POLICY FORUM: GENETICS

DNA Patenting and Licensing

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Patenting provides important incentives for research and development leading to advances in genetic tests and treatments. Nonetheless, there is concern that patents on gene sequences and their applications threaten research and impede availability of new medical innovations (*1*). Because little is known about patenting and licensing of genetic inventions, we conducted a telephone interview study of firms and nonprofit institutions. We sampled U.S. institutions holding three or more U.S. patents issued since 1990 in U.S. patent class 435/6 (molecular biology, involving nucleic acid) and containing the term "Seq. I. D." in the claims (*2*), identifying 48 firms and 62 nonprofit institutions. We selected the 10 companies and 10 nonprofits holding the greatest numbers of patents and a random sample of 22 companies and 22 nonprofits from the remainder, and we included one institute in the National Institutes of Health (NIH). We oversampled firms because of a concern that company executives would be less willing to participate.

Representatives from 19 of the 32 companies and 27 of the 33 nonprofit institutions participated ($\chi^2 = 3.96$, $P = 0.047$). Our final response rates were 19/48 firms (40%) and 27/62 (44%) nonprofits. There were no significant differences in participation rates between the 10 firms and 10 nonprofits holding the most patents and the remainder of the samples. Quantitative estimates regarding invention disclosures, patents, and licenses were provided by 33 respondents (72%).

Nonprofits appeared to generate more genetic discoveries than firms, consistent with earlier findings by Thomas *et al.* (*3*, *4*). Nonprofits, however, were less likely than firms to file patent applications. With one extreme outlier excluded, companies reported that they had received an average of 37 invention disclosures (range = 0 to 100) and had filed an average of 32 patent applications (86%) in the prior 2 years. Nonprofits received an average of 163 disclosures (range = 1 to 600) and filed an average of 24 applications (15%). This is consistent with a study indicating that from 1986 to 1990, Stanford, Columbia, and the University of California system had patent filing rates between 15 and 17% (*5*).

Responses suggest that differences in filing rates are attributable to divergent goals of patenting. Firms are more likely to adopt broad patenting strategies to build portfolios that have market value, that can be used to block competitors, or that defend the firm's ability to work in a particular field. Nonprofits were more likely to assess the market value of an invention before filing. Several respondents from nonprofits reported filing provisional patent applications to retain rights to an invention while exploring whether there was a market for the invention and a potential exclusive licensee willing to pay patenting costs. No nonprofits reported patenting for defensive reasons.

Regarding licensing, companies were nearly as likely to have granted licenses to genetic patents (42% of patents) as nonprofit institutions (51%). However, firms reported that an average of 27% of all licenses granted were exclusive, while nonprofits reported an average of 68% (Kolmogorov-Smirnov test for equality of distributions $P = 0.001$). This is consistent with an earlier study documenting the use of exclusive licensing by nonprofits for a small sample of genetic diagnostics patents (*6*). For comparison, a 1999 survey of academic technology transfer executives showed that roughly 50% of licenses granted by universities were exclusive (*7*), while only about 22% of licenses granted by the NIH in 2001, and less than 16% of active licenses managed by the NIH Office of Technology Transfer, are exclusive (*8*). Thus, the use of exclusive licenses of sequence-based inventions by nonprofit institutions appears to exceed that of firms for the same technology, as well as the use by universities and the NIH for all technologies.

The differences in licensing practices may reflect several phenomena: (i) Nonprofits may prefer exclusive licensing in order to minimize licensing expenses and to maximize short-term revenues. (ii) For federally funded research, nonprofits must give licensing preference to small firms, under the 1980 Bayh-Dole Act (*9*), and small, particularly start-up, businesses may depend on exclusive rights to establish a competitive advantage and to ensure access to high-risk capital. (iii) Firms may be less likely to license targets for downstream development (*10*). (iv) Nonprofit institutions (primarily universities) may be generating different types of inventions than companies. For example, universities may generate more basic genetic discoveries useful primarily as targets for development of therapies. Numerous respondents noted a difference between research tools and research targets, stating that tools useful to performing research should be made broadly available [like the Cohen-Boyer patent on recombinant DNA (*11*)], while exclusive licensing may be necessary to promote investment in downstream development.

These results do not mean that university inventions are likely to be tied up by exclusive rights. Only a small fraction of university inventions are patented; most would be freely available upon publication. In contrast, nearly all commercial inventions are patented, and only a minority (31%) of these were reported to be licensed to others on nonexclusive terms.

The incentives for commercialization of invention provided by the Bayh-Dole Act seem to result in a focus by nonprofit recipients of federal research support on short-term profits and high-risk exclusive licensing. Further study is needed to examine differences between university and company research and patent portfolios; whether frequent use of exclusive licenses by universities is justified by the need to stimulate investment in downstream product development or whether exclusive licensing has simply become a default method for efficiently transferring technology; whether the body of university invention that is not being patented should be patented, and whether it is being disseminated to the relevant communities; and on the long-term efficiency of exclusive licensing on product development and the effects, if any, on competition.

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