on the practice, study, and teaching of gene-based diagnostic tests in academic medical centers.

With completion of the sequencing of the human genome and the rapid emergence of human proteomics, there can be no doubt about the salience to biomedical research and medical practice of patent law, its practice by the U.S. Patent and Trademarks Office (PTO), and its creation and interpretation by the Supreme Court and, much more often, by the Court of Appeals for the Federal Circuit (CAFC, the appellate court that hears appeals of all patent decisions rendered in U. S. district courts). Although these matters tend to be arcane and not generally well understood outside the patent community, they are of critical importance to the future of medicine and need to be better comprehended by the academic medical community and society at large.

To this point, it is instructive to recall some observations made in a plenary address delivered by U.S. Supreme Court Justice Stephen Breyer at the 2000 Whitehead Policy Symposium on genes and society. Justice Breyer posed the question:

> How best can legal institutions—which must give answers—interact with science—which so often poses difficult questions? *What I want to emphasize is the importance of making difficult science-related choices only when there has been extensive, informed development of the relevant legal and policy issues prior to decision* [emphasis added].[4]

Justice Breyer went on to note the extensive public discussion that had taken place before the Supreme Court delivered its decision on physician-assisted suicide, and contrasted that with issues in contemporary genetics.

> By way of contrast, let me mention two sets of issues, arising from developments in genetics, that may not yet have been subject to the kind of public discussion and debate that help to assure the soundness of a public policy decision. The first set arises out of genetic discoveries that permit doctors to forecast an increased likelihood that certain individuals will develop cancer.[5]

The second set of issues involves patent law. The Justice observed:

> If an inventor creates a product or process that is "useful," "novel," "non-obvious" and which does not consist of laws of nature, natural phenomena or abstract ideas," then the patent law, in return for disclosure, grants the inventor a twenty-year monopoly over that product or process. This patent law approach is a one-size-fits-all approach. The question is, does it fit the world of genetic research?
>
> The most difficult question is deciding when . . . products of genetic research reflect only discovery of an existing aspect of nature . . . and when they amount to a protectable invention or useful device . . .

> It might be more helpful to ask instead how well patent law's sub-classifications and precedents here fit patent law's basic job. That job is developing financial incentives that, as they operate in the marketplace, will encourage useful discovery and disclosure without unduly restricting the dissemination of those discoveries, hindering the circulation of important scientific ideas, or scattering ownership to the point where it inhibits the use of the underlying genetic advance. And—if patent law's legal categories do not well match that law's basic objectives where genetic research is at issue—how should the law be changed? The best answers will arise when the legal issue is focused by previous conversations between science, business, economics, and law. Neither courts nor legislatures may yet find wise answers in the absence of such earlier interaction.[6]

Accordingly, we (DK and SH) decided to undertake a project to gather and disseminate authoritative information to inform our understanding and that of our members about these complex and controverted patent issues. With the generous support of the Alfred P. Sloan Foundation, and following wide consultation, we commissioned four papers from nationally recognized experts. It was our original intention to disseminate these papers as an AAMC monograph. Subsequently, we were delighted when the editor-in-chief of *Academic Medicine* proposed that we develop a special issue of the journal to address these matters. Among other advantages, this opportunity ensured that the papers would be indexed in the biomedical literature, and would therefore be citable. It also enabled us to solicit five additional papers to elaborate the issues further, as well as to offer commentary, from diverse experts in the field.

THE ARTICLES AND COMMENTARIES

This special issue of *Academic Medicine* is organized to allow readers to progress through an orderly sequence of our contributors' views and perspectives on the issues of gene patenting. These views range from a strong defense of the current system to criticism of certain aspects of current patent practices and proposals for reform. We begin with an insider's view of the patent system by George Elliott, a practice specialist in the U.S. Patent and Trademark Office (PTO) with broad experience in science policy. Elliott provides a primer on patent review, from its statutory requirements to its implementation in the issue or decline of a patent. He also describes the important role played by the courts in their continuing reinterpretation of the patent law. Elliott concludes by emphasizing that enforcement and licensing of patents lie wholly outside of the PTO's purview, and that social questions about access to patented subject matter—such as the practice of patented gene-based diagnostic tests—must be addressed in other forums.

The second article, "Human Gene Patents," provides a lucid justification of the legal and policy rationale controlling the issue and enforcement of gene patents and their adjudication in the courts. Goldstein and Golod describe the scope and limitations of gene patents and the types of exemptions that have been proposed or allowed. They point out that there is no U.S. statutory exemption for non-commercial research on patented subject matter, but note that a narrow, judicially-created exemption does permit use of patented subject matter for non-commercial ("philosophical") purposes. However, they argue that patents (and licenses) on gene-based diagnostic tests are properly enforceable and do not permit academic or other clinical practitioners to practice such tests without license or other authorization from the patent holder. Restrictions hold wherever the delivery of the service generates revenues and is thereby deemed to be "with commercial intent," regardless of use of the testing procedure and the clinical data obtained in education and research.

Recognizing that members of the lay public may be perplexed by patenting of human genes already existing in nature, Goldstein and Golod trace the statutory basis and case law supporting patents on compositions of matter that have been isolated and purified away from their naturally occurring contexts. They also correct the misperception—too common in media reports and editorials on this issue—that a patent holder may "own" a person's genes. They make the important point that ownership of intellectual property associated with genes is separate from ownership of tangible property, i.e., of the naturally occurring genes themselves. The authors note the different commercial utilities of isolated human gene sequences and argue that it is impossible "to create an effective legal system that distinguishes between the different classes of human genes or the different institutions of discovery."

The third article, by Murashige, focuses on the workings of the patent system with respect to research tools, and addresses the "uneasy alliance" between patent holders and academic or basic researchers with respect to the use of such tools, whose chief utility is to advance further laboratory research. Recognizing the complex mix of not-for-profit and commercial research organizations conducting genomic research, Murashige compares the advantages attributed to the patenting system—providing incentives for finance and development and spurring creativity—with the disadvantages perceived by the academic community. The latter include impediments to the communication of research findings, often very onerous transaction costs in obtaining biological research materials, retardation or inhibition of research dependent upon patented research tools, and an overall loss of efficiency in the research system.

Murashige argues that the options for mitigation of this

problem are limited to legislative restriction, or "carve out," of certain subject matter from patentability, or strengthening the criteria used in review of patent applications, especially non-obviousness and utility, which involve a high degree of judgment. She illustrates the issues by informative comparison of the U.S. system with that of the European Community and other jurisdictions that differ in what they permit to be patented and in their procedures for application and review. Murashige is pessimistic about the former approach, noting that federal appellate court decisions during the past two decades have steadily expanded the interpretation of patentable subject matter. With respect to tightened review criteria, she views the PTO's recently revised utility standard as perhaps the most practical remedy for addressing concerns about proliferation of overlapping or unspecific gene patents.

Finally, Murashige, like Goldstein and Golod, examines proposed options for "post-patent solutions," such as legislative or other restrictions on licensing. There are only two legislative exemptions from patent infringement: for research required to seek regulatory approval of generic versions of patented drugs prior to expiration of the patent, and for physicians practicing a patented method of treatment. While acknowledging the judicially created "research exemption" applied to non-commercial research, Murashige notes that crafting a precise and unambiguous definition of research is a difficult challenge in any proposed statute for a broad research exemption. She concludes that the most reasonable approaches include stanching the flow of superfluous or undeserved patents through more stringent review of claims, and compelling patentees with claims to research tools to offer non-exclusive licenses at reasonable rates.

In the fourth article, Barton, in his tightly reasoned analysis, is troubled by the recent judicial extensions of patentable subject matter into increasingly intangible areas, such as business methods and genomic information. With respect to the latter, he argues that patents on single nucleotide polymorphisms (SNPs), variations in DNA sequences that may be correlated with distinctive phenotypes useful in medical diagnosis and pharmacotherapy, and on computer-based genomic information, databases, or manipulation procedures "may seriously interfere with medical research." He proposes redress through test litigation, seeking reversal of certain CAFC decisions, and/or a legislative research exemption for using SNPs in medical research, "including contexts in which medical research and clinical practice are substantially intertwined," such as in academic medical settings.

Barton notes that genomic patenting may affect the development of novel therapeutic proteins, or the use of genomic information in medical research and practice. It is the latter application that is especially troubling. He reviews the current status of patent law, focusing on the statutory criteria and how they have recently been interpreted by the courts, and notes that several of the underlying legal doctrines "could be changed or be interpreted in ways more favorable to the conduct of research." He gives special attention to the criterion of patentable subject matter, where he argues that recent decisions by the CAFC have eroded the long-held interpretation that patents on laws of nature, scientific principles, and methods of doing business were prohibited. In considering approaches to protect medical research, Barton proposes that patenting of "information about the world or of abstract methods of using such information" be prohibited.

Barton offers two plausible directions of reform. The first is to seek either a narrow statutory exemption permitting patented genomic information to be used freely "when the research purpose is substantial compared with the diagnostic purpose," or a statutory exemption, or compulsory licensing, for use of genomic information for all diagnostic purposes. The second approach is to seek amendment of the patent statute, and Barton offers language to accomplish this purpose. He concludes that although more ambitious, the second approach may be more feasible because it would likely be supported by many in the scientific and medical research communities, as well as those in the business community concerned about business methods patents.

The final commissioned paper, "The Economics of Human Genome Patents," provides a broad, authoritative economics perspective on the issues. Scherer explores the cost and benefits of human gene patents and how these are distributed among the diverse participants. He presents empirical data on the importance of patents in inciting innovation across industrial subgroups and notes the special importance of patents to the pharmaceutical, biotechnology, and some categories of the chemical industries. He analyzes the economic bases and consequences of patent policy in pharmaceuticals, which require a protracted and expensive process of development and testing but that can be relatively cheaply and competitively imitated once they are approved and disclosed, and contrasts them to patents on DNA sequences or other elemental information that are far "upstream" in the product development pathway.

Of particular interest are the results of a survey conducted by Scherer of gene sequence grants issued by the PTO during a 33-month period from 1998 to 2001. Of the patents originating in the United States, the most frequent use category was "for human use," and the next most frequent was as research tools. About one third of the patents originating in the United States claimed human genome sequences, which were coded as having combinations of treatment, diagnostic, preventive, and gene therapy applications. Notably, universities were the most frequent recipients of human-use patents, and the second most frequent recipients of patents on human DNA sequences.

Scherer then provides an erudite summary of the economics of patent policy, emphasizing its complexity. Particularly informative is his analysis of the not-uncommon case in which an upstream, enabling invention of little commercial value proves indispensable to one or many downstream inventions of substantial commercial value. Even more complicated is the case in which the downstream product(s) rests on the shoulders of multiple antecedent inventions. How to allocate appropriately the economic returns among the upstream and downstream inventors is a challenging problem for economic theory, as well as in contemporary biomedical research, and is perhaps most familiarly embodied in licensing and cross-licensing disputes involving "reach-through" and "reach-back" rights. Such disputes can generate enormous transaction costs. They may become increasingly frequent and vexing with respect to the scope and overlap of patent claims on human gene sequences.

On the basis of his analyses, Scherer argues strongly that genome patent claims should be interpreted narrowly. He recognizes the fragility of the research exemption but argues that although it is an imperfect policy instrument, its preservation is highly desirable. Scherer is particularly concerned with ensuring that the development of new (therapeutic) products is not blocked or retarded by a multiplicity of prior patent claims, but he is pessimistic that the diversity of participants in biotechnology will provide a "sufficient community of interest to organize comprehensive low-royalty cross-licensing" regimes. Accordingly, he suggests mandatory arbitration as one mechanism for resolving such problems.

To provide further insight into these matters, and to obtain reactions to the reasonableness and the practicability of the commissioned authors' respective recommendations, we invited the views of several commentators who find themselves on the front lines of these issues in their academic, commercial, or other professional duties. Copies of the commissioned manuscripts were shared with professor Arti Rai of the University of Pennsylvania Law School, Mr. Lee Bendekgey and Dr. Diana Hamlet-Cox of Incyte Genomics, Inc., and professor Rebecca Eisenberg of the University of Michigan Law School. Additional comments were solicited from Dr. Debra Leonard, professor of pathology at the University of Pennsylvania, whose remarks do not address the papers, but rather present the perspective of a leading participant in molecular diagnostics and the practice, research, and teaching of gene-based diagnostic tests.

Rai argues that the most fruitful way to consider the issues of human gene patents is from the perspective of research tools. She notes that the analyses invited by the AAMC universally consider the argument that intellectual property protections may inhibit or preempt further basic or clinical research on patented DNA sequences. Rai points out that research tools may themselves be end products, or they may be research platforms that can have a profound impact on science and technology (e.g., the Cohen–Boyer patent on recombinant DNA technology and the recent University of Wisconsin patent on human embryonic stem cells) and that "economic analysis suggests that broad patents on research platforms impose costs that may outweigh the usual benefits of stimulating invention and development."

Rai argues that the problem with adopting a research-exemption approach is the commingling of research and commercial activity even in nonprofit institutions, and notes that gene-based diagnostic testing is a case in point. She prefers to use the statutory standards to restrict the scope of patent claims on research platforms, and to this end she examines both the recently strengthened utility standard adopted by the PTO and the use of the description and enablement standard by the CAFC to narrow patent scope.

Although narrowing the scope of claims on upstream research would be a desirable step, it would not solve the problem of assembling multiple upstream patents on research tools required for product development, e.g., DNA microarrays that detect the expression of scores of genes. Rai agrees with Scherer that the prospects for pooling patents—and thus consolidating licensing requirements—in the biopharmaceutical industry seem low. She applauds such recent efforts by the NIH as publishing all raw human genome sequence data immediately and urging its grantees not to patent research platforms and to make the sharing of research tools less onerous by adopting simplified, uniform Biological Materials Transfer Agreements. Finally, acknowledging the profound behavioral effect on publicly funded investigators and institutions of the Bayh–Dole Act, which permits institutions to retain title to inventions made with federal research grants, Rai suggests that it may be necessary to amend the Act to give federal agencies more authority to limit, or even eliminate, the patenting of publicly funded research platforms.

Bendekgey and Hamlet-Cox, in contrast, argue directly against the putative disadvantage of patents on research tools, whether platforms or not. Patent law, they argue, does not and should not make distinction between inventions whose chief utility is to advance further research and development and other inventions. Given the fundamental rationale of the patent system to promote innovation, protections for research tools should be of no less importance than protections for other inventions or discoveries. They further posit that there is no convincing evidence that gene patenting has inhibited research, or that patent "thickets" and royalty stacking have yet proved problematic, or that the various undesirable consequences feared by other contributors to this issue have occurred. They challenge the research community to demonstrate empirically any diminution of research and development in genomics arising from gene patents.

With respect to gene-based diagnostic tests, Bendekgey and Hamlet-Cox deny that patents will restrict access to or widespread implementation of these tests. They argue that economic incentives provide a likely motivation for patent holders to make such tests widely available and on reasonable terms. Moreover, they note that some types of misuse or abuse of patent exclusivity, if they do occur, are already prohibited by federal antitrust and other law, or, if in the area of health care, may be subject to redress by health law and regulation. It is not clear, they argue, whether exempting physicians from infringement in practicing patented gene-based diagnostic tests, such as is proposed in recent legislation, would benefit patients directly in lower costs for the service, or would primarily benefit rival organizations performing these tests.

Many of the recommendations made by the invited authors are based on distinctions between the nature and type of research or invention (e.g., "upstream" vs. "downstream" research, research tools, etc.). Bendekgey and Hamlet-Cox note that the patent system does not distinguish between genomics and other categories of research and technology. "It has never been the role of the patent system," they note, "to establish industrial policy with respect to any particular category of invention or sector of the economy."[7] As strong proponents of gene patents, they assert more plainly than any of our other contributors what is at the heart of the research community's concerns:

> As with any other composition of matter (as compared to a claim to a process or method of use), all that is required by the Patent Statutes, as well as over 200 years of patent law, . . . is that a single utility be disclosed by a patent applicant in order to obtain a patent claim to the composition of matter for all uses.[8]

Nonetheless, Bendekgey and Hamlet-Cox do note that given that U.S. universities are the leading holders of human-use gene patents, and the role of federal funding in biomedical research, the universities, either voluntarily or as a result of modification of the Bayh–Dole Act, could adopt a policy that mandated non-exclusive licensing on standard terms of their gene patents for research. They posit that such a step would address many of the concerns that other authors have raised.

Eisenberg begins her cogent analysis of these issues by noting the peculiar timing of the controversy over gene patenting. In contrast to other expansions of the definition of "patentable subject matter," such as to life forms and business methods, where apprehension closely followed patent issue, concerns about gene patents were delayed by a decade. Eisenberg attributes this delay to change in the nature of those patents. The initial wave of patents was on genes that directed the synthesis of therapeutic proteins. But during the last decade these patents have evolved to include diagnostic products of mixed clinical and research use; upstream discoveries far from end-product development; and "routine research results obtained through a mechanized process requiring no more than ordinary skill on the part of the inventors." She reviews the controversy that has arisen over the patenting of gene-based diagnostic tests, with its implication both for biomedical research and medical practice, and concludes that "in this challenging strategic environment, it is not clear that the owners of disease gene patents will converge with the social interest in promoting continuing technological progress."

Eisenberg then turns her attention to the patenting of genes as research tools, and observes that "with this shift, patenting genes started to look less like patenting end products and more like patenting scientific information." (We find it ironic that this controversy was initiated not by industry but by the NIH, when, coincident with the advent of high-throughput DNA sequencing, it filed patent claims on expressed sequence tags, ESTs, with no plausible utility other than research tools, an action vehemently opposed by nobelist James D. Watson, who resigned his position as the first director of the Human Genome Project.) Although the NIH established the precedent, industry was quick to follow suit, and many thousands of EST patent claims soon flooded the PTO.[9] Eisenberg shrewdly adds that "the gene patenting controversy arose during a period of rapid and uneasy change in the culture of academic biomedical research from a tradition of open science to a more restrictive, proprietary enterprise."

That author, who chaired the NIH Working Group on Research Tools,[10] echoes Scherer[11] in discussing the difficulty in appropriately capturing the economic value that research tools provide to researchers, and accordingly, the social utility of patenting them, especially when "the invention would, in all likelihood, have soon become freely available in the public domain through the efforts of others working in the field." She reminds us that skepticism about the wisdom of patenting research tools has been voiced on occasion even by the staunchly pro-patent pharmaceutical industry.

Eisenberg concludes her essay by addressing the statutory patent standard of non-obviousness with respect to the results of high-throughput DNA sequencing "that can be (and is) performed by modestly competent research technicians in a mechanized discovery process." She criticizes the holdings of the CAFC in the 1990s, reversing its own precedents, that blunted the applicability of this criterion, and she captures the central concern of those troubled by current patent practice by noting that

> it is regrettable that the approach of the Federal Circuit has eviscerated an important requirement for patent protection

> during the years when most of the human genome was sequenced. As a result, the patent system has encouraged researchers to race along pathways made obvious by their predecessors to complete the relatively easy step of DNA sequencing, laying patent claims along the way that will dominate more challenging scientific work that has yet to be done.[12]

Leonard, who directs the Molecular Pathology Laboratory at a leading academic medical center, provides a personal perspective on the impact of human gene patents on medical practice and research. She points out that there are three major potential utilities for gene discoveries: in diagnostics, therapeutics, and prevention. Of these, use of the knowledge to perform a diagnostic laboratory test is the fastest, simplest, and cheapest to develop. For laboratory physicians, especially those in academia, knowledge of an association between a specific mutation and susceptibility to human disease is all that is required for them to implement a laboratory developed (commonly dubbed "home-brew") gene-based diagnostic test. No special reagents or equipment are needed beyond those already available to the laboratory, no patented composition of matter need be purchased, and there need be nothing unique or novel about the test process itself. In other words, once information about a gene sequence or mutation is in public domain, implementation of the diagnostic test based on the gene is well within the capability of, and obvious to, a practitioner with ordinary skill in the art.

In contrast, Leonard recognizes the effort, time, and expense required to bring a diagnostic test kit to market, and supports the patenting of such products. She notes that most laboratory physicians would prefer to use such kits, both for convenience and for assurance of quality control of the components provided by the manufacturer. However, Leonard argues that the current practice of patenting, and thereby controlling the use of, a piece of basic scientific information, namely, that a mutation is correlated with a human disease, leads to unprecedented and unjustified restrictions of accepted medical practice that are bad for patient care, medical research, and the public health. She proposes that, if necessary, society mandate non-exclusive licenses for testing services at reasonable royalty rates, and that physicians be allowed to continue to provide gene-based diagnostic testing for their patients.

CODA: PUBLIC VS. PRIVATE SCIENCE

A striking aspect of the papers presented in this special issue of *Academic Medicine* is their alternating views of the benefits to society from proprietary versus nonproprietary genomic information, which rest on deeply seated legal, economic, and cultural foundations. More broadly, these dichotomous views encompass other "research tools," especially those transforming tools dubbed "platform technologies," and, even further, reach the much larger question of the societal advantages of proprietary versus nonproprietary *science* and the future organization, shape, and conduct of scientific research, especially in academic institutions. Accordingly, to conclude this set of articles, we thought that readers would benefit from the insightful context and perspectives provided by Rebecca Eisenberg, a law professor (and also a commentator for this issue, noted above), and Richard Nelson, a professor of international and public affairs, business, and law, in "Public vs. Proprietary Science: A Fruitful Tension?" That article is reprinted here from *Daedalus* by permission of the American Academy of Arts and Sciences and by courtesy of the authors.

Eisenberg and Nelson examine the presumption that basic scientific research is most effectively utilized when the findings of that research are openly disseminated without significant restriction, while research with more practical application should be the prerogative of private enterprise for development in new products or applications. Private-sector control of this knowledge ensures that users who eventually benefit from the technology help compensate the costs of its development. Venerable and fruitful distinctions between commercial research (e.g., involving industry and the patent system) and non-commercial research (e.g., universities and public grants) have been predicated on this model.

However, many fields of cutting-edge science and high technology now seamlessly interact, and even basic (or fundamental) research increasingly touches upon or foreshadows practical applications. Advances in molecular biology generally, and in genomics particularly, lie squarely in these areas of intersection between basic research and application. Moreover, institutional boundaries that once reasonably sharply demarcated basic research from technological development have grown porous, especially in recent decades in biomedicine, with more academic research finding application in industry. The Bayh–Dole Act has accelerated—as it was intended to—the rate at which academic laboratories and investigators transfer research discoveries to industry. This has also given many investigators and their universities an intensifying remunerative interest in their research from royalty payments, equity interests, and other relationships.

Eisenberg and Nelson examine the Human Genome Project and rival industry sequencing efforts as a case in point of the new political economy of scientific research—and as a possible remedy to our concerns. Since the inception of the Human Genome Project, there has been general agreement among researchers that the project would be most advantageous to science if the sequence data were made publicly available, quickly and without restriction. A series of research and consortial agreements, some involving publicly funded scientists and industry, and some spurred by industry,

ensured public access to Genbank, as well as to some EST and cDNA libraries, and to SNPs. By virtue of depositing this information rapidly into the public domain, and thereby making it prior art, and by other preventive actions, these projects helped to ensure that the information would not be patented.

Eisenberg and Nelson conclude that many of these arrangements required federal agencies and some universities to "maneuver around" the Bayh–Dole Act, suggesting, at least implicitly, that provisions of the Act might be ripe for revisiting. Also, in several cases, most notably genomic sequences and the SNPs consortium, in a surprising reversal of roles, it was industry (represented by major pharmaceutical companies) that initiated or helped enable the project to ensure open and unencumbered access to information, the type of access that has historically been the provenance of academia and the raison d'être of academic research. Eisenberg's and Nelson's plea, echoed here, is to reassert the value of public science as a broadly valuable and enabling social commitment, not limited simply to the products or technologies it spawns. As such, public (and academic) science remains a source of critical and independent thought, a shared archive, the foundation for educating future generations of scientists, and a source of future discoveries and technologies yet unseen.

CONCLUSION

The use of current patent law and practice to permit the privatization of increasingly upstream biomedical scientific information has implications for the future of medical research and practice that have received, despite valiant efforts by NIH policymakers to facilitate the sharing of research tools, comparatively little attention in the wider public debate on the ethical, social, and legal implications of genomic research or the protection of genetic information. Decisions that may have profound social consequences for the disposition and use of human genomic information in medical research and practice are largely being made—contrary to U.S. Supreme Court Justice Breyer's admonition—in the context of arcane patent litigation that is opaque to those who are not members of the patent bar, or otherwise "patent aficionados."

We believe that the articles and commentaries presented in this special issue of the journal will provide valuable assistance to the academic medical community and other non-patent experts in better understanding the many dimensions of these profoundly important and complicated issues. We hope they will promote informed public conversation that is long overdue, and better position the academic medical community to engage in dialogue with the legal and business communities, and others, in the spirit of Justice Breyer's challenge.

Note added in proof: To underscore the timeliness of this theme issue, the Court of Appeals for the Federal Circuit in October 2002 issued a troubling decision (Madey v. Duke University) that sharply narrows, if not eliminates, the applicability of the fragile, common law "research exemption" to universities. The Court held that the conduct of academic research "further[s] the institution's legitimate business objectives," and that "our precedent does not immunize any conduct that is in keeping with the alleged infringer's legitimate business, *regardless of commercial implications*" [emphasis added].

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ENDNOTES

[1]For example, the Patent Act of 1952, the Bayh–Dole Act of 1980, and the Hatch–Waxman Act of 1986.

[2]See for example, the Committee on Intellectual Property Rights in the Knowledge-Based Economy, of the National Academies of Science, Board on Science, Technology, and Economic Policy, Washington, DC.

[3]"Joint U.S.–U.K. statement to ensure that discoveries from the human genome are used to advance human health," by President Bill Clinton and Prime Minister Tony Blair, March 14, 2000. The White House Press Office.

[4]Breyer SG. Genetic advances and legal institutions. Journal of Law, Medicine & Ethics, Special Supplement, 2000, 28;4:23–8. The supplement reports Selected Proceedings of "Genes and Society: Impact of New Technologies on Law, Medicine, and Policy," Whitehead Policy Forum, Cambridge, MA, March 2000.

[5]Ibid.

[6]Ibid.

[7]Bendekgey L, Hamlet-Cox D. Gene patents and innovation. Acad Med. 2002;77:1373–80.

[8]Ibid.

[9]In January 2001, the PTO heightened its standard for the utility criteria, which will diminish the number of these EST patents eventually issued. The new standard is discussed by several of the authors.

[10]Another author included in this issue, John Barton, also served as a member of the NIH Working Group on Research Tools.

[11]Scherer FM. The economics of human gene patents. Acad Med. 2002;77:1348–67.

[12]Eisenberg RS. Why the gene patent controversy persists. Acad Med. 2002;77:1381–7.