EXHIBIT 6

View from the Bench: Patents and Material Transfers

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Scholars have argued that the growing number of patents on research inputs may now impede upstream, noncommercial research by creating an "anticommons" in which rights holders may impose excessive transaction costs or make the acquisition of licenses and other rights too burdensome to permit the pursuit of scientifically and socially worthwhile research (*1*, *2*). Alternatively, owners of the rights over key upstream discoveries may restrict follow-on research through the exercise of exclusivity (*3*, *4*). The prospect of financial gain from upstream research has raised the further concern that academics are becoming more reluctant to share information, findings, or research materials (*5*, *6*). In 2003, a small-sample interview study suggested that, despite numerous patents on upstream discoveries, academic researchers have accessed knowledge without the anticipated frictions (*7*). Receiving material requested from other researchers could, however, prove problematic (*8*, *9*).

The *Madey* v. *Duke* decision of 2002 raised anew the question of the impact of research tool patents on biomedical research by clarifying that there was no general research exemption shielding academic researchers from infringement liability (*10*). This very visible decision and continuing concerns over the impact of research tool patents on academic science prompted our current study.

We report findings from a survey of 414 biomedical researchers in universities, government, and nonprofit institutions (*11*). In this group of academic, biomedical researchers, 19% currently receive industry funding for their research (representing 4% of their research budget); 22% applied for a patent in the past two years, with an average of 0.19 patent applications per year per respondent; 35% have some business activity [i.e., have participated in negotiations over rights to their inventions, have begun developing a business plan, had a startup, had a process or product in the market, or had licensing income].

LOGISTIC REGRESSION PREDICTING RECEIVING REQUESTED MATERIAL

Variable	Estimate
Scientific competition	–0.058 ± 0.029*
Academic supplier	0.007 ± 0.005
MTA	0.012 ± 0.004**
Patented	0.005 ± 0.007
Patent status unknown	–0.004 ± 0.004
Drug	–2.217 ± 0.683**

Values ± SEM. *$P < 0.05$; **$P < 0.01$.

Although common, patents in this field are not typically used to restrict access to the knowledge that biomedical scientists require. To begin with, few academic bench scientists currently pay much attention to others' patents. Only 5% (18 out of 379) regularly check for patents on knowledge inputs related to their research. Only 2% (i.e., 8) have begun checking for patents in the 2 years since *Madey* v. *Duke*, which suggests little impact of the decision. Five percent had been made aware of intellectual property (IP) relevant to their research through a notification letter sent either to them or their institution, which differs little from the 3% who reported having received such notification 5 years ago (prior to the *Madey* v. *Duke* decision). Furthermore, although 22% of respondents report being notified by their institutions to respect patent rights (versus 15%, 5 years ago), such notification did not appreciably affect the likelihood of checking for patents—5.9% of those receiving such instruction checked for patents versus 4.5% of those not receiving instruction.

Only 32 out of 381 respondents (8%) believed they conducted research in the prior 2 years using information or knowledge covered by someone else's patent. However, even for the few who were aware of others' patents, those third-party patents did not have a large impact on their research. Of the 32 respondents who were aware of relevant IP, four reported changing their research approach and five delayed completion of an experiment by more than 1 month. No one reported abandoning a line of research. Thus, of 381 academic scientists, even including the 10% who claimed to be doing drug development or related downstream work, none were stopped by the existence of third-party patents, and even modifications or delays were rare, each affecting around 1% of our sample. In addition, 22 of the 23 respondents to our question about costs reported that there was no fee for the patented technology, and the 23rd respondent said the fee was in the range of $1 to $100. Thus, for the time being, access to patents on knowledge inputs rarely imposes a significant burden on academic biomedical research.

Our research thus suggests that "law on the books" need not be the same as "law in action" if the law on the books contravenes a community's norms and interests (*9*, *12*). Although the new survey did not explicitly ask respondents their opinions about a research exemption, our results suggest that infringement remains of only slight concern. In contrast, research on clinical diagnostic testing (*13*, *14*) suggests that when the research is itself also a commercial activity, patent holders are more likely to assert and clinical researchers more likely to abandon infringing activities.

In addition to examining access to others' intellectual property, we consider the extent to which scientists can access the tangible research materials and data created by other labs, highlighted as another source of friction that may be impeding biomedical innovation (*5*, *8*, *15*). Indeed, concerns about increasing noncompliance with material transfer requests have prompted the National Institutes of Health to issue guidelines designed to encourage the exchange of materials created with federal funding (*16*).

About 75% of our academic respondents made at least one request for a material in the past 2 years. On average, academics made about seven requests for materials to other academics and two requests to industry labs in the past 2 years. However, 19% of our respondents report that their most recent request for a material was denied (*17*). Moreover, noncompliance with such requests appears to be growing (see supporting online text). Campbell and colleagues (*5*) reported that, among genomics researchers, about 10% of requests were denied in the 3 years, 1997–99. For the

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genomics researchers in our sample, the denial rate for 2003–04 was 18% (95% confidence interval, ±3.7%).

Over a 1-year period, an average of one in six respondents reported that delays in receiving materials from other academics caused at least one project they were working on to suffer a greater than 1-month delay, a substantial delay in a fast-moving research field. Noncompliance by other academics with research input requests resulted in about 1 in 14 scientists abandoning at least one of their projects each year.

We conducted two regression analyses to probe the reasons for noncompliance (see supporting online text). The first examined whether the respondent's most recent request was satisfied (see table, p. 2002). Statistically significant predictors of noncompliance included a measure of scientific competition (i.e., the number of competing labs) and whether the requested material was itself a drug. The patent status of the requested material had no significant effect on noncompliance. A second analysis with other variables—particularly characteristics of the prospective supplier—examined predictors of the number of times the respondent failed to comply with requests (see table, this page). Here, the burden of compliance (i.e., number of requests per dollar of funding); scientific competition; and commercial orientation (i.e., whether the respondent has engaged in any of the business activities listed above) increase the likelihood of noncompliance. Finally, the number of respondent publications, indicative of respondent eminence or the opportunity cost of responding, also increases the likelihood of noncompliance.

In addition to these regressions, we also asked respondents directly why they denied requests. The major self-reported reasons for noncompliance included the cost and/or effort involved and protecting the ability to publish, with commercial incentives much less prominent (*5*, *18*). We find, however, the multivariate regression analysis to be more credible than the self-reported relationships for the following reasons: (i) it uses a more objective measure of commercial orientation, while controlling for the effects of other variables and (ii) it is less likely to be influenced by a "socially desirable response bias" that leads academics to subordinate less socially desirable incentives (e.g., commerce) compared with more desirable ones (e.g., intellectual challenge) (*19*).

We also considered costs and burdens associated with material transfer agreements (MTAs). Only 42% of requests required an MTA, and only 11% of requests for research inputs led to an MTA negotiation lasting more than 1 month. Moreover, in almost all cases, there was no immediate fee for the requested material. However, for 8% of research input requests, negotiating the MTA stopped the research for more than 1 month. Although MTAs do not commonly entail delays or impose fees, they frequently come with conditions. MTAs, especially from industry suppliers, often include demands for reach-through rights of some form. Of executed MTAs, 29% had reach-through claims, and 16% provided for royalties. Twenty-six percent of MTAs imposed publication restrictions. Requests for drugs were the most likely to yield such a restriction, with 70% of such agreements including some restriction on publication of the research results using the transferred drug.

As a case study, we also collected data from an additional 93 academic scientists who are conducting research on one of three signaling proteins (CTLA-4, EGF, and NF-κB) that are patent-intensive research areas with enormous commercial interest, involving large pharmaceutical firms, small biotechnology firms, and universities. These are the very conditions where issues of access to IP should be evident. Although the incidence of adverse consequences due to restricted access to IP was more manifest here than in the random sample, it was still infrequent (only 3% of respondents reported stopping a project in the past 2 years because of a patent). On the other hand, access to materials was even more problematic in these areas than in the random sample (*18*). For example, 30% of researchers in these fields did not receive their last requested material.

Our results offer little empirical basis for claims that restricted access to IP is currently impeding biomedical research, but there is evidence that access to material research inputs is restricted more often, and individual research projects can suffer as a consequence. To the extent that any redirection of a scientist's research effort or reallocation across investigators because of denied access impedes scientific progress, this is cause for concern. In contrast, if such redirection reduces duplicative research or increases the variety of projects pursued, social welfare may even increase (*20*, *21*). In addition, it is not clear whether patent policy contributes to restricted access to materials, although the commercial activities fostered by patent policy do seem to restrict sharing, as do the burden of producing the materials and scientific competition.

Scientific progress in biomedicine may be well served by a study of the welfare impacts of restrictions on material transfers, and, if warranted, greater diligence in the monitoring and enforcement of the applicable NIH guidelines.

NEGATIVE BINOMIAL REGRESSION PREDICTING NUMBER OF REFUSALS TO SEND REQUESTED MATERIAL

Variable	Estimate
Commercial orientation	0.010 ± 0.004*
Scientific competition	0.078 ± 0.040*
Publications	0.075 ± 0.037*
Request burden	0.038 ± 0.019*
Budget	0.008 ± 0.042
Industry funding	0.006 ± 0.005
Drug discovery	0.000 ± 0.007
Male	–0.008 ± 0.004†

Values ± SEM. *$P < 0.05$; †$P < 0.10$.

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Supporting Online Material

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