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# **Real Impediments to Academic Biomedical Research**

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### **Executive Summary**

Numerous scholars have expressed concern over the growing "privatization of the scientific commons" represented by the growth in academic patenting. Even before the Bayh-Dole Act and the pervasive patenting of academic science, however, there was an earlier concern over the extent to which the drive for recognition among scientists and competition for priority and associated rewards also limited contributions to the scientific commons. This suggests the utility of a more open-ended consideration of the different factors-not just patentingthat might affect knowledge flows across scientists. In this paper, we use a simple economic perspective that emphasizes the benefits and costs of excluding others from research results and analyze the empirical evidence on exclusion in biomedical research. We suggest, first, that one might distinguish between legal and practical (i.e., lower cost) excludability-and that practical excludability, at least in the world of academic research, may have little to do with patents. At the same time, however, we suggest that excludability may indeed be a real concern for academic and, particularly, biomedical research, but to understand where and how it occurs, we need to look beyond patents to consider additional ways in which flows of knowledge and other inputs into research may be restricted (including secrecy and control over materials). We do find restrictions imposed on the flow of information and materials across biomedical researchers. While patents play some role, they are not determinative. What appears to matter are both academic and commercial incentives and effective excludability. Exclusion is rarely associated with the existence of a patent in academic settings, but is more readily achieved through secrecy or not sharing research materials.

# I. Introduction

American universities have rapidly increased the patenting and licensing of their discoveries over the past twenty years. Patents issued to American universities have grown almost an order of magnitude, from 434 patents issued to universities in 1983 to 3,259 in 2003, and the preponderance of these were in biomedicine. In addition, total annual licensing revenue from university inventions increased from about \$200 million in 1991 to about \$1.3 billion in 2003.

While the Bayh-Dole Amendment of 1981 and subsequent legislation facilitated this growth, the growth also reflected the expansion of patentable subject matter to include academic discoveries in a number of domains, particularly the life sciences, but also software. The growth of patenting also reflects a strengthening of ties between universities and commerce more generally during this period, reflected partly in a growth of industry support for academic research, but also in increased interest on the part of some academic institutions in licensing and other strategies to raise revenues for their institutions.<sup>1</sup>

Numerous scholars (e.g., Nelson 2004, 2006; Dasgupta and David 1994; Mowery et al. 2004; Eisenberg 2003; among others) have expressed concern over this growing "privatization of the scientific commons" (Nelson 2004, 456), represented by the growth in academic patenting. Their concern is that such privatization may undermine the norms and institutions of "open science" and scientific advance itself by, among other things, restricting access to the upstream discoveries and understandings that are essential inputs to subsequent research (cf. Andrews et al. 2006).

Scientists' actions to restrict others' access to their discoveries, data, instruments, and other research inputs are not, however, new. Long before the Bayh-Dole Act and the widespread patenting of academic science, scientists have limited their contributions to the scientific commons out of concern over their ability to gain credit and recognition for their work (Merton 1973; Hagstrom 1965, 1974). Even Galileo, for example, was careful to limit access to his telescope in order to preserve his priority and ensure credit for subsequent discoveries (Biagioli 2006).

In this paper, we review our own empirical findings and those of others to consider the degree to which the different types of inputs into academic biomedical research—including others' patented and unpatented discoveries, materials, data, and know-how—may be restricted. We also consider the different means through which such restrictions may be imposed, including patents, but also secrecy or simply withholding materials or data. Third, we also try to arrive at some understanding why scientists may impose such restrictions by adopting an economic framework that features the scientists' expected costs and benefits of excluding others. In this simple framework, costs may be tied, for example, to how readily different means of control, such as patents or secrecy, can be implemented. Also, potential benefits may include academic benefits such as eminence, promotion, and so on that come from priority of discovery or the financial benefits that may be realized from the commercialization of an academic's discoveries.

Our consideration of a broad range of research inputs raises a question about the degree to which, and what aspects of, scientific research contributes to a "scientific commons," even absent patents. Of course, what had been traditionally located in this "commons" were published research findings that were available for use by others. What has presumably alarmed Nelson and others about the diffusion of academic patenting is that there is now a legal basis for excluding others from using such published information and findings. In this paper, as noted in the preceding, we are concerned not only, however, with access to patented knowledge, but also to unpatented inputs into research since not all the information or research inputs that are usefully exchanged across scientists—such as materials, unpublished findings, data, or know-how—are patented or even patentable. And for those research findings and inputs that are patented, we distinguish between the legal and "practical" (i.e., readily achievable) excludability conferred by patents and examine the degree to which patents actually restrict access.

To prefigure the following discussion, we indeed observe restrictions imposed on the flow of information and materials across biomedical researchers. The observed forms of exclusion are consistent with the notion that scientists impose restrictions on access to findings and research inputs in response to the expected costs and benefits of such exclusion. We also find that both academic and commercial incentives matter. Of particular importance for current policy discussions, we find that exclusion in academic settings rarely involves the assertion of a patent, but is more typically associated with secrecy or the withholding of research materials, suggesting that the means of restriction employed and the sorts of flows involved (i.e., knowledge, materials, data) depend upon the associated costs. We also find, however, that even where the cost of imposing a restriction is low, as through the withholding of materials, the vast majority of academics comply with requests, suggesting either that academics also benefit from such sharing or that powerful social norms around sharing still apply.

#### II. Why Knowledge Flows Matter

How might limiting access to research findings or inputs affect scientific advance? This can occur in several ways. As Nelson (2004) argues, limiting the use of upstream discoveries in follow-on research to solve a particular problem will constrain the number of researchers working on a problem and, hence, the range of approaches pursued and capabilities deployed. In the face of ex ante uncertainty surrounding the best way of solving technical and scientific problems, a restricted set of approaches or scientists may compromise the performance attributes of whatever solution is arrived at ex post (cf. Evenson and Kislev 1976; Nelson 1982), relative to what might have been.<sup>2</sup>

Restricted access to the fruits of others' research may also limit the realization of complementarities or efficiencies across researchers. For example, knowledge of a promising cell receptor implicated in some disease process may well offer important guidance to other researchers in the field who could potentially build on that discovery. And some of those researchers may have special skills or access to other specialized assets (such as libraries of compounds or special patient populations) that confer special advantages in the use of that knowledge. Restrictions on access to that target that foreclose or limit others' use of that discovery may thus prevent the combining of these complementary assets and capabilities and, in turn, compromise follow-on discovery.

Restrictions on knowledge flows could also impede efficiencies realized through the elimination of duplicative research. Such efficiencies may take the form of knowing that someone else has succeeded in achieving a particular outcome that you were working on in your own lab, with the consequence that it was no longer useful to keep at it. Alternatively, knowledge that a particular approach had failed may spare others the cost of pursuing that approach.

Although restrictions placed on the flow and exchange of research findings and inputs may impede scientific progress in the different ways outlined in the preceding, they need not. There is a potentially important offsetting effect associated with such restrictions. Scientists' ability to limit or delay access to their findings, materials, data, and know-how may increase the expected returns to their research and thus increase the incentive to do the research to begin with. Although the empirical literature provides no sense of the importance of this appropriability incentive effect, its possibility suggests a trade-off between the benefits that society and even individual scientists may derive from the free flow of knowledge and other research inputs, versus any incentive-dampening effect that may be associated with such flows.

# III. The Payoff to Exclusionary Practices and Priority of Discovery

To understand why academic scientists might restrict access to either their discoveries or research inputs, we start by characterizing the payoffs to such behavior. We suggest that one perceived payoff from such exclusionary behavior is a greater likelihood of coming up with a discovery first. Indeed, priority of discovery has been widely recognized for decades as a motivation for scientific research and stressed in the seminal writings of Merton (1957) as well as in the more recent writings on the economics of science by Dasgupta and David (1987, 1994) and Stephan (1996).

But what is the payoff from winning a priority race? Clearly, it redounds to an academic's reputation among his or her peers and, in turn, professional esteem or eminence. In addition to gratifying the scientist emotionally, the esteem of peers also confers tangible benefits of academic promotion, including the award of tenure, career security, and endowed chairs, as well as the prospect of outside income gained through consulting and speaking fees (see Stephan 1996). When eminence is of a sufficient level, it can materially affect income, and when it also confers job mobility across institutions, it can raise income quite substantially, depending upon the field. Eminence yields the other tangible benefit of conferring an advantage in the competition for grants whose awards are importantly influenced by the reputation of the applicants. Depending on the field, grants can be critical to the conduct of academic research itself. This is surely true of biomedicine, where researchers may require lab space, equipment, and access to materials, animals, and possibly human subjects.

The benefits conferred by priority are also not of a one-time character. Rather, as pointed out by Merton (1968) in his discussion of the Matthew effect in science, they are self-reinforcing (see also Allison and Stewart 1974; Cole and Cole 1973). Reputation influences the award of grant money that is essential to the conduct of research—and hence the ability to come up with the next discovery, which in turn redounds to reputation. Reputation not only affects support. It also affects an academic's ability to attract quality students, who, in turn, affect the researcher's ability to succeed, and so on. Thus, there is a cycle in which significant publication begets resources, which enables subsequent research and publication, which reinforces reputation, and so on. Thus, the rewards to priority are not only substantial at a point in time, but over time, importantly influencing the arc of scientific careers (Allison and Stewart 1974; Cole and Cole 1973).<sup>3</sup> As a consequence, scientists are motivated not only by the rewards to priority for any given discovery, but also by the expectation of the follow-on findings that a given discovery may open up.

Traditionally, the prospect of priority of discovery is seen as motivating dissemination and access rather than secrecy and exclusion. Building on Merton's (1957) earlier insight, Dasgupta and David suggest that the virtue of the priority-based system is that, to generate the private good of reputation in a priority-based system, scholars must publish and, hence, make available their findings for all to see and—at least until recently—to use.<sup>4</sup> They state, "Priority creates a privately-owned asset—a form of intellectual property—from the very act of relinquishing exclusive possession of the new knowledge" (Dasgupta and David 1987, 531, as cited in Stephan 1996, 1206). Stephan and Levin (1996, 1206) further argue that this system based on reputation also provides an incentive to the scholar to encourage wider dissemination to further augment their reputation, thus providing "a mechanism for capturing the externalities associated with discovery." Thus, the suggestion is one of a felicitous consistency between the achievement of the reputational benefits of priority and social welfare.<sup>5</sup>

Yet the objective of priority of discovery and the academic reputation that devolves from it advance disclosure only to a point. While academic scientists will typically disclose that which is required to persuade the scientific community of the merit and validity of their discoveries, there are intermediate inputs into that work that are often not disclosed or otherwise made publicly available, including data, materials, knowledge of methods, and other information. Following Stephan (1996) and Eisenberg (1987), we suggest that scientific competition may dampen researchers' willingness to disclose or share these various inputs that are potentially vital to others' work.<sup>6</sup>

In addition to the returns to exclusionary behavior that might redound to a scientist's academic career, another potential payoff to exclusionary behavior is the prospect of financial gain from the commercialization of discoveries—a benefit that has become more salient with the proliferation of university-based start-ups and licensing income over the past twenty-five years in the life sciences. The concern here is that such commercial motives may provide not only incentives for restricting dissemination of research inputs, resembling the effect of scientific competition, but may also compromise academics' interest in disclosing their discoveries either fully or promptly when such disclosure diminishes a proprietary commercial advantage.<sup>7</sup>

The observation that the prospect of commercial returns may compromise an academic's motive to fully and promptly disclose their research findings raises the question for academics of the degree to which commercial and academic incentives to disclose research conflict. The interaction of these two sets of incentives is complicated. On the one hand, the two motives may work together to reinforce the drive to disseminate research findings and undermine it at the same time (or in different settings). In some contemporary academic research communities, commercial activity still does not accord status, and rarely does it confer academic promotion (Berkovitz and Feldman 2006). Indeed, commercial activity can detract from the esteem of academic peers and, hence, provide lower levels of reputational and associated rewards. Zucker and Darby (1996) suggest, however, that in biomedicine, commercial motives may reinforce academic motives of priority and publication because it tends to be the recognized "star scientists" who play dominant roles in founding start-ups based on academic discoveries. Even if scientists require publication to establish or reinforce their "star" status, commercial motivation may nonetheless compromise the coincidence between their academic ambitions and full dissemination of the details of their discoveries. A start-up's success will necessarily depend upon a proprietary advantage, whose source is typically some sort of know-how or information that is not publicly available. Although Zucker and Darby (1996) argue that there is a strong tacit element in biomedical research that star scientists are able to keep private and exploit as the basis for founding firms, not only tacit elements may be kept private.

# IV. How Academics Appropriate the Returns to Discovery and Implications for Flows of Knowledge and Other Inputs

In this section, we briefly consider how academics increase their ability to appropriate academic and commercial returns to discovery and the implications of these different strategies for flows of knowledge and other research inputs.<sup>8</sup> One strategy that strengthens a scientist's ability to achieve dominance in a field, through either the quality or speed of discovery, includes the deployment of complementary capabilities, which can include able students, lab infrastructure, and access to financial support. Academic reputation itself can be considered a complementary asset inasmuch as it confers more ready access to resources and to journal outlets. Such reliance on complementary capabilities does not, in itself, compromise disclosure of either findings or the exchange of research inputs—and may actually accelerate both.

A commonly featured strategy among academics that does dampen knowledge and material flows is secrecy (Merton 1957). This can take several forms. One is refusing to discuss ongoing research until priority has been established through publication (Hagstrom 1974; Walsh and Hong 2003).<sup>9</sup> Such secrecy can be taken further by limiting the disclosure of research findings through publication delay or incomplete publishing (Blumenthal et al. 1997; Walsh, Jiang, and Cohen 2006).<sup>10</sup> Researchers may also withhold the data upon which published findings are based or withhold supplemental information that is useful but not typically provided in the publication (such as phenotypic information or protein structures). Researchers may also limit the distribution of difficult-to-obtain material research inputs or the material embodiments of research findings (such as new materials, equipment, cell lines, etc.) in order to protect the discoverers' advantage in conducting any research that may build upon the prior discovery (Campbell et al. 2002; Walsh, Cho, and Cohen 2007).<sup>11</sup> There is also tacit and other private knowledge generated in the course of conducting research that scientists may be reluctant to disseminate.

Academics (and their institutions) may also use patents to restrict access to published findings and research inputs, typically to enable the commercialization of discoveries through the creation of start-ups or licensing to existing firms. Indeed, a key feature of patented discoveries is that, though disclosed, they cannot in principle be used by others without permission.<sup>12</sup> In addition to conferring a legal basis for restricting access to scientific discoveries, patents may also increase a researcher's *incentive* to restrict access by enabling the commercialization of his or her discoveries.<sup>13</sup>

The ways in which patents may restrict knowledge flows may be distinguished on the basis of whether it is a question of gaining access to one or a small number of patents, perhaps associated with some foundational discovery, or gaining access to a large number of patents. Merges and Nelson (1990) and Scotchmer (1991) highlight the possibility that, where innovation is cumulative, the assertion of patents on key upstream discoveries may significantly restrict follow-on research.<sup>14</sup> The patenting of numerous, individually less significant discoveries may also impede academic research. Although their focus is largely on commercial projects, Heller and Eisenberg (1998) and Shapiro (2000) suggest that the patenting of a broad range of research tools that researchers need to do their work has spawned "patent thickets" that may make the acquisition of licenses and other rights too burdensome to permit the pursuit of what should otherwise be scientifically and socially worthwhile research, (engendering a tragedy of the "anticommons" [Heller and Eisenberg 1998]).15

# V. What We Know about Restrictions on Flows of Research Inputs in Biomedicine

In this section, we review the empirical evidence on restricted access to research inputs where such inputs can include the research findings of others, information and data, and research materials of a more intermediate character. As noted in the preceding, we will broaden our consideration of restricted flows of research inputs beyond patented discoveries. We do this because not all the information or research inputs that are usefully exchanged across researchers are patented or even patentable. Moreover, we consider the material flows as well as knowledge flows across biomedical researchers because restrictions on material sharing can have many of the same effects on scientific advance as restrictions on the use of disembodied knowledge. We focus on three types of restrictions distinguished by the nature of the research input in question. The first is the use of patents to deny access to published knowledge. The second is the use of secrecy to keep all or part of a research result from being published immediately or to keep proprietary control over data and other unpublished knowledge inputs. Finally, there is the use of control over research materials to deny access to the inputs for follow-on research.

#### Access to Patented Findings and Techniques

We begin with restrictions on published information associated with patents. Because patents confer the right to exclude others from practicing the patented invention, they can be used to prevent other scientists from making use of published research results if those results are also patented (cf. Ducor 2000; Murray and Stern 2005).

Patent-related restrictions on access to knowledge of a discovery can take numerous forms. Any positive price for access to intellectual property potentially restricts access. In addition to licensing fees, restrictions may also be imposed through terms of exclusivity and other conditions of use (e.g., reach-through terms, demands for coauthorship, etc.) as well as the transactions costs highlighted by Heller and Eisenberg (1998) that potentially impose a burden on researchers. Another way in which patents can restrict access is by simply signaling a possibility of infringement liability and, in turn, litigation, with its attendant costs. Eisenberg (2003) suggests that the growth of patenting of upstream discoveries by universities and firms may now impede follow-on academic and other research, particularly since the *Madey v. Duke* decision, which made it clear that academic research does not confer any shield against infringement liability. Similarly, Andrews et al. (2006) argue that the recent Supreme Court ruling in the *LabCorp v. Metabolite* case shows that basic facts of nature are patentable and that such patents will impede scientists' ability to conduct their research.

Several studies have attempted to estimate the incidence of such patent-related access restrictions, including both the problem of accessing a small number of patents associated with fundamental upstream discoveries as well as the problem of acquiring rights to a multitude of complementary technologies. First, one might ask whether knowledge and other inputs to biomedical research are commonly patented. Indeed, there are a large number of patents associated with genes, for example. A recent study found that nearly 20 percent of human genes had at least one patent associated with them, and many had multiple patents (Jensen and Murray 2005). Another study estimated that in the United States, over 3,000 new DNA-related patents are issued each year (National Research Council 2005, figure 4-1). Prior work on licensing of university-based inventions suggests that the majority are licensed exclusively (AUTM 2000; Henry et al. 2002; Pressman et al. 2006).<sup>16</sup> Thus, the preconditions for patents restricting access exist in biomedical research.

Studies that have examined the incidence of access or anticommons problems find them, however, to be rare, even for industry scientists, and especially so for academic scientists (Nagaoka 2006; Nicol and Nielsen 2003; Straus 2002; Walsh, Arora, and Cohen 2003a; Walsh, Cho, and Cohen 2005; Walsh et al. 2007). For example, in their limited, interviewbased study, Walsh et al. (2003b) find that, although complaints about access to patented technologies and findings are not rare (about one-third of their respondents mentioned some issue regarding limits on accessing others' intellectual property [IP]), such limitations never caused the academic scientists among their interviewees to stop a promising line of research. Finally, they find no evidence of academics being excluded from research due to patents on research inputs (although the sample of academics in that study was small and not representative). Walsh et al. (2003b) also find virtually no instances of industrial or academic researchers being stopped due to an inability to gain access to a large number of patents needed for a research project. In a subsequent survey research study using a much larger, random sample of academic biomedical researchers, Walsh, Cho, and Cohen (2005, 2007) confirm these earlier qualitative results for academics with the finding that only 1 percent of academic researchers (i.e., those in universities, nonprofits, and government labs) report having to delay a project, and none abandoned a project due to others' patents, suggesting that neither anticommons nor restrictions on access were seriously limiting academic research.<sup>17</sup> Another piece of evidence both partially explaining this finding and suggesting that academics appear to be little concerned with the possibility that their research may be infringing others' patents is that only 5 percent of the academic scientists surveyed regularly check for relevant patents.<sup>18</sup> With the important exception of gene patents that cover a diagnostic test, the Walsh et al. finding that patents have rarely blocked academic research have been replicated with other samples and in other countries (Straus 2002; Nicol and Nielson 2003; Nagaoka 2006; Walsh et al. 2007).<sup>19</sup>

Even if patents do not stop ongoing research, the very prospect of a thicket or restricted access may dissuade researchers from choosing particular projects and limit lines of attack in that way. To explore this possibility, Walsh, Cho, and Cohen (2007) asked academic respondents to assess the importance of reasons that may have dissuaded them from moving ahead with the most recent project that they had seriously considered but had not pursued. The most pervasively reported reasons why projects are not pursued include lack of funding (62 percent) or being too busy (60 percent). Scientific competition (too many others working on the problem) was also an important reason for not pursuing projects (29 percent). Technology control rights, such as terms demanded for access to needed research inputs (10 percent) and patents covering needed research inputs (3 percent), were significantly less likely to be mentioned. Respondents doing research on drugs and therapies were, however, somewhat more likely to report that unreasonable terms demanded for research inputs were an important reason for them not to pursue a project. These results are broadly consistent with Sampat's (2004) and, especially, Murray and Stern's (2005) findings of a decrease in the citations to a paper (on the order of 10 percent of expected citations) after the published result is patented, particularly because the latter study sampled from a population of scientists working closer to downstream and commercial applications.<sup>20</sup> These several results suggest that there may be some redirection of effort away from areas where there are patents on research results, especially in more commercially motivated domains. The overall social welfare implications of this redirection are, however, uncertain as there is both a potential loss from having fewer people work on a problem and a potential gain from having a socially more diverse research portfolio (Cole and Cole 1972; Dasgupta and Maskin 1987).

#### Limits on Practical Excludability of Patented Knowledge

An important reason why patents do not limit access to published research results is that researchers in firms and academia employ a suite of "working solutions" to the access and anticommons problems (Walsh et al. 2003a). Within firms, in addition to licensing (Pressman et al. 2006), these "working solutions" include inventing around, locating research and development (R&D) facilities in jurisdictions where the research tool patents in question have not been applied for, challenging questionable patents, and using the technology without a license.<sup>21</sup> Although Walsh, Arora, and Cohen (2003a) and Walsh et al. (2007) cannot know the rate at which academics may have actually infringed patents, the existence of numerous research tool patents noted in the preceding and the fact that academics rarely check for patents suggest that academics commonly use technology without a license, although perhaps unknowingly. It has been suggested, however, that academics' use of patented technology without a license reflects an inappropriate and possibly unstable practice (Eisenberg 2003; National Research Council 2003, 2005). It is important to remember, however, that the stability of this unlicensed use is supported by a combination of the difficulty of enforcing patents due to the secrecy of research programs, the cost of litigation, and a common interest among patent owners in allowing such use. Patent owners may engage in "rational forbearance" (National Research Council 1997) of others' possible infringement both because the infringing research can add value to the patent and because forbearance can generate goodwill that is needed to encourage information exchange with other researchers in the field (Kieff 2001; Walsh, Arora, and Cohen 2003a).<sup>22</sup> Because research communities are often small and reputation is important (even for industry scientists), aggressive enforcement of patent rights may be too costly if it undermines the goodwill that is essential to others' future cooperation (for sharing information, materials, and informal access to patented technologies).23

Thus, the low incidence of access or anticommons problems relative to the large numbers of researchers or projects that may be at risk should not come as a surprise.<sup>24</sup> A key factor preventing such a failure in academic settings in particular (though also true of industrial research) is that it is hard to detect infringement or enforce the right to exclude if it is detected. Assuming that a patent owner can even detect an unauthorized use of one of his or her patented discoveries by another researcher, sending a warning letter may have little impact, and a lawsuit is an expensive and risky proposition, with the expected payoff (injunction against research that is finished and "reasonable royalties" on a small scale use of the research tool) quite small, especially when weighed against the cost of substantial legal fees as well as the possible loss of the patent right. Thus, although a patent may confer a legal right to exclude, it does not confer "practical excludability" in academic research settings. As we will see, the same is not true for control over privately held research materials, data, or not-yet-published results. In these cases, excludability is more readily achieved.

#### Practically Excludable Research Inputs

In this section, we begin to consider the degree to which we observe restrictions on access to privately held research inputs, including materials, data, or unpublished research findings. Access to others' research materials in particular is vital to the conduct of biomedical research (cf. Furman and Stern 2005). Walsh et al. (2007), for example, report that over the two-year period, 2003 to 2004, academic researchers in genomics and proteomics reported making an average of nine requests for materials, seven to other academics and two to industry scientists. Examples of material inputs are an organism (e.g., OncoMouse), a cell line (e.g., human embryonic stem cells), a protein (e.g., purified eurythropoetin), or a drug (e.g., a statin for studying the cholesterol cycle). Examples of unpublished information of use to other researchers include phenotypic information on a mouse or the three-dimensional structure of a protein.

As suggested in the preceding, due to the challenges and disadvantages of asserting patents, it is costly to control the use of patented discoveries in academic biomedical research settings. In contrast, it is much less costly in academic settings to control the use of privately held materials and data where such inputs are difficult to replicate.<sup>25</sup> Detection of the use of such inputs is not difficult because a prospective user must request the input. Moreover, the owner must actively cooperate with the prospective user to provide access. This requirement of active cooperation provides owners of privately held inputs more control and less expensive means of control over access relative to owners of IP. An owner of a material or data, for example, can deny access by simply not responding to a request, effecting exclusion at little cost. Also, the burden of initiating the exercise of control over access falls on the owner in the case of patented knowledge, whereas, for materials or other privately held inputs, it falls on the prospective user who must submit a request. Finally, compared to owners of "pure" intellectual property, owners of materials and other privately held inputs face greater out-of-pocket costs to satisfy rather than deny requests as granting typically entails replication of materials, shipping, preparing data, and so on. Thus, the costs of excluding others from using materials, data, unpublished findings, and so on are much less than excluding others from accessing patented discoveries.

In the following sections, we discuss the limits on access to unpublished information and materials to demonstrate empirically that these are more practically excludable research inputs as compared to pure intellectual property.

#### Scientific Secrecy: Withholding of Unpublished/Intermediate Findings

There is evidence of significant secrecy among university researchers with regard to unpublished findings or data (Blumenthal et al. 1997; Campbell et al. 2002; Walsh and Hong 2003; Walsh, Cho, and Cohen 2005). As noted in the preceding, the employment of a range of strategies to protect the rewards from priority has long been known in science. Hagstrom (1974) notes that this type of secrecy was common in science, even in the 1960s, especially in experimental biology. Walsh and Hong (2003) find that secrecy has increased in physics, mathematics, and, especially, in experimental biology from the 1960s to the 1990s, along with concern over scientific competition. These several examples suggest that such secrecy is endemic in science and especially so in experimental biology.

In addition to scientific competition, commercial incentives can also motivate secrecy. Walsh et al. (2007) report that 7 percent of the academic biomedical researchers surveyed acknowledged that, in order to protect the commercial value of an invention or discovery, they delayed publication of their research results for more than one month at least once in the last two years. Four percent reported that during the last two years they, at least once, decided not to publish a result in order to protect the commercial value of their findings.<sup>26</sup>

#### **Restricting Access through Control over Materials**

There is also evidence that scientists are often denied access to others' research materials. Walsh et al. (2007) find that, as reported by those making requests, 19 percent of recent requests were not fulfilled and that at least 8 percent of respondents had a project delayed due to inability to obtain timely access to research materials (compared to less than 1 percent who were delayed by inability to obtain a patent license). Furthermore, Walsh et al. (2007) find that, among genomics researchers, the rate of withholding research materials appears to have increased from 10 percent of requests in the 1997 to 1999 period (Campbell et al. 2002) to 18 percent (±3.7 percent) of requests in the 2003 to 2004 period, possibly reflecting a significant increase in a short time. This failure to receive requested research materials can have a negative impact on individuals' research programs (Campbell et al. 2002; Walsh, Cho, and Cohen 2005).<sup>27</sup> Campbell et al. (2002) reported, for example, that 28 percent of all geneticists reported they had difficulty replicating published results, and 24 percent had their own publication significantly delayed. Walsh et al. (2007) find that one in nine scientists had to abandon a project each year due to an unfulfilled request for materials or information. Thus, where practical excludability exists, we see some evidence that it is being exercised. These findings raise the question of what motivates scientists to exclude others from using their materials and other inputs.

#### **Reasons for Restricted Access**

As pointed out in the preceding, scientists may be motivated to exclude others from using their materials or information by scientific competition, commercial motivation, or both. Furthermore, our cost/benefit perspective suggests that the likelihood of excluding depends in part on the cost of complying with a request, both in terms of the risk of losing priority races or commercial benefits and the burden of compliance.

Empirical work has examined the causes of withholding behaviors. One consistent finding is that industry funding is associated with delayed publication (Bekelman, Li, and Gross 2003; Blumenthal et al. 1997; Campbell et al. 2002; Cohen, Florida, and Goe 1994; Cohen et al. 1998). Walsh, Jiang, and Cohen (2007) find that publication delay is associated with commercial activity and ties to small and medium enterprises (SMEs) and that excluding information from publications is associated with industry funding. Blumenthal et al. (1997) and Campbell et al. (2002) find that commercial activity (including but not limited to patenting) is associated with withholding research results. Thus, the evidence suggests that the prospect of diminished commercial gains from research findings tends to increase the rate of excluding others from access through the use of withholding practically excludable research results.

This benefit/cost perspective can help explain not only the higher rates of excluding others from access to materials or unpublished results and data as compared to patented knowledge, but can also help us understand the correlates of complying with requests for these practically excludable research inputs. The costs of providing materials to fellow researchers potentially include, for example, a diminished advantage for the achievement of priority of discovery, lost commercial opportunities, and the effort and cost burden of actually complying with the request.<sup>28</sup> Using our survey data, we tested two models of sharing of materials and data, one from the point of view of those trying to receive the data or material (consumers) and one from the point of view of those asked to provide the data or materials (suppliers; Walsh, Cho, and Cohen 2007). A key finding, from both the consumer and the supplier models, is that greater scientific competition (measured by the number of labs that are competing with the lab for publication priority), and thus the greater the chance that compliance might cost a lead in a priority race, is associated with lower probability of providing access to the research material or unpublished data.<sup>29</sup> For those who have been asked to send materials or information, a prior history of commercial activity is also associated with an increased likelihood of noncompliance with the request, suggesting that a potential loss of competitive advantage in the market increases exclusionary practices. We also find that the burden and costs of compliance with requests for data or materials (measured by the number of requests, controlling for lab funding) reduces compliance (see also Campbell et al. 2002). Those with more publications in the last two years are also more likely to exclude, perhaps because the opportunity cost of spending time complying with requests is higher for those who are more productive.

From the point of view of those trying to acquire materials, we find that being asked to sign a materials transfer agreement (MTA) is associated with a *greater* likelihood of receiving the material or information. It is likely that compliance is lower in the case where there is no MTA because the person who was the object of the materials request simply did not respond. In other words, this finding is consistent with the claim that, in the case of material or unpublished information, even passive resistance provides practical excludability. On the other hand, while being asked to sign an MTA is associated with greater access, less sharing is associated with restrictive terms in the MTA (that raise the cost of accepting the material), including demands for publication review (which may reduce the ability to turn the material into recognition through a future publication) and royalties (which may reduce the commercial payoff of future results). Finally, we find that whether a material is patented does not appear to affect access.<sup>30</sup> Thus, not only do patents per se rarely restrict academics' access to scientific knowledge, as shown in the preceding, but they also do not appear to be associated with restricted access to materials or unpublished information.

Although some evidence suggests that the norm of sharing research materials and results may be weakening in biomedical research, sharing is still common, with the average academic researcher in biomedical fields making three to four requests per year, about 80 percent of which are fulfilled (as reported by those making requests). The strength of this norm is impressive once one considers that compliance often involves costs, including out-of-pocket expenses (for copying and sending materials, which can be significant in the case of a genetically modified animal) as well as the risk of losing a competitive advantage (either academic or commercial) by sharing access to a material that may be key to future success.

#### VI. Reflections on Empirical Findings

As shown in the preceding, academics are rarely excluded from using others' patented published research—largely because they rarely know whether a published discovery is patented or not and are apparently not that concerned. They simply want to get their work done. Thus, legal excludability due to patents does not appear in practice to impose an important impediment to academic research in biomedicine, and much of what's published continues to reside effectively (if not legally) in the public domain. What is private and excludable, however, are those inputs into scientific research that are privately possessed and often difficult to replicate, such as materials and data. In our view, the key issue is the impact of reputation-driven science on access to such privately held research inputs.

As suggested by Eisenberg (1987) and supported by the empirical findings of Walsh, Cho, and Cohen (2007), biomedical researchers can achieve their reputational objectives while retaining proprietary control

of data, materials, and some methods. Such inputs do not simply provide the basis for a given publication, but also a stream of ongoing work, making the researcher all the more reluctant to relinquish his or her control, as doing so may compromise the researcher's ability to claim priority growing out of future work.

As reported in Walsh et al. (2007), it is to materials and data that biomedical researchers will occasionally refuse access to others, and whether such materials are patented appears to have little to do with whether they are shared. Such inputs into the research process are often not part of the "scientific commons." Others can be excluded from accessing these inputs—and are, notwithstanding the strictures of granting agencies and journals such as *Science* and *Nature*.<sup>31</sup>

Although academics will sometimes exclude others from using their research inputs when they can, such exclusion is still observed, however, only in a minority of instances. As noted in the preceding, about four-fifths of requests for materials by academic biomedical researchers to other academics are satisfied (Walsh et al. 2007). An obvious question is why do four-fifths of academic researchers comply with requests for research inputs in light of reasons and ability not to? One possibility is that academics also benefit from such sharing, perhaps by realizing complementarities and efficiencies from participating in networks based on reciprocal exchange. Norms also play an important role. We observe, however, that the incidence of priority-driven restrictive practices and presumably the strength of norms around sharing are not uniform in science (e.g., Walsh and Hong 2003). As documented by Sulston and Ferry (2002) in their discussion of the development of rules for the dissemination of genomic sequence data, norms regarding disclosure, data sharing, and so on can differ sharply even between related scientific communities.<sup>32</sup> Clearly, there are norms of exchange that apply to different degrees across individuals and communities, and it is not clear why such norms take hold for some individuals and in some settings but not in others.

#### VII. Implications

Although academic research—especially in published form—has some elements that fit the common characterization of a public good—satisfying the conditions of nonexcludability and nonrivalry in use—other important elements, notably its inputs and reputational effects, do not. All of these benefits are individually appropriable returns to scientific research. What we observe in the empirical results reported in the preceding for academic biomedical research is that where excludability appears to be readily enforced for privately possessed inputs into biomedical research, it sometimes is, and this is especially manifest in the sharing of materials and, to some extent, data.

We have argued that academic biomedical scientists work at least partly for private (academic and commercial) rewards, and these incentives may drive how they interact and cooperate with the scientific community. The notion that researchers make decisions about the sharing of materials and knowledge to maximize academic and commercial priority-linked rewards provides a simple way of thinking about the factors that might drive the sort of withholding and other behaviors that have now been studied by many. A number of the findings from the Walsh et al. study make sense from this vantage point, including the negative effect of the out-of-pocket costs of compliance with requests for materials as well as the negative effect of the intensity of competition across labs on compliance. This perspective also explains the greater likelihood of exclusion for privately held materials and other research inputs as compared to patented, published findings in that the costs of exclusion are much less for the former than for the latter. On the benefits side of this framework, it also appears that researchers' expected payoffs to behaviors that might favor the winning of priority races may stimulate exclusionary practices. For example, the Walsh et al. (2007) results suggest that where the expectations of commercial returns to academic discoveries are higher, the more likely it is that an academic scientist will engage in withholding behavior.

There are important factors, however, that may affect biomedical researchers' exclusionary behaviors that have not been considered in any broad-based empirical studies. For example, as noted in the preceding, offsetting the negative incentive effect of any diminished potential for achieving priority of discovery, sharing may also allow academics to benefit from the inflow of information, materials, and ideas that come with participation in relationships and networks that involve the reciprocal exchange of such research inputs. The impact on behavior of the potential realization of such complementarities from mutual exchange has not, however, been examined. Another related factor is the social disapproval and associated sanctions that may be a significant cost of withholding behavior. Indeed, we conjectured in the preceding that the observation of withholding behavior in only a minority of instances can be at least partly explained by powerful social norms that guide the conduct of biomedical research.<sup>33</sup> We do not, however, have direct statistical evidence on the strength or role of such norms in contemporary biomedical research.

Another important omission from prior work, however, is a consideration of the role that government and other funding of biomedical research might play in affecting noncompliance with requests for materials, data, and so on. Consider, for example, a possible impact of higher levels of National Institutes of Health (NIH) funding on exclusionary behavior. If the expected marginal payoff to exclusionary practices increases with the level of NIH funding by conferring an advantage in the competition for more sizable grants (perhaps by qualifying the applicant uniquely to carry out the proposed project), then growth in NIH funding may stimulate exclusionary behaviors, especially if funding is concentrated in larger, but fewer, grants. Indeed, this raises the possibility that the rapid run-up in NIH funding over the past decades may itself account for some of the increase in noncooperative behaviors observed among academic scientists in biomedicine.<sup>34</sup> Of course, numerous other factors could have affected changes in withholding behavior during this same period, including the growing emphasis on commercial spin-offs from academic medicine. Moreover, there are reasons to believe that NIH funding and associated policies could have dampened such behaviors as well.35

Regarding the impact of public and other funding, the more general point is that such funding may affect the way scientific research is done, its cooperative character, and, in turn, its efficiency. Indeed, federal agencies and other granting institutions understand the nature of the incentives discussed in the preceding that condition the conduct of the research itself. The NIH reflected this understanding when it imposed requirements on its grantees regarding the sharing of data and materials (NIH 1999). Notwithstanding the question about the degree to which such strictures are enforced, one must be cognizant, however, about the effect of such policies that compel the sharing of materials, data, and other privately held information on the incentives to do the research.

The imposition of strictures designed to dampen exclusionary practices raises the question of the net effect of such practices on scientific progress. As suggested in the preceding, the answer turns on the tradeoff between the efficiency and complementarity benefits of knowledge exchange, on the one hand, versus the possible appropriability incentive effects of such on the other. If academics are deprived of their ability to keep these research inputs private, will that diminish their expectation of the payoff to their research?<sup>36</sup> And, if so, will that dampen their incentive to conduct the research to begin with?<sup>37</sup> Although one would think that public subsidy and the expectation of intrinsic rewards might diminish the likelihood of such an outcome, the question has not been empirically explored in any systematic fashion.<sup>38</sup>

In addition to compelling the exchange of materials and research inputs, one might consider other institutional schemes that increase the scientists' incentives to share materials, data, and other inputs. One might consider, for example, supporting the expansion of biomedical resource centers (BRCs) and online databases. Furman and Stern (2005) show that, by reducing the cost of accessing materials (as well as certifying quality), depositing materials in a BRC results in a significant increase in citations to scientists, especially in later years, after most publications are no longer actively cited.<sup>39</sup> Given the ease of access and reputational benefits associated with shared repositories, it may be worth exploring how to expand their use. It may be that greater subsidies to these institutions would allow them to take on greater numbers of materials and would encourage scientists to switch from peer-to-peer exchanges to institutionally mediated exchanges.

#### VIII. Conclusion

Our results suggest that, in biomedicine, there is little basis to be concerned over access to others' published research results. In contrast, academics are able and willing to exclude others from using research inputs, especially materials and unpublished information where exclusion is a simple matter. Even these practically excludable research inputs are, however, shared in the majority of cases. Where academics do exclude others from the use of inputs, the means of exclusion are typically secrecy and control over materials. Patents are a less effective means of exclusion because their enforcement involves a costly process of search and legal challenges, with few associated benefits. In contrast, control over information or materials can confer exclusivity at low cost, even through such passive means as not responding to requests. We also find that while commercial motives can generate noncooperative behavior, such behavior is also endemic to the reputation-reward system of academic science.

Our simple logic that focuses on the expected costs and benefits to noncooperative behaviors suggests we should expand our purview beyond patents when we try to understand what might drive such behaviors across academic researchers. Rather, when considering policy reforms designed to promote the free flow of research inputs across academics, we should examine the underlying determinants of the costs and benefits of sharing versus excluding and the associated incentives to conduct the research to begin with.

# Endnotes

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1. Indeed, Mowery et al. (2004) suggest that the Bayh-Dole Amendment was itself partly an outgrowth of the pursuit of licensing relationships on the part of a handful of universities.

2. The basic proposition developed by Evenson and Kislev (1976) and Nelson (1982) is that the more approaches to a given technological objective that are tried, the greater the likely contribution to technical advance (in terms of improvements in product quality or performance, or manufacturing costs) of the approach that is ultimately selected by the market (or some other mechanism or authority). In other words, society may not be best served by having, for example, only Geron trying to employ human embryonic stem cell technology to create pancreatic replacement tissue.

3. Owen-Smith (2003) also shows that this accumulative advantage process works at the level of institutions competing for prestige as well and, in this respect, aligns the incentives of academics and their institutions.

4. Merton (1957, 640) states, "Once he has made his contribution, the scientist no longer has exclusive rights of access to it. It becomes part of the public domain of science. Nor has he the right of regulating its use by others by withholding it unless it is acknowledged as his. In short, property rights in science become whittled down to just this one: the recognition by others of the scientist's distinctive part in having brought the result into being."

5. As Merton ([1957] 1973, 292) put it, "Then are found those happy circumstances in which self-interest and moral obligation coincide and fuse."

6. Exclusionary practices can be attenuated due to the social opprobrium that they may elicit. But recognizing the power of these incentives not to share, granting agencies, scientific journals, and even foundations try to compel the beneficiaries of their various functions to disclose their data, methods, and materials (Eisenberg and Rai 2006).

7. Researchers may, for example, delay announcing a discovery until a patent application has been filed or possibly until the application is published. In the case of the OncoMouse, for example, Leder (funded by DuPont as well as NIH) submitted a patent and delayed publication. This actually cost him scientific priority over Palmiter and Brinster (whose paper was published four months before Leder's and about the same time as Leder's patent application) but gave Harvard (and DuPont) patent priority (Murray 2006). Palmiter and Brinster did not file for a patent, even though they had industry funding.

8. These "academic appropriability strategies" are roughly analogous to the appropriability strategies employed by firms to protect the profits due to industrial innovation documented by Levin et al. (1987) and Cohen, Nelson, and Walsh (2000). Biagioli (2006) provides a wonderfully detailed account of the different "appropriability strategies" employed by Galileo to increase his academic credit and authority.

9. "To maintain his property, Descartes implores his friend Mersenne, 'I also beg you to tell him [Hobbes] as little as possible about what you know of my unpublished opinions, for if I'm not greatly mistaken, he is a man who is seeking to acquire a reputation at my expense and through shady practices'" (quoted in Merton 1957, 652).

10. Merton (1957), for example, cites scientists long ago submitting sealed manuscripts to learned societies or announcing results in code in order to establish priority without tipping off their competitors:

In the seventeenth century, for example, and even as late as the nineteenth, discoveries were sometimes reported in the form of anagrams—as with Galileo's "triple star" of Saturn and Hooke's law of tension—for the double purpose of establishing priority of conception and of yet not putting rivals on to one's original ideas, until they had been further worked out. . . . As late as the nineteenth century, the physicists Balfour Stewart and P. G. Tait reintroduced this practice and "to secure priority . . . [took] the unusual step of publishing [their idea] as an anagram in *Nature* some months before the publication of the book." (Sir J. J. Thompson, *Recollections and Reflections* [London: G. Bell, 1936, 22; quoted in Merton ([1957] 1973, 315)

A more recent example comes from research on superconductivity, where Paul Chu was accused of deliberately introducing a "typo" into his two papers submitted to *Physical Review Letters* (substituting Yb [ytterbium] for Y [yttrium] in a key formula) in order to throw off reviewers, who were also potential competitors. He also applied for a patent after submitting the papers. Although reviewers are supposed to keep manuscripts confidential, news of the discovery leaked (although the leak included the mistaken formula). Chu then corrected the error before submitting the final proofs to the journal, causing some who followed the (incorrect) leaked formula to accuse Chu of deliberately trying to throw them off the trail. Others in the field say that, even if it was the honest mistake Chu said it was, they would understand someone doing this deliberately in such a high-stakes race as superconductivity was in the late 1980s, with Nobel prizes and possibly substantial commercial applications at stake (Kolata 1987; see also Fox 1994).

11. For example, due to dissatisfaction over not receiving proper scientific credit for contributing avian flu samples, Chinese scientists became very reluctant to share these valuable research materials, saying that they would conduct the research themselves in order to ensure they received the credit for any discoveries in this important research field (Zamiska, February 24, 2006, A1, A6).

12. Ironically, although patents may enable the realization of financial returns to discovery, they also protect the information that is disclosed and thus may motivate more disclosure, at least as compared with secrecy.

13. Patents covering published results may also reduce the incentive of other researchers to do follow-on research, not because they cannot access the results, but because they may have to share the rents associated with any follow-on discoveries with the patent holder if the prior patent blocks the follow-on invention. This reduced incentive for exploiting a particular published discovery may partially explain the Murray and Stern (2005) and Sampat (2004) findings that patented results are less likely to be cited.

14. Such foundational discoveries may be either rival-in-use or not. An example of a foundational discovery that is not rival-in-use is the method of recombinant DNA, or

polymerase chain reaction (PCR) technology, both of which have wide applications. A foundational discovery that may well be rival-in-use and that offers the promise of creating—and replacing—different types of human tissue is that of human embryonic stem technology. This is rival-in-use in the sense that if, for example, one firm builds on that technology to create pancreatic tissue, that product would clearly compete with another firm creating the same type of tissue, even if the particular way in which the technology had been employed differs.

15. More generally, where follow-on research depends on access to numerous patents, the transactions costs and accumulated licensing fees may also restrict access to domains of research that would build on such upstream developments. For example, some research programs dedicated to discovering therapies or drugs require access to numerous targets that may be associated with a particular disease process. If each target is patented and a license fee is charged, the accumulated licensing fees can restrict access, perhaps significantly.

16. Pressman et al. (2006) find, however, that many of these "exclusively" licensed patents are licensed to more than one firm (either divided by field of use or geography, or sometimes in series), which suggests that access restrictions may not be as severe as the condition of exclusivity might suggest.

17. If we use as the denominator only those scientists who knew of a relevant patent, 16 percent had been delayed, though none abandoned a project. It is not clear which is the appropriate risk set, all researchers or only those who explicitly knew of a relevant patent.

18. This number is not reported to have increased significantly since the *Madey v. Duke* decision, nor does it differ significantly between scientists that had been alerted by their institutions to check for patents compared to those that did not receive such instruction.

19. In the area of gene patents covering a diagnostic test, there are more instances of patent assertions that impede research (Cho et al. 2003; Merz et al. 2002). For example, Merz et al. (2002) find that 30 percent of clinical labs report not developing or abandoning testing for the hemochromatosis gene (HFE) after the patent was issued. Cho et al. (2003) find that 25 percent of labs had abandoned one or more genetic tests due to patents, with Myriad's patents among the most frequently mentioned. This activity is, on one level, a competing commercial activity, and, hence, it is not surprising to find the patent owner asserting his rights. To the extent, however, that clinical research is intimately integrated with diagnostic testing, especially in the U.S. funding system, demands by patent owners to exclusive rights to conduct tests could affect the progress of science in these areas (Cho et al. 2003). Furthermore, the potential for problems of access may be diminishing due to a declining number of patents granted on these technologies in the last few years (especially in Europe and perhaps in Japan). Part of this decline may be due to firms recognizing that the high cost of acquiring large numbers of these patents may not be justified (Hopkins et al. 2007).

20. Murray and Stern (2005) based their analysis on a sample of "patent-paper" pairs based on publications in *Nature Biotech*, which tends to be more downstream in its orientation. More generally, the causes and implications of this relationship between patents and citations are, however, unclear. In particular, is this drop in citations a result of a change in research practices or simply of citation practices (i.e., an unwillingness to announce infringement in print)? Even if it is the former, does this simply reflect the change in incentives, leading researchers (especially industry researchers) to redirect their efforts into less-encumbered research areas?

21. The relatively small number of these gene patents that have been issued in Europe and Japan suggests that "going offshore" may be a relatively straightforward solution for global pharmaceutical firms (Hopkins et al. 2007).

22. For example, Human Genome Sciences (HGS) has a key patent related to the chemokine (C-C motif) receptor 5 (CCR5), which is an important research tool for studying HIV infection. However, the relation between this patented receptor and HIV infection was discovered by NIH researchers, who were using the patent without a license. HGS's reaction to this infringement is telling. Rather than sue for infringement, the firm welcomed this unlicensed use of its technology, which made the patent substantially more valuable. And the firm's owner declared he would welcome additional research by university and government researchers and would even provide necessary research tools (Marshall 2000).

23. The case of the OncoMouse is illustrative. Murray (2006) describes this as a very small, close community that was morally outraged by the licensing terms that DuPont (and by extension, Leder and Harvard) were demanding for access to this technology. Interestingly, this is not a case of withholding access (because anyone could use the technology if they would agree to the terms, the most onerous of which was a reach through claim on future discoveries as well as publication review and requirements to give regular progress reports to DuPont). Rather, it was the violation of the mouse community's norms of free exchange of materials that seems to have led to loud protests and to NIH stepping in to renegotiate access terms. And it may have been DuPont's outsider status that led them to ignore these reciprocity norms and aggressively assert their patent rights.

24. For firms, either an anticommons failure or blocked or expensive access to some foundational patented discovery requires not that any one strategy for overcoming such problems be unavailable, but that the entire suite of working solutions be ineffective.

25. If the input is difficult to duplicate on your own, the owner of that input may be able to readily exclude others from using their research input. Indeed, as noted in the following, Walsh et al. (2007) found that it was predominantly the lack of capabilities or the time and cost involved—more than the existence of a patent on a desired material—that leads scientists to make requests for materials rather than duplicating the materials themselves.

26. There is the possibility that these figures could understate the incidence of incomplete or delayed publication due to social desirability response bias.

27. While possibly hurting the researchers who make such requests, denial of requests does not necessarily hurt society. For example, if such denials lead to less duplicative research and a greater variety of projects undertaken, society may be better off as a consequence (cf. Walsh, Arora, and Cohen 2003a).

28. As discussed in the following, Furman and Stern (2005) also suggest that such provision can also confer reputational benefits.

29. Walsh and Hong (2003) and Blumenthal et al. (2006) also find that scientific competition is associated with excluding others from using materials, data, or ongoing research results.

30. Walsh and Hong (2003) find a similar result that patents are not associated with greater secrecy about ongoing research.

31. Priority-driven attention to secrecy on the part of academics is ironically reinforced by the practices of major scientific journals as well, including *Science* and *Nature*, which strictly regulate what may or may not be disclosed from an accepted manuscript prior to publication and how that disclosure might occur.

32. The extraordinary openness associated with the Human Genome Project (daily publishing of sequence data) was the result of a contentious negotiation within the community, with many arguing that those conducting the research, even though it was publicly funded, should have a period of exclusivity over the data (Sulston and Ferry 2002).

33. Indeed, Robert Cook-Deegan (personal communication) suggests that such disapproval is institutionalized in the NIH study sections that evaluate grant proposals in that a reputation for not providing data to other scholars can apparently, under some circumstances, affect the award of grants or the terms under which a grant is awarded.

34. As noted in the preceding, Walsh et al. (2007) observed that, for similar samples of academic genomics researchers, noncompliance appears to have grown from about 10 percent of requests in the 1997 to 1999 period (Campbell et al. 2002) to 18 percent in the 2003 to 2004 period. At the same time, NIH constant-dollar obligations for academic research more than doubled, jumping from \$6.6 billion dollars (denominated in constant 2000 dollars) in 1997 to \$13.5 billion in 2003 (National Science Board 2006).

35. For example, if, in certain fields, NIH grants had become sufficiently plentiful and widely distributed, then researchers may actually have perceived a diminution in competition for them. Of course, NIH guidelines regarding the sharing of data and materials, discussed in the following, could also dampen the incidence of exclusionary practices.

36. When recommending that scientists provide unrestricted access to data and materials associated with published results, the National Academy of Sciences (2003) recognized the importance of considering the effect of such policies on scientists' incentives when they took the unusual step of providing a minority report, arguing that it was appropriate for authors to withhold research inputs in order to ensure that the author can individually appropriate the scientific and commercial potential in his or her discoveries. This minority report highlights the legitimacy within the scientific community of some forms of restricted access and emphasizes the complexity of balancing the norms of sharing with the need to provide incentives.

37. The case of the Alliance for Cell Signaling (AfCS) is illustrative. This project is attempting to map all of the cell signal pathways and provide open access to results, even before publication in journals (Abbot 2002). To accomplish this, the AfCS has hired a team of researchers to conduct the analyses and post the results. Project members are not allowed to submit papers to journals until at least one month after posting the data for public use. We wonder if such hired-hand research is sufficient incentive for an academically ambitious young scholar. Or, to put it differently, would a premier academic scientist recommend this position to his or her most promising students (Cohen 2005; cf. Rai 2005)?

38. See Cohen and Sauermann (2007) for a discussion of the importance of considering intrinsic incentives for understanding individual researcher performance.

39. This observation raises the possibility that scientists are acting irrationally when they withhold in order to ensure greater reputational benefits. However, this possibility must be tempered with the understanding that both commercial and reputational benefits, especially in the short term, might be better served by closely controlling distribution of one's research results.

# References

Abbot, A. 2002. Into unknown territory. Nature 420 (6916): 600-601.

Allison, P. D., and J. A. Stewart. 1974. Productivity differences among scientists: Evidence for accumulative advantage. *American Sociological Review* 39:596–606.

Andrews, L., J. Paradise, T. Holbrook, and D. Bochneak. 2006. When patents threaten science. *Science* 314:1395–96.

Association of University Technology Managers (AUTM). 2000. AUTM Licensing Survey. Norwalk, CT: AUTM.

Bekelman, J. E., Y. Li, and C. P. Gross. 2003. Scope and impact of financial conflicts of interest in biomedical research. *Journal of the American Medical Association* 289:454–65.

Berkovitz, J., and M. P. Feldman. 2006. Entrepreneurial universities and technology transfer: A conceptual framework for understanding knowledge-based economic development. *Journal of Technology Transfer* 31:175–88.

Biagioli, M. 2006. Galileo's instruments of credit: Telescopes, images, secrecy. Chicago: University of Chicago Press.

Blumenthal, D., E. G. Campbell, M. S. Anderson, N. Causino, and K. S. Louis. 1997. Withholding research results in academic life science: Evidence from a national survey of faculty. *Journal of the American Medical Association* 277:1224–28.

Blumenthal, D., E. G. Campbell, M. Gokhale, R. Yucel, B. Clarridge, S. Hilgartner, and N. A. Holtzman. 2006. Data withholding in genetics and the other life sciences: Prevalence and predictors. *Academic Medicine* 81:137–45.

Campbell, E. G., B. R. Clarridge, M. Gokhale, L. Birenbaum, S. Hilgartner, N. A. Holtzman, and D. Blumenthal. 2002. Data withholding in academic genetics. *Journal of the American Medical Association* 287:473–80.

Cho, M. K., S. Illangasekare, M. A. Weaver, D. G. B. Leonard, and J. F. Merz. 2003. Effects of gene patents and licenses on the provision of clinical genetic testing services. *Journal of Molecular Diagnostics* 5:3–8.

Cohen, W. M. 2005. Does open source have legs? In *Intellectual property rights in frontier industries: Software and biotechnology*, ed. R. W. Hahn, 159–75. Washington, DC: AEI-Brookings Joint Center for Regulatory Studies.

Cohen, W. M., R. Florida, and R. Goe. 1994. University-industry research centers in the United States. Pittsburgh: Carnegie Mellon University

Cohen, W. M., R. Florida, L. Randazzese, and J. Walsh. 1998. Industry and the academy: Uneasy partners in the cause of technological advance. In *The future of the research university*, ed. R. Noll, 171–99. Washington, DC: Brookings Institute.

Cohen, W. M., R. R. Nelson, and J. P. Walsh. 2000. Protecting their intellectual assets: Appropriability conditions and why U.S. manufacturing firms patent (or not). NBER Working Paper no. 7552. Cambridge, MA: National Bureau of Economic Research, February.

Cohen, W. M., and H. Sauermann. 2007. Schumpeter's prophecy and individual incentives as a driver of innovation. In *Perspectives on innovation*, ed. F. Malerba and S. Brusoni, 73–104. Cambridge, UK: Cambridge University Press.

Cole, J. R., and S. Cole. 1972. The Ortega hypothesis. Science 178:368-75.

------. 1973. Social stratification in science. Chicago: University of Chicago Press.

Dasgupta, P., and P. A. David. 1987. Information disclosure and the economics of science and tech. In *Arrow and the ascent of modern economics theory*, ed. G. Feiwel, 519–42. New York: New York University Press.

------. 1994. Toward a new economics of science. Research Policy 23:487-521.

Dasgupta, P., and E. Maskin. 1987. The simple economics of research portfolios. *Economic Journal* 97:581–95.

Ducor, P. 2000. Coauthorship and coinventorship. Science 289:873-75.

Eisenberg, R. S. 1987. Proprietary rights and the norms of science in biotechnology research. *Yale Law Journal* 97:177–231.

------. 2003. Patent swords and shields. Science 299:1018–19.

Eisenberg, R. S., and A. K. Rai. 2006. Harnessing and sharing the benefits of statesponsored research: intellectual property rights and data sharing in California's stem cell initiative. *Berkeley Technology Law Journal* 32:1188–1214.

Evenson, R. E., and Y. Kishlev. 1976. A stochastic model of applied research. *Journal of Political Economy* 84:265–81.

Fox, M. F. 1994. Scientific misconduct and editorial and peer review processes. *Journal of Higher Education* 65:298–309.

Furman, Jeffrey L., and Scott Stern. 2006. Climbing atop the shoulders of giants: The impact of institutions on cumulative research. NBER Working Paper no. W12523. National Bureau of Economic Research, Cambridge.

Hagstrom, W. O. 1965. The scientific community. New York: Basic Books.

------. 1974. Competition in Science. American Sociological Review 39:1-18.

Heller, M. A., and R. S. Eisenberg. 1998. Can patents deter innovation? The anticommons in biomedical research. *Science* 280:698-701.

Henry, M. R., M. K. Cho, M. A. Weaver, and J. F. Merz. 2002. DNA patenting and licensing. *Science* 297:1279.

Hopkins, M. M., S. Mahdi, P. Patel, and S. M. Thomas. 2007. DNA patenting: The end of an era? *Nature Biotechnology* 25:185–87.

Jensen, K., and F. Murray. 2005. Intellectual property landscape of the human genome. *Science* 310:239–40.

Kieff, F. Scott. 2001. Property rights and property rules for commercializing inventions. *Minnesota Law Review* 85:697–754.

Kolata, G. 1987. Yb or not Yb? That is the question. Science 236:663-64.

Levin, R. C., A. K. Klevorick, R. R. Nelson, and S. G. Winter. 1987. Appropriating the returns from industrial research and development. *Brookings Papers on Economic Activity*, Issue no. 3:783–831.

Marshall, E. 2000. Patent on HIV receptor provokes an outcry. Science 287:1375-77.

Merges, R. P., and R. R. Nelson. 1990. On the complex economics of patent scope. Columbia Law Review 90:839–916.

Merton, R. K. 1957. Priorities in scientific discovery. American Sociological Review 22:635-59.

——. 1968. The Matthew Effect in Science. *Science* 159:56–63.

Merz, J. F., A. G. Kriss, D. G. B. Leonard, and M. K. Cho. 2002. Diagnostic testing fails the test. *Nature* 415:577–79.

Mowery, D. C., R. R. Nelson, B. N. Sampat, and A. A. Ziedonis. 2004. *Ivory tower and industrial innovation: University-industry technology transfer before and after the Bayh-Dole Act.* Palo Alto, CA: Stanford University Press.

Murray, F. 2006. The Oncomouse that roared: Resistance and accommodation to patenting in academic science. Massachusetts Institute of Technology. Mimeograph.

Murray, F., and S. Stern. 2005. Do formal intellectual property rights hinder the free flow of scientific knowledge: An empirical test of the anti-commons hypothesis. NBER Working Paper no. 11465. Cambridge, MA: National Bureau of Economic Research, July.

Nagaoka, S. 2006. An empirical analysis of patenting and licensing practices of research tools from three perspectives. Paper presented at OECD conference, Research Use of Patented Inventions, Madrid, Spain.

National Institutes of Health, Department of Health and Human Services. 1999. Principles and guidelines for recipients of NIH research grants and contracts on obtaining and disseminating biomedical research resources: Final notice. *Federal Register* 64 (246): 72090–96.

National Research Council. 1997. Intellectual property rights and research tools in molecular biology. Washington, DC: National Academies Press.

———. 2003. Sharing publication-related data and materials: Responsibilities of authorship in the life sciences. Washington, DC: National Academies Press.

-------. 2005. Patenting and licensing of genomic and proteomic innovations. Washington, DC: National Academies Press.

National Science Board. 2006. Science and engineering indicators. Washington, DC: GPO.

Nelson, R. R. 1982. The role of knowledge in R&D efficiency. *Quarterly Journal of Economics* 97:453–70.

-------. 2006. Reflections on "The simple economics of basic scientific research": Looking back and looking forward. *Industrial and Corporate Change* 15:903–17.

Nicol, D., and J. Nielsen. 2003. Patents and medical biotechnology: An empirical analysis of issues facing the Australian industry. Centre for Law and Genetics Occasional Paper no. 6. Hobart, Australia: University of Tasmania.

Owen-Smith, J. 2003. From separate systems to a hybrid order: Accumulative advantage across public and private science at research one universities. *Research Policy* 32:1081–1104.

Pressman, L., R. Burgess, R. M. Cook-Deegan, S. J. McCormack, I. Nami-Wolk, M. Soucy, and L. Walters. 2006. The licensing of DNA patents by US academic institutions: An empirical survey. *Nature Biotechnology* 24:31–39.

Rai, A. 2005. "Open and Collaborative" research: A new model for biomedicine. In *Intellectual property rights in frontier industries: Software and biotechnology*, ed. R. W. Hahn, 131–58. Washington, DC: AEI-Brookings Joint Center for Regulatory Studies.

Sampat, B. N. 2004. Genomic patenting by academic researchers: Bad for science? Paper presented at the Conference on Academic Entrepreneurship, Roundtable of Engineering Entrepreneurship Research, Atlanta, GA: Georgia Institute of Technology.

Scotchmer, S. 1991. Standing on the shoulders of giants: Cumulative research and the patent law. *Journal of Economic Perspectives* 5:29–41.

Shapiro, C. 2000. Navigating the patent thicket: Cross licenses, patent pools, and standardsetting. In *Innovation policy and the economy*, ed. A. Jaffe, J. Lerner, and S. Stern, 119–50. Cambridge, MA: MIT Press.

Stephan, P. E. 1996. The economics of science. Journal of Economic Literature 34:1199–1235.

Stephan, P. E., and S. G. Levin. 1996. Property rights and entrepreneurship in science. *Small Business Economics* 8:177–88.

Straus, J. 2002. Genetic inventions and patents: A German empirical study. Paper presented at BMBF and OECD workshop, Genetic Inventions, Intellectual Property Rights, and Licensing Practices. Berlin, Germany.

Sulston, J., and G. Ferry. 2002. *The common thread*. Washington, DC: National Academies Press.

Walsh, J. P., A. Arora, and W. M. Cohen. 2003a. The patenting and licensing of research tools and biomedical innovation. In *Patents in the knowledge-based economy*, ed. W. M. Cohen and S. Merrill, 285–340. Washington, DC: National Academies Press.

-------. 2003b. Working through the patent problem. *Science* 299:1020.

Walsh, J. P., C. Cho, and W. M. Cohen. 2005. The view from the bench: Patents, material transfers and biomedical research. *Science* 309:2002–2003.

Walsh, J. P., W. M. Cohen, and C. Cho. 2007. Where excludability matters: Material versus intellectual property in academic biomedical research. *Research Policy* 36:1184–1203.

Walsh, J. P., and W. Hong. 2003. Secrecy is increasing in step with competition. *Nature* 422:801–2.

Walsh, J. P., H.-I. Huang, K. Hasegawa, K. Motohashi, T. Yamagata, and M. Ueno. 2007. Research tool access in the age of the IP Society: Results from a survey of Japanese scientists. In *Research tools and academic research: An International symposium.* Tokyo, Japan.

Walsh, J. P., M. Jiang, and W. M. Cohen. 2007. Publication in the entrepreneurial university. Paper presented at the American Sociological Association annual meeting, August 12, 2007, New York.

Zamiska, N. 2006. How academic flap hurt world effort on Chinese bird flu. Wall Street Journal, A1.

Zucker, L. G., and M. R. Darby. 1996. Star scientists and institutional transformation: Patterns of invention and innovation in the formation of the biotechnology industry. *Proceedings of the National Academy of Sciences* 93:12709–16.