

# **Patents, Spillovers, and Competition in Biotechnology**

David H. Austin

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Resources for the Future  
1616 P Street, NW  
Washington, D.C. 20036  
Telephone: 202-328-5000  
Fax: 202-939-3460  
Internet: <http://www.rff.org>

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## Abstract

I perform an event study on 600+ patents awarded primarily to 20 leading biotechnology firms and find significant changes in market values at the time of the awards. Adjusting for partial anticipation of events, I estimate that core technology patents in highly contested research areas are expected to generate between \$13 and \$21 million of economic value. They also generate spillover benefits for the patentee's rivals—presumably including knowledge transfers—valued at \$3 to \$6 million per firm. Awardees may appropriate only half of private benefits, although I observe negative spillovers for some high-profile awards. Most patents have no significant market impact.

**Key Words:** innovation, patent value, spillover, competition, event study

**JEL Classification Numbers:** G14, O31, O34, L65

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# Patents, Spillovers, and Competition in Biotechnology

David H. Austin\*

## 1. Introduction

This paper analyzes stock market effects of individual biotechnology patent awards. Incentives for firms to innovate depend partly on the potential value of the resulting patents and their impact on rival firms. Patents also convey information about the abilities and prospects of the firms, and they define intellectual property rights. Valued for all of these reasons, patents have been an important way for biotechnology firms to raise equity capital and venture capital.<sup>1</sup> However, by patenting, firms risk generating knowledge spillovers to rival firms. This paper presents the first empirical measurement of the economic importance of patents for patentees and their rivals.

Earlier studies have correlated patents with changes in the market values of firms by using annual counts of successful patent applications as a proxy for the quantity of innovation in the filing year. Such data are not suitable for my analysis, as the aggregation obscures technological details that my study design requires. Because firms face different rivals for different patents, those data also do not permit the examination of rival effects.

This study exploits in new ways the rich information contained in patent documents. In addition to disaggregating the data, which allows me to explain patent value as a function of content, I also analyze patent grants rather than applications. There is an obvious timing difference in that it has taken an average of almost three years to process patent applications in biotechnology.<sup>2</sup> I use patent grants primarily because the market responds to them. They are public information, widely and quickly disseminated.

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<sup>1</sup> It often takes years for biotechnology firms to develop products that will generate consistent revenue streams. For them, patents are an important way of signaling their prospects and attracting investment capital (Lerner 1995a).

<sup>2</sup> The average lag is two years; the lag was nine months in my sample.

Biotechnology is an ideal field for this analysis. New drug research is highly competitive, and the firms place great importance on their patents; a priori it is not clear whether the patents should help or harm rival firms. Trajtenberg (1990) suggests that individual patents play an important role in the dynamics of industry sectors: “The whys and hows of cross-sectional results regarding the structural characteristics of mature sectors ... cannot really be understood except in light of how those sectors evolved into their observed equilibrium; ... [disaggregated] patent data ... seem to be particularly well suited to trace that process.”<sup>3</sup> This observation is particularly apt for biotechnology, where firms have relied heavily on patent protection and patents seem to have played an important role in its evolving market structure.

Like *Drosophila melanogaster*—the fecund fruit fly that speeds genetic research—biotechnology firms are prolific innovators. This study is organized around a mere 20 leading firms, yet they won nearly 600 patents in the first decade of commercial activity. In the early 1990s, seven of them dominated national rankings of research intensity.<sup>4</sup> Although this sample does not represent patents as a whole, the market forces and cross-firm effects that it illustrates may also exist in other industries.

I find that the market values of firms rise significantly when patenting occurs in contested research areas, especially where several firms have had successful clinical trials. Core technology patents in any of these areas appear to be valued between \$13 and \$21 million. Most of these patents are also viewed as benefiting rival firms. Knowledge spillovers must flow most readily between firms doing similar research, and here I show that these individual patents may be a direct pathway, generating economic values of roughly \$3 to \$6 million per rival firm. Some high-profile patents are viewed as harmful to rival firms and may have much higher own valuations. Most of the other patents in the sample do not generate significant market effects.

The paper is organized as follows: Section II reviews the relevant economics literature. Section III describes my theoretical model, which motivates the empirical analysis described in Section IV. I discuss sample selection and data in Section V, and present the regression results in

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<sup>3</sup> Trajtenberg (1990), p. 215.

<sup>4</sup> Five of the top ten American firms in 1991 R&D spending per employee were biotechnology companies—Biogen (1), Genentech (2), Genetics Institute (4), Amgen (6), and Chiron (9)—as were six of the top seven companies in 1991 for R&D-to-sales—Centocor (1), Chiron (2), Biogen (3), Genetics Institute (4), Genentech (5), Immunex (7). (*Business Week* 6/29/92, p.105). All of these firms are in my sample.

Section VI. In Section VII, I use these results in simulating the theoretical model and deriving implicit patent values. Section VIII offers concluding remarks.

## 2. Literature Review

The empirical literature contains several different approaches to analyzing patent data. Schankerman and Pakes (1986) and Lanjouw (1993) analyze European patent renewal fees in a cross-industry setting and estimate patent values over time. Lanjouw (1998) develops a dynamic, stochastic discrete choice model of optimal renewal decisions that recognizes that firms may need to protect patents from infringement. Lanjouw finds that, on average, the annual value of patent protection is roughly 10% of the associated R&D expenditures and, as in the two earlier studies, the distribution of patent values is highly skewed.

Renewal fee data are useful for distinguishing between high- and low-valued patents, and for estimating the time path of a patent's value. A patent will not be renewed if the fee exceeds its value. The fees, however, are very low relative to the values of important patents, so although their identities can be inferred from the renewals, their values cannot be estimated directly. Analysis of the U.S. data has not been possible because renewal fees were instituted only recently. See Lanjouw, Pakes, and Putnam (1996) for a detailed survey of these studies.

Several papers link individual patent characteristics to the private value of the patent. Lerner (1994) finds that the breadth of patent protection is associated positively with firm valuations in a set of privately held, venture-backed biotechnology firms.<sup>5</sup> Austin (1993) identifies a small, positive effect of patent breadth on the market values of a set of publicly traded biotechnology firms by using a similar measure of breadth.

Other studies have examined the relationship between the annual market returns of a firm and the total patent applications that eventually result in patents that the firm filed that year. Griliches (1981) finds that surprises in a firm's annual total are related positively to changes in its market-to-book value ratio and that "a successful patent is worth about \$200,000" (Griliches 1984). Because U.S. patent applications are not announced, these studies are inconclusive about whether patents or the underlying research or innovations are driving observed changes in firm

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<sup>5</sup> Lerner's patent-scope proxy is a function of the number of technological areas under which the patent is classified.

value.<sup>6</sup> For instance, Pakes (1985) argues that when a firm receives a patent it “indicates that events have occurred that increase the firm’s market value by \$810,000.” Griliches, Pakes, and Hall (1987) find a strong cross-sectional relationship between the annual patent applications of firms and changes in market value. They also find a weaker but significant relationship between year-to-year changes in successful patent applications and returns to equity. See Hall (1999) for a recent survey of this literature, a central conclusion of which is that patents are a proxy for R&D success, that they add information beyond measures of total R&D activity, and that this information has a positive market value.

Empirical research on the effects of patents on other firms has focused on R&D spillovers rather than market effects. Jaffe (1986) notes that a firm’s number of patents per dollar of R&D, and its returns to R&D, tend to be higher if it is “close” to other research firms in technology space. Megna and Klock (1993) find that patent stocks for 11 rival semiconductor firms have negative effects on the market-to-book value ratios for other firms, while their R&D expenditures have positive effects. Jaffe, Trajtenberg, and Henderson (1993) find geographically localized patterns to R&D spillovers, as measured by patent citations. Finally, Cockburn and Henderson (1994) find that R&D investment in the presence of rival firms is not winner-take-all. Rather, own research productivity is correlated positively with the research outcomes of rival firms. They interpret this finding as evidence for widespread R&D spillovers. Most of these studies are consistent with firms benefiting from the patents of rival firms, though there is also evidence that patent rights can impose costs on rival firms. Griliches (1990) contains a thorough survey of the earlier empirical literature on patent value.

### 3. Model

This section describes the general theoretical framework underlying my empirical analysis. I develop a model of stock market excess returns in which the prior expectations by investors about patentable research, and the odds of patenting by firms in the face of competition, are capitalized into the firms’ stock prices. I simulate the model that assumes a

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<sup>6</sup> The Japanese and European patent offices publish pending patent applications 18 months after the earliest filing worldwide. Because U.S. firms often file overseas for patents on significant innovations, the domestic stock markets may develop expectations about corresponding U.S. patents. Working papers in circulation may also yield clues. Applicants for U.S. patents have a year to file after a paper is circulated. Applications in Europe and Japan must precede publication of the paper, and the one-year anniversary of the earliest worldwide filing.

range of values for the unobservable priors and yields estimates of private patent value and spillover effects implicit in the excess returns.<sup>7</sup>

Consider  $N$  firms racing for a patent. If the identities of the firms are known, then investors' priors about each firm's likelihood of winning the patent, and about the value of that patent, are reflected in the firms' pre-patent stock prices.<sup>8</sup> Let  $p$  be the market's prior probability that a patent will issue,  $0 \leq p \leq 1$ .<sup>9</sup> If the research is not observed, or is believed not to be patentable, then  $p = 0$ . If a patent is anticipated, investors' symmetric priors that it will go to a particular firm equal  $1/N$ . Asymmetric expectations are also permitted.

Let a patent's expected present discounted value, on the day it issues, be  $V > 0$ , the net present value of the stream of rents from products embodying the innovation, plus any resulting revaluation of the firm's other assets. Some of them—especially intangible ones—may complement the innovation or be revalued as the patent updates the firm's quality signal. Rents are net of revenues in the absence of the patent.<sup>10</sup>

A new patent may raise or lower the values of the  $(N - 1)$  rival firms. Their values will decline if investors expected that the patent might be issued and if the expected own value share  $V/N$  dominated the expected net spillover benefits share  $C(N-1)/N$ ; that is, the net effect (benefits less costs) of losing times the odds of losing. A patent may impose both costs and benefits on rival firms and raise R&D costs by foreclosing research avenues, or induce infringement litigation, but the patent discloses knowledge that might complement the rivals' research. The sign of the rival effect is an empirical issue.

If investors' prior probabilities are symmetric with respect to the  $N$  firms, then as the patent is issued, each firm's market value will reflect patent expectations according to:

$$\text{Patent Premium} = p \cdot \left( V \cdot \left( \frac{1}{N} \right) - C \cdot \left( \frac{(N-1)}{N} \right) \right)$$

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<sup>7</sup> I use the term "spillover" to refer to any economic benefit accruing to another firm due to a patent and not limited to knowledge spillovers.

<sup>8</sup> Many biotech innovations are discoveries of genetic sequences for known proteins or of processes for synthesizing natural proteins, and thus may be anticipated to a degree. It is plausible that investors know who is racing because the information is published in *BioScan*.

<sup>9</sup> Because  $p$  is not observable, I ignore its possible time-dependency.

<sup>10</sup> Many biotech patents issue before FDA approval is won (or requested), and uncertainty about that process affects the valuations of those patents. Most biotechnology products are protected by a host of patents.



The premium reflects the expectation  $p$  that a patent will issue, times the patent's expected effect on each firm. Note that  $C < 0$  implies a *benefit* to the other firms.<sup>11</sup>

Once investors learn the outcome of the patent race, the winner and losers are revalued according to expressions (1) and (2) below. Unanticipated information creates excess returns, or differences between predicted and observed prices. For the patentee, these equal:

$$OWN\ EFFECT = V \cdot \left(1 - \left(\frac{p}{N}\right)\right) + C \cdot \left(\frac{p \cdot (N-1)}{N}\right) \quad (1)$$

The change in the patentee's market value consists of the reversal of the rival effect in  $C$  and the addition of the remaining patent value  $V$ , net of the portion already capitalized.<sup>12</sup>

The values of the losing firms will change according to:

$$RIVAL\ EFFECT = -V \cdot \left(\frac{p}{N}\right) - C \cdot \left(1 - \frac{p \cdot (N-1)}{N}\right) \quad (2)$$

The first term reflects a firm's failure to win the patent, and the loss of the market premium given it might win. The second term gives the expected cost of its rival's patent, net of the portion already capitalized. For unanticipated patents,  $p = 0$  and the excess returns are simply  $V$  for the patentee and  $C$  for each losing firm.

As  $N$  is the only observable parameter in the model in the simulations that assume values of  $p$  to solve the equations for  $V$  and  $C$  given the data.

If investors have (correct) asymmetric priors about the patentee, this model will understate  $V$  and  $C$ , which would be capitalized more fully than implied by the symmetric model. If investors correctly put extra weight  $1 < \alpha < N$  on the eventual patentee given that a patent will issue, priors for the other firms' collective chances of winning will drop to  $(N - \alpha)/N$ . Adding an asymmetric prior  $\alpha$ , the model becomes:

$$OWN\ EFFECT = V \cdot \left(1 - \frac{p\alpha}{N}\right) + C \cdot \left(\frac{p \cdot (N - \alpha)}{N}\right) \quad (1')$$

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<sup>11</sup> "C" is a mnemonic for the "cost" of losing a patent.

<sup>12</sup>  $V$  could be negative if the patent disappoints expectations of its probable scope or content.

$$RIVAL\ EFFECT = -Vp \cdot \left( \frac{N - \alpha}{N \cdot (N - 1)} \right) - C \cdot \left( 1 - p \cdot \left( 1 - \frac{(N - \alpha)}{N \cdot (N - 1)} \right) \right) \quad (2')$$

To solve for  $V$  and  $C$  in the asymmetric model,  $\alpha$  must be simulated along with  $p$ .

The asymmetric model applies to several research areas in the data. For instance, Genentech has dominated competitors in research on human growth hormone and tissue plasminogen activator, a treatment for heart attack and stroke. In simulations I subject  $\alpha$  and  $p$  to sensitivity analysis.

#### 4. Empirical Framework

These models suggest that excess returns depend on patent values, expected effects on rivals, the number of rivals, and the identity of the patentee (own or rival). I assume that values and rival effects depend on characteristics of the patents, and I have data on presence or absence of recombinant DNA (rDNA) content; breadth; the protein with which the patent is associated, if any,<sup>13</sup> and the number of firms active in the research field. I interact these characteristics with indicators of patentee identity relative to the firm being observed.

Excess returns take the following form:

$$EXCESS\ RETURN = F((rDNA, breadth, significance; protein; N) * (OWN; RIVAL; NEUTRAL))$$

The first three characteristics in this equation enter the model in interaction with the fourth, a “protein” indicator variable that controls for patents on some aspect of protein synthesis, including genetic sequences. Proteins researched by only one of the sampled firms are not captured by this variable, which picks up about 15% of the patents. The OWN, RIVAL, and NEUTRAL effects also refer only to these protein patents, as those relationships are defined in terms of the proteins. The own effects of all “nonprotein” patents are captured by the intercept term. I expect the positive own effect of a protein patent is greater than the effects of its other patents, which do not relate directly to products.

Slightly more than half the patents in the sample have rDNA content.<sup>14</sup> Others cover equipment, procedures, novel drug use, or nonrecombinant chemical discoveries. I hypothesize

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<sup>13</sup> Biotechnology drugs are based on proteins, or amino-acid sequences.

<sup>14</sup> See the Data section for definitions and sample statistics.

that own rDNA patents are more valuable because they involve core technologies. Their marginal effect on rival firms is indeterminate a priori; rDNA patents often include codified amino acid sequences that may facilitate knowledge spillovers.

The greater the scope or breadth of a patent, the more intellectual property it controls. I expect patent breadth to be associated positively with own returns and negatively with returns to rival firms.

The third variable controls for “significant” patents and related mean shifts in the dependent variable. This variable does not reflect any particular patent characteristic. The empirical literature shows that patent values are highly skewed, with very few high-value patents. I proxy for a significant patent by whether or not it was described in the *Wall Street Journal* (*WSJ*)<sup>15</sup> and expect the own *WSJ* effect to be positive. Many of these patents are major, blocking patents on gene sequences or production processes, and I expect their effect on rival firms to be negative.<sup>16</sup>

Finally,  $N$  is the number of competitors in each research area. As  $N$  increases, own effects should increase and rival effects should shrink in absolute value. This follows from the theoretical model.<sup>17</sup>

As implemented econometrically, the dependent variable is the excess return from the standard Capital Asset Pricing Model (CAPM), expressed in percentage terms.<sup>18</sup> The model assumes explicitly that patent value is independent of firm size. Firms have varying levels of resources for exploiting patents but can license them to the highest bidder. All else equal, a patent will affect more strongly the stock price of a more highly leveraged firm, but there are no

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<sup>15</sup> A referee has suggested that this variable may be endogenous with excess returns. In my sample, about one in four *WSJ* patents gave own, first-day excess returns above +2%, twice as frequently as with other protein patents, but negative or zero returns were just as likely among *WSJ* patents. I will not emphasize the *WSJ* results, treating them, with caveats, as a possible upper-bound on outlier valuations.

<sup>16</sup> See the appendix for a description of the *WSJ* patents.

<sup>17</sup> Differentiating (1) and (2) with respect to  $N$ , it is clear that the larger is  $N$ , the greater the surprise that a particular firm patents—meaning higher own excess returns—and the less of a surprise that other firms do *not* patent, minimizing those excess returns.

<sup>18</sup> Patent grants are announced immediately, and a three-day event window captures their full impact. Even before web browsers, same-day information about new patents could be retrieved electronically. To match the dependent variable I normalize the independent variables by pre-event firm value, logged to give a better fit and reduce heteroskedasticity (which is inversely proportional to firm size). Normalizing the intercept term merely inflates the other coefficients without changing the results.

significant cross-firm differences in bond-to-equity ratios here, because the firms did not use debt financing.

Thus, I estimate

$$R_{it} = \delta_0 + \sum_v \delta_v \cdot D_{vt} + u_{it} \quad t = 1, \dots, T, \quad (3)$$

where  $R_{it}$  is the firm  $i$  excess return from an event at time  $t$ , and the  $D_{vt}$  are the interaction dummies. The  $D_{vt}$  also include an indicator variable to control for events subsequent to joint venture or licensing agreements between erstwhile rivals;  $u_{it}$  is a mean zero random error, and  $\delta_0$  and  $\delta_v$  are parameters to be estimated.

The dependent variable  $R_{it}$  is the time  $t$  CAPM residual:

$$R_{it} \equiv (r_{it} - r_{ft}) - (\hat{\alpha}_{it} + \hat{\beta}_{it} (r_{mt} - r_{ft})), \quad (4)$$

$R_{it}$  is measured from one trading day prior to the event to two days after it.<sup>19</sup> I estimate  $\hat{\alpha}_{it}$  and  $\hat{\beta}_{it}$  by fitting the CAPM to 244 days of data ending the fifth trading day before the event;  $\hat{\beta}_{it}$  estimates the volatility of firm  $i$ 's stock relative to the S&P 500. Finally,  $r_{it}$  is the return on shares in firm  $i$  at time  $t$ ;  $r_{ft}$  is a risk-free rate of return (inflation-adjusted 30-day T-Bill rate); and  $r_{mt}$  is the return on the value-weighted Nasdaq index. The CAPM also includes a serially uncorrelated, mean zero random error term.

## 5. Data

The study design requires the identification of competing firms, which is a manageable task because the study involves only one industry. Biotechnology is a good subject because the firms patent fervently and defend their claims.<sup>20</sup> The results, though particular to biotechnology, suggest that patents are not anticipated highly, and that this type of event study can be repeated for other industries.

Among the 20 leading biotechnology firms in this study, there has been competition in at least 17 research areas from which every major biotechnology drug so far has originated. The 20

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<sup>19</sup> See Brown and Warner (1985). I use the Nasdaq composite index as the market measure, because all of the firms in the sample traded in that market. In the late 1980s, Genentech switched to the NYSE.

<sup>20</sup> There has been an extraordinary amount of patent litigation in biotechnology (Lerner 1995b).

firms were selected because, as of December 1988, they were the most highly valued, publicly traded firms.<sup>21</sup> The date is midway between the last of three early waves of initial public offerings in biotech (IPOs), in 1986, and the end of the sampling frame in 1991.<sup>22</sup> By 1992 these firms had received 565 patents; the data include another 69 awarded for competing—or complementary—innovations by outside firms and organizations. Stock price data come from the Center for Research in Securities Prices (CRSP).

These data span the first decade of commercial biotechnology. Innovations from that time have been important in determining the competitive positions of these firms. Dominant in cross-industry rankings of R&D intensity, the firms also dominate biotech patent-holder lists. Almost half of nearly 800 patents awarded by 1988 to more than 100 biotech firms belong to a firm in my sample.<sup>23</sup>

*BioScan*, a quarterly trade publication, reveals that progress has been unequal over the 17 research competitions. Some have produced FDA-approved drugs, while others have stalled in clinical trials. For nine areas, at least two rivals had reached the final Stage III of clinical trials by the end of the sampling period. RIVAL and NEUTRAL effects are sharper in those areas, and, in terms of patents, firms have been much more productive. Seventy-six percent of the protein patents in the sample—and about 80% of rDNA, broad, or *WSJ* patents—were awarded in these areas. I limit the regression analyses to the nine proteins.<sup>24</sup>

I identify patents with specific proteins by keyword searches of patent titles and abstracts, and company press releases. This technique matches 121 patents, or 21%, with one of the 17 protein families—an average of 7 patents per protein. The other 444 patents either relate to proteins only one firm was researching or are not associated with any protein.<sup>25</sup> The same keywords identify the other 69 patents.

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<sup>21</sup> See Table A1 for the list of the 20 firms. I limited the sample to firms with a primary focus on pharmaceutical or medical diagnostic products.

<sup>22</sup> Sampled firms went public, mostly in 1981, 1983, and 1986.

<sup>23</sup> In Lerner's 1994 list, the 20 firms in my sample had 345 patents by 1989 and by 1992, two of them, Genentech and Cetus, each had more than 100. The other 18 firms averaged 16 patents.

<sup>24</sup> See Table A2 for the 17 proteins for which the sampled firms have competed, and the 9 featured in the results.

<sup>25</sup> For example, patent 4824641, awarded to Cetus for "carousel and tip." In all, about 30 or 40 proteins were being pursued by about 250 commercial firms. (*U.S. News and World Report*, 11/24/86, p. 52).

None of the patents cover all aspects of a protein molecule or of its uses.<sup>26</sup> None is linked to more than one protein, and no protein is covered by only one patent. When a “protein patent” is issued, I observe stock prices of the patentee, its rivals, and the remaining neutral firms. Rivals are in-sample firms that are active in research on the protein to which the new patent relates.<sup>27</sup> For patents not related to any of the nine featured proteins, I measure own effects only, because rivalries are not defined.

U.S. patents are issued only on Tuesdays, many on the same day. Following standard practice, I drop most such patents.<sup>28</sup> The remaining 416 generate 1,670 “events.” Most patents generate a single own event, whereas protein patents generate up to 20 events, one per firm. The overlap exclusions slightly favor protein patents, which generate about 26% of OWN events.

Table 1 reports mean excess returns on 86 protein patents and 59 nonoverlapping, ancillary-search patents. These generate 86 OWN, 480 RIVAL, and 856 NEUTRAL events.<sup>29</sup> An average of 4 to 5 firms compete for each protein, which leaves as many as 16 neutral firms, depending on their IPO dates. It is not surprising that returns are highest for own, protein patents, whereas a RIVAL mean of 0.6% hints at positive spillovers from these patents.<sup>30</sup> I investigate this finding in greater depth in the regressions. The table also shows mean returns from the 248 patents not associated with a study protein.

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<sup>26</sup> This is the root cause of much biotech patent litigation. For instance, in 1987, two U.S. patents issued on erythropoietin (EPO) a commercially valuable, natural enzyme that stimulates red blood cell production. First, Genetics Institute received a patent on a synthesizing method, then Amgen patented EPO’s genetic sequence. Each patent potentially blocked the other. With huge returns at stake, the firms litigated. Amgen prevailed four years later and, thanks to EPO, became the world’s largest biotech company.

<sup>27</sup> Some rivalries are modulated by joint-venture or other agreements. *BioScan* lists these, and I control for them in the regressions.

<sup>28</sup> I do not exclude OWN or RIVAL events that coincide just with NEUTRAL events. I also exclude NEUTRAL events and “non-protein” patents occurring within one week of OWN and RIVAL events, which may influence them. These exclusions make no qualitative difference.

<sup>29</sup> Ancillary patents generate no own events.

<sup>30</sup> As a check on the model specification, randomly selected days yield a mean-zero excess return as expected.

**Table 1. Mean Percent Excess Returns to Patent Grants  
Three-day event window**

Patent type	N	Mean	Standard deviation	Minimum	Maximum
Full, non-overlapping patent sample	1670	0.61	6.05	-24.4	32.9
<i>Not protein patents:</i>					
OWN	248	0.63	5.89	-21.8	21.5
<i>Protein patents:</i>					
OWN	86	1.25	7.02	-24.39	32.88
RIVAL	480	0.60	5.44	-16.03	29.56
NEUTRAL	856	0.55	6.32	-23.11	31.18

The regressions estimate shadow values for patent characteristics—breadth, rDNA content, and a *WSJ* announcement—that I described earlier. I define 36 patents as “broad,” which means they belong to three or more international classification (ICN) categories.<sup>31</sup> There are 48 rDNA patents, which are those classified into special categories U.S. 930 or 935 for “recombinant DNA” or “genetic engineering.” Because these categories were not defined until 1984, they miss several patents. Finally, 16 patents, about 5% of the final sample, were discussed in the *WSJ*. This press coverage, usually just a few inches of column space, typically occurred the day after the patent issued. Several patents were discussed later or were given more space.<sup>32</sup>

<sup>31</sup> An ICN-based measure is validated in Lerner (1994) for four or more categories. This stricter definition applies to fewer than 10% of the protein patents, only one of which is not also an rDNA or *WSJ* patent.

<sup>32</sup> The *WSJ* criterion captures four patents from Lerner’s (1994) list of 13 “seminal” biotechnology patents. Twelve of those patents issued to firms in my sample. Not all of them are protein patents, which leaves too few patents in the regression sample for meaningful statistical analysis. If one ignores possible overlapping events, own excess returns for the twelve average 5.1%, while average rival returns are zero.

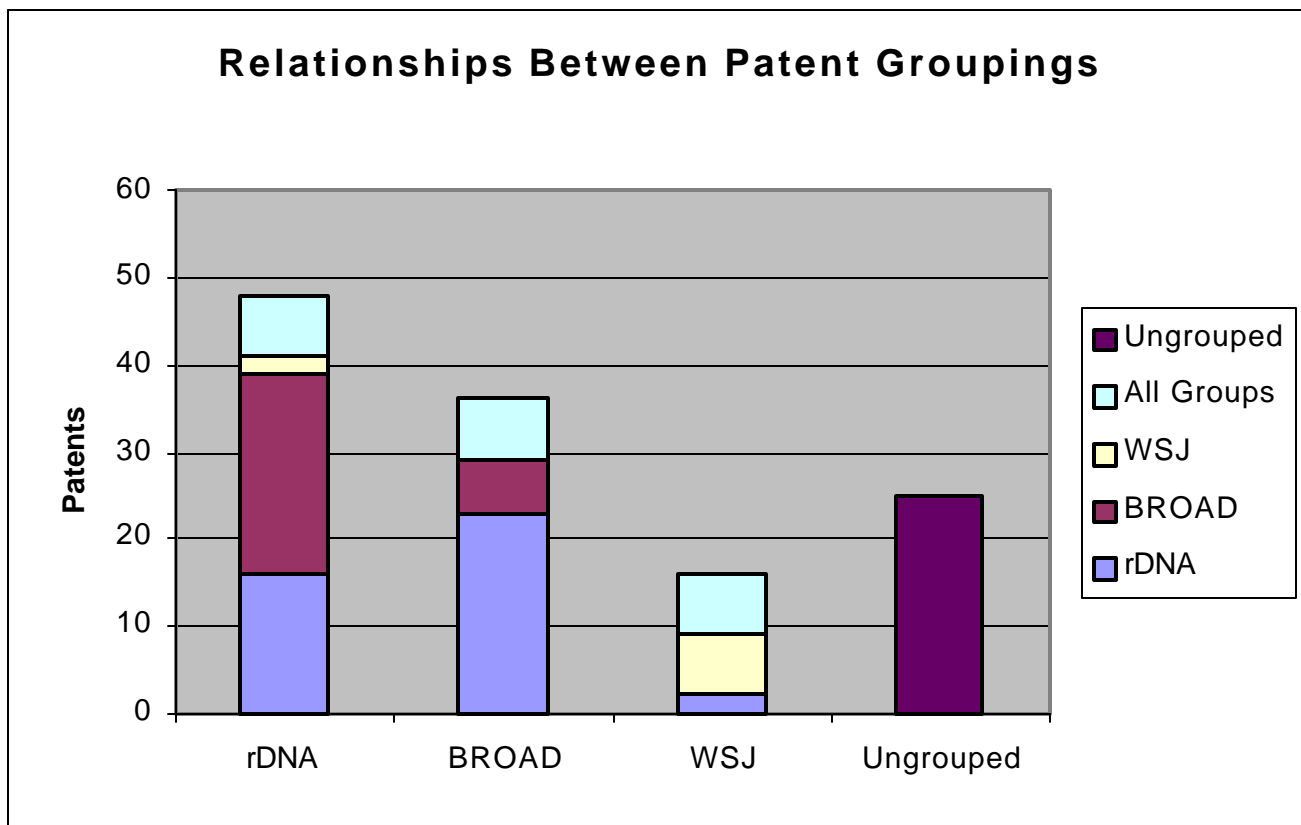


Figure 1. Cross-classification relationships for 86 protein patents



Figure 1 describes the relationships among these variables. The left column shows that of 48 rDNA patents, 23 are broad patents, 2 were announced in the *WSJ*, 7 belong to all three groups, and 16 are rDNA only. The next two columns can be read the same way. The final column shows that 25 of 86 protein patents are not broad, have no rDNA content, and were not announced in the *WSJ*. These groupings are for all 17 proteins; results for the subset are almost identical.

## 6. Regression Results

The regressions begin with a simple specification distinguishing between only so-called protein patents and the other patents.<sup>33</sup> The protein dummy is interacted with indicators of firms' identities vis-a-vis the patentee, because stock price reactions are observed for every firm when a protein patent is awarded.

Table 2 presents these results. Regression (I) essentially reprises Table 1, although it is so only for research areas that had two firms at or beyond Stage III. The OWN coefficient shows that these patents are significantly more highly valued than other biotech patents, which raises the market values of the patentees by an average of 1.85%, or \$8.3 million, for these firms.<sup>34</sup> This effect, significant at the 1% level, is large but it understates the true valuations. I derive full, implicit values in the next section.

These patents seem also to produce positive spillover benefits for other firms. *NEUTRAL* captures the effect of patents awarded in areas unrelated to a firm's own research. When a protein patent issues, the market values of neutral firms increase by \$0.6 million on average, which is statistically significant at the 7% level. This finding could reflect expected knowledge spillovers, but it might also be a sign that the patents, in general, have increased investor confidence in biotechnology firms.<sup>35</sup>

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<sup>33</sup> For these regressions, the latter group includes patents from the eight research areas in which one or fewer firms had reached Stage III in clinical trials. This boosts membership to 269 patents while reducing the number of protein patents to 65. Cf. Table 1. The ancillary patents are included in these regressions but do not qualitatively affect the results.

<sup>34</sup> I back these numbers out by de-normalizing the regression coefficients. Models including *N* in the interactions, as suggested by the theoretical model, produce identical results but do not fit the data as well and exhibit greater heteroskedasticity.

<sup>35</sup> Revaluation of "neutral" firms may drive Mitchell and Mulherin's (1994) finding of a small, positive relationship between the number of stories (of all types) appearing in the *WSJ* and aggregate returns to securities that day. Such

The RIVAL effect gives evidence that suggests positive spillovers to direct competitors of a rival patentee. The effect is larger than the NEUTRAL effect, but is not estimated as precisely: When a rival firm wins a patent, the values of the other firms active in the same area increase by an average of \$1.7 million.<sup>36</sup> The difference between rival and neutral effects may reflect the greater value of spillovers to competitors, for whom the knowledge is more relevant. Differences with the own effect are statistically significant at 5%.

I control for erstwhile RIVAL events that are subject to joint venture or patent licensing agreements. The sign and magnitude of the joint venture (JV) effect are consistent with these agreements, in the sense that the effect on a firm's market value of a JV partner's patent or a licensed patent is almost identical to the effect of the firm's own protein patents.

Limiting the firm effects to nine research areas and paring away the eight others in which less progress had been made boosts the coefficients by 25%–35% compared with the full 17 research areas. The proximate reason why these patents are more valuable could be because innovations in these nine research areas are closer to market. Possible reasons for that, in turn, might be because those markets are bigger, consumer willingness to pay is higher, or the innovations offer greater quality improvements over conventional substitutes.

Although model (I) is significant statistically, its adjusted R-squared is very small. Distinguishing between OWN, RIVAL, and NEUTRAL effects explains less than 1% of the variation in excess returns across firms and patents. The CAPM model, of which excess returns are the residuals, explains about 70% of the variation in stock prices. Patents significantly affect prices, but these models explain at best less than 3% of residual variation.

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revaluations are acknowledged explicitly, within limits, in biotechnology: "There are only so many times you can [r]evalue a whole industry based on one or two companies' news," says Rick Stover, biotech analyst ... ."

<sup>36</sup> Despite its smaller coefficient, the rival effect is greater than the neutral effect because in the nine research areas, the firms are larger than average. The patentees are worth \$420 million on average; rival firms, \$276 million—thus, larger firms have also patented more often in these races; and neutral firms, \$85 million.

**Table 2. Effect of Biotechnology Patent Grants on Firm Values**  
**Dependent variable: firm excess returns**

	I		II		III		IV		V	
Variable	Est / (s.e.)		Est / (s.e.)		Est / (s.e.)		Est / (s.e.)		Est / (s.e.)	
<b>INTERCEPT</b>	0.125 (0.212)		0.124 (0.212)		0.130 (0.212)		0.123 (0.211)		0.127 (0.210)	
<b>OWN</b>	23.942 *** (8.457)		19.058 * (10.93)		2.299 (13.166)		7.616 (9.292)		-15.338 (13.742)	
<b>RIVAL</b>	6.181 (4.000)		8.650 (5.000)		-0.755 (6.449)		7.933 * (4.000)		0.867 (6.000)	
<b>NEUTRAL</b>	6.883 * (3.844)		9.023 * (4.849)		-3.273 (5.975)		4.286 (3.963)		-5.065 (5.985)	
<b>OWN-broad</b>			11.396 (16.13)							
<b>RIVAL-broad</b>			-5.285 (6.993)							
<b>NEUTRAL-broad</b>			-4.303 (5.940)							
<b>OWN-rDNA</b>					34.914 ** (16.385)				36.673 ** (16.278)	
<b>RIVAL-rDNA</b>					10.620 (7.000)				10.889 (7.000)	
<b>NEUTRAL-rDNA</b>					14.330 ** (6.479)				13.383 ** (6.447)	
<b>OWN-WSJ</b>							81.349 *** (19.778)		82.497 *** (19.733)	
<b>RIVAL-WSJ</b>							-21.280 * (12.551)		-21.648 * (12.520)	
<b>NEUTRAL-WSJ</b>							22.944 ** (9.273)		21.768 ** (9.267)	
<b>JV AGREEMENT</b>	18.217 (13.339)		17.508 (13.37)		21.305 (13.389)		18.808 (13.250)		21.853 * (13.299)	
<b>N</b>	1667		1667		1667		1667		1667	
<b>Adj R-sq</b>	0.0047		0.0039		0.0098		0.0182		0.0233	
<b>F</b>	2.971		1.924		3.359		5.423		4.983	
<b>Prob &gt; F</b>	0.0185		0.0622		0.0015		0.0001		0.0001	

Notes: Heteroskedasticity-consistent standard errors in parentheses

**Firm effects are for patents in nine areas with multiple firms in Stage III clinical trials**

**RHS variables interacted with  $[\ln(\text{firm value})]^{-1}$**

\* significant at 10% level; \*\* 5%; \*\*\* 1%

Model (II) shows that broad protein patents may be more valuable to the patentee than narrow ones and that they may be less helpful to other firms, although these incremental effects do not differ significantly from the effects of all protein patents. All else equal, broader property rights restrict the utility of knowledge spillovers and enhance the appropriateness of a patent, and these results are consistent with this. *F*-tests show that the OWN effects of broad patents are significant at the 1% level and also different from their effects on RIVAL firms and NEUTRAL firms at 5%.<sup>37</sup>

Model (III) examines rDNA patents and reveals that the interesting effects in model (I) are due to these core patents. Model (III) also explains twice as much variation in the dependent variable. When rDNA patents issue, market values increase by \$12.6 million—more than 50% larger than the model (I) estimate, which is now seen to average high- and low-value patents. The NEUTRAL effect is one-third larger at \$0.8 million, as is the RIVAL effect, here \$2.5 million. The incremental effects of the OWN and NEUTRAL rDNA coefficients are significant at 5%, while the RIVAL rDNA coefficient is not significant at conventional levels (tail probability 14%). *F*-tests confirm that total effects of all three events, combining the protein and rDNA coefficients and the intercept, are significant statistically (RIVAL at 5%, the other two at less than 1%) and that, once again, OWN effects are the largest by a significant margin.

Regression (IV) controls for mean shifts from blockbuster patents. One in five of the protein patents in the nine featured races that were noted in the *WSJ*, usually the day after they issued. As Figure 1 shows, more than half of the *WSJ* patents are broad and have rDNA content. Own firm values increase an average of \$29.4 million for *WSJ* patents, which is nearly two-and-a-half times the rDNA effect and is strongly significant at the 1% level. The effect for NEUTRAL firms is also more than twice as large, at \$1.9 million, and is also highly significant. These effects differ in degree from their counterparts in regression models (I)–(III), but the RIVAL-*WSJ* effect differs in kind. When a rival wins a *WSJ* patent, a firm's value declines by an average of \$2.5 million, or almost \$4.5 million relative to the NEUTRAL firms in the sample. The RIVAL coefficient is significant at the 10% level. *F*-tests for differences between all of the effects are significant at the 1% level.

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<sup>37</sup> The slightly stronger definition of breadth used by Lerner (1994) should produce larger effects, but they cannot be implemented here due to sample-size limitations.

Many of the *WSJ* patents have given the patentee a monopoly or a strong competitive advantage in selling the embodying drug. The RIVAL effect may indicate that the patents are viewed as winner-take-all prizes with market-power implications that are expected to dominate any spillover benefits. The *WSJ* criterion accounts for almost four times as much variation as the basic model.

First-day, pre-publication reactions to *WSJ* patents are no stronger than average, and this criterion does not appear endogenous. The valuations could reflect excessive responses to the *WSJ* events, subject to later correction, but the valuations are also consistent with the high status of most of these patents. The *WSJ* results do not represent biotech patents as a whole, and caveats about the *WSJ* results should be kept in mind.

The final model (V) includes both the rDNA and the *WSJ* effects, which overlap only somewhat. The interaction effects are changed little from models (III) and (IV), and they imply that the effect of *WSJ* patents with rDNA content is about 16%, or \$4.8 million, greater than for other *WSJ* patents. The explanatory power of model (V) is the largest of the five, by about 30%.

These results indicate that certain, well-defined kinds of biotechnology patents induce significant market responses of magnitudes consistent with characteristics of those patents. In the next section, I simulate the theoretical model to derive implicit market valuations for these patents, given that they may be anticipated partially. Event analysis of corresponding patent applications yields no evidence of excess returns, even by using longer event windows. If U.S. patent applications are a source of anticipation about pending patents, the information either does not coincide with the event or is treated as highly uncertain.<sup>38</sup>

## 7. Simulations

The theoretical model (see Section III) comprises two equations in three unknown parameters, including returns  $V$  from winning a patent and  $C$  when a patent is awarded to another firm. Here, I use trial values for the third unknown parameter,  $p$ , prior expectations by investors that a patent will issue, to solve the model given observed market effects.

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<sup>38</sup> For the application event analysis, I use a 10-day window (-5, +5). Anticipation could come from firms announcing their patent applications or early notification of pending patents, which may precede a patent by several months. In my sample, it took an average of 34 months for the patent office to process a successful application, meaning that overseas applications, if filed simultaneously, would be published on average 16 months before the U.S. patent issues.

Subtracting model Equation (2) from (1) yields  $C = OWN\ EFFECT - RIVAL\ EFFECT - V$ , which by substitution leads to a single expression in  $V$ :

$$V \cdot N \cdot (1 - p) = RE \cdot p \cdot (N - 1) - OE \cdot (p \cdot (N - 1) - N) \quad (3)$$

$OE$  and  $RE$  are observed excess returns: OWN and RIVAL, respectively.  $N$  is the number of firms in a research area. I assume  $N = 6.6$ , the average number in my sample over nine areas. Algebra yields the implicit valuations reported in the top-half of Table 3 for low, medium, and high values of  $p$ .

The alternative model assumes that investors put extra weight on the eventual winners' odds of patenting correctly. Manipulating (1') and (2') does not yield tidy expressions, but the model can be solved for  $V$  and  $C$  when an assumption is made about the weight  $\alpha$ . Simulations show that the results are not very sensitive to this parameter. Table 3 presents the basic model, which corresponds to the equal-weighting case  $\alpha = 1$ , and it presents  $\alpha = 5$ , which is close to its maximum allowable value of  $N$ .

**Table 3. Average Patentee Benefits,  $V$ , and Rival-Firm Costs (benefits),  $C$   
Nine biotechnology research areas (see Table A2)**

<i>patentee prior factor</i>	<i>patent prior</i>	<i>(I) all protein patents</i>		<i>(III) rDNA patents</i>		<i>(IV) WSJ patents</i>	
		<i>V</i>	<i>C</i>	<i>V</i>	<i>C</i>	<i>V</i>	<i>C</i>
<b><math>\alpha = 1</math></b>	<b><math>p</math></b>	<b><math>V</math></b>	<b><math>C</math></b>	<b><math>V</math></b>	<b><math>C</math></b>	<b><math>V</math></b>	<b><math>C</math></b>
<i>All firms equally prior-weighted</i>							
	<b>0.1</b>	\$8.60	(\$2.00)	\$13.05	(\$2.95)	\$29.65	<b>\$2.35</b>
	<b>0.5</b>	\$11.00	(\$4.40)	\$16.63	(\$6.53)	\$31.65	<b>\$0.35</b>
	<b>0.9</b>	\$32.60	(\$26.00)	\$48.87	(\$38.77)	\$49.64	(\$17.64)
<i>Patentee prior weight <math>\alpha/N</math>, all other firms weighted <math>(N - \alpha)/N</math>, for <math>N = 6.6</math></i>							
<b><math>\alpha = 5</math></b>	<b><math>p</math></b>	<b><math>V</math></b>	<b><math>C</math></b>	<b><math>V</math></b>	<b><math>C</math></b>	<b><math>V</math></b>	<b><math>C</math></b>
	<b>0.1</b>	\$9.03	(\$1.92)	\$13.71	(\$2.83)	\$31.74	<b>\$2.72</b>
	<b>0.5</b>	\$14.11	(\$3.84)	\$21.39	(\$5.68)	\$46.73	<b>\$3.05</b>
	<b>0.9</b>	\$42.68	(\$24.20)	\$64.30	(\$36.02)	\$98.51	<b>\$8.91</b>

*\$ millions*

If patents are highly anticipated, their true market values are much higher than the observed changes in firm valuations. Excess returns reflect only the portion of patent value not already capitalized into stock prices before the event, or 10% when  $p = 0.9$ . With equally weighted firms, the present discounted own value of a protein patent with rDNA content would average \$49 million. Implausibly, expected spillovers per rival would be nearly as high. If the patentee's identity were also highly anticipated, the implicit valuations of these patents would be about 30% higher, although spillovers would be a little lower. To put this figure in perspective, valuing all of the protein patents at \$64 million—for  $\alpha = 5$ ,  $p = 0.9$  and rDNA content—and the others at \$0, the sampled firms' patent portfolios would have been worth between one-third and one-half of the firms' then-market capitalizations.

Startup biotech firms are often valued largely for their intangible assets. Attributing \$800 million of Genentech's then-\$2 billion market capitalization to its patents might be defensible if one assumed revenues would be \$0 without them. Such high valuations depend on aggressive assumptions, however, and finding comparable rival benefits is not so easily defended.

For lower values of  $p$ , the estimates are more conservative and less elastic with respect to  $p$  and  $\alpha$ . At  $p = 0.1$ , they are fairly insensitive to  $\alpha$  and average about \$9 million for all own protein patents, or about \$13 million for just rDNA patents. For  $p = 0.5$ , the estimates vary a little more with  $\alpha$  and range from \$11 to \$14 million or \$17 to \$21 million, respectively. From this calculation, I conclude that \$9 million is a conservative estimate of protein-patent values. Those lacking rDNA content are worth much less, whereas my central estimate for the rDNA protein patents is about \$17 million.<sup>39</sup>

Even at \$9 million, own patent values would be tenfold the largest estimate in the literature. There are several possible reasons for this estimate. It is likely that patents are unusually important in biotechnology, whereas earlier studies are based on many industries and do not include biotech. Also, averaging annual changes in firm value over many patents inevitably produces a low estimated value per patent, because I, and others, show that most

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<sup>39</sup> The lower  $p$  assumption produces more plausible value and appropriability estimates, and it is also more consistent with the significant NEUTRAL effects in the regressions, which cannot be explained by surprises in the identity of the patentee.

patents are not very valuable. Finally, the patents in Table 3 are for innovations in core technology and are even more valuable than average biotechnology patents.<sup>40</sup>

For  $p = 0.1$ , and regardless of  $\alpha$ , spillover benefits for rival firms are about \$2 to \$3 million, or \$3 to \$6 million for rDNA patents, which account for no more than about one-fourth the level of corresponding own values. Corresponding estimates for neutral biotechnology firms, not shown, range from \$0.7 to \$1.0 million. I observe more than five rivals per patentee, which suggests that the patentees appropriate somewhat less than half the total benefits of their patents. On average, though, only two or three of the rivals are in the firm sample, where spillovers may be greater. Outside firms include a competitive fringe, which may benefit less from spillovers; and public research institutes such as National Institutes of Health, where incentives to exploit spillovers may be lower than in the private sector. Thus, appropriateness may be higher than that strictly implied by the spillover estimates.

## 8. Summary and Conclusions

Patents generate rents for patent-holders and may impose externalities on their rivals. This paper presents the first direct empirical evidence on the private economic value of these effects. I find that new patents often induce significant firm revaluations, especially for the patentee and its competitors. This paper demonstrates that as a rule, patents are not highly anticipated and that an event study of patent grants can be an appropriate way to value them.

I perform the study on an original sample of more than 600 biotechnology patents awarded to primarily 20 leading firms. I create a theoretical framework for interpreting the results by modeling how expectations about future patents and patent-holders affect market values. My estimates of the underlying patent valuations are, however, relatively insensitive to parametric assumptions about these prior expectations, within a range of plausible values.

Depending on those assumptions, I find market valuations of between \$9 and \$14 million each, for patents in leading—and highly competitive—research areas, which include erythropoietin, colony-stimulating factors, human growth hormone, and hepatitis-B vaccine. These “protein” patents comprise about 12% of the sample. I also find that in general, these

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<sup>40</sup> The final column shows that for  $\alpha = 1$ , *WSJ* patents impose net costs on rivals averaging \$2.3 million, versus neutral-firm benefits of \$2.4 million. Spillovers to rivals may exceed those to neutral firms but be offset by other costs. Neutral-firm benefits are \$1.2 million, \$1.9 million, \$4.3 million if  $p = 0.5$ , and \$6.2 million, \$9.4 million, and \$21.5 million if  $p = 0.9$ .



patents generate net spillovers valued from \$2 to \$4 million per patent per rival firm. The patentees in my sample usually appropriate less than half of the private returns to their patents. I also find that neutral biotech firms receive spillovers valued about one-third as highly.

Most of these effects appear to be due to a subset of these patents for innovations in recombinant DNA or genetic engineering. These patents are valued at between \$13 and \$21 million and yield \$3 to \$6 million in spillovers to rivals. A few “seminal” patents—and others also noted in the *WSJ*—received much higher valuations and were, atypically, expected to impose net *costs* on rival firms. Finally, 88% of the patents are not related to the contested proteins and generate excess returns that are not significantly different from zero.

That just one-eighth of the patents should have significant economic value is consistent with earlier research, although here I also explain patent value as a function of content. The valuations seem rational, in the sense of responding to characteristics—possibly including patent breadth—that I deemed, a priori, to be desirable. My central estimate of about \$17 million in own value exceeds earlier estimates by more than an order of magnitude. This finding can be defended by comparing the value of the patents to the total capitalized values of the patent-holders, and on the basis of the importance of the patents in generating revenues. In my sample, the firms always held multiple patents on a product by the time they began selling it.

My spillover results are also consistent with earlier empirical research, which shows that rival firms’ R&D productivity is mutually beneficial. My findings suggest that individual patents may be a direct pathway for knowledge spillovers and that these, too, can have significant economic value—my central estimate is about \$4 million per rival firm for the more valuable patents. Except in a few high-profile cases, the market does not seem to treat patents as winner-take-all prizes. In my current research, I find evidence that even for the *WSJ* patents, from which the market appears to expect negative spillovers, patenting by rival firms is slowed only temporarily.

This research contributes to a broader understanding of the role patents play in firms’ strategic interactions, and in shaping the evolving market structure in biotechnology. Biotechnology patents—valuable assets with direct and immediate effects on the patentees and their rivals—seem to merit the importance placed on them by innovating firms.

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## Appendix

**Table A1. Top U.S. Biotechnology Firms  
By December 1988 Market Value**

Rank	Firm	Market value (\$000,000)	Sales (\$000)	Rank by sales	Patents as of 11/91
1	Genentech	1,289.4	341.7	1	103
2	Amgen	555.8	69.2	2	30
3	Cetus *	283.3	57.6	4	170
4	Genetics Institute	222.1	19.8	9	41
5	Centocor	178.6	62.9	3	18
6	Biogen	164.2	26.7	6	23
7	Chiron	151.7	28.5	5	24
8	Xoma	140.3	6.7	15	13
9	Cambridge Biotech	139.5	4.2	21	5
10	Molecular Biosystems	137.9	5.0	20	7
11	Immunex	94.2	20.9	8	26
12	NeoRx	81.0	6.0	16	26
13	Genzyme	68.1	21.6	7	6
14	Calif. Biotechnology	65.7	13.3	10	12
15	Repligen	47.5	7.6	14	31
16	Synergen	41.2	8.6	12	5
17	Integrated Genetics †	31.6	12.5	11	10
18	Oncogene Scientific ‡	25.8	5.9	17	0
19	Bio-Technology General	17.4	5.4	19	10
20	Monoclonal Antibodies §	16.3	8.5	13	2

Source: William O'Neil & Co., 12/16/88

\* Purchased by Chiron, December 1991

† Merged with Genzyme, August 1989

‡ Prior to 1992 Oncogene licensed patents from other firms only

§ Monoclonal Antibodies merged with Quidel in January 1991

Table A2. Seventeen Research Areas with Multiple, In-Sample Rivals

Protein	Patent-holders (Patents through 11/91)	Other Rival Firms	Description †
Colony Stimulating Factors (CSFs) *	Amgen, Cetus, Immunex, Genetics Institute (GI), 3 outside sample. <b>(17 in-sample patents + 3 outside)</b>	Biogen, Genzyme, Integrated Genetics	Regulate production of red blood cells; immunomodulators.
Erythropoietin (EPO) *	Amgen, GI, Integrated Genetics (IntG), 2 outside sample <b>(7+2)</b>	Biogen, BioTech General, California Biotech (Scios)	Alternative to blood transfusions in dialysis patients.
Factor VIII *	Chiron, Genentech, GI, 2 outside <b>(6+5)</b>	Biogen, IntG	Lacking in hemophiliacs. Biotech product eliminates HIV risk of natural substitute.
Hepatitis B vaccine *	Amgen, Biogen, Genentech, IG, 7 outside <b>(6+8)</b>	Chiron	Based on monoclonal antibodies.
Human Growth Hormone (hGH) *	Genentech, Biotech General, 3 outside <b>(10+3)</b>	Biogen, Scios, Chiron	Short stature, osteoporosis, renal failure, burns, obesity. No risk of disease with synthetic hGH.
Imaging MAbs*	Centocor, Cetus, Molecular Biosystems, NeoRx, XOMA <b>(10+N/A)</b>	Genentech	Diagnostic aid. Monoclonal Antibodies (MAbs) are specific for particular antigens.
Septic Shock MAbs *	Cenotcor, XOMA <b>(2+0)</b>	(None)	Indicated for post-surgical bacterial invasion.
Gamma Interferon (IFN-g) *	Amgen, Biogen, Genentech, 6 outside <b>(7+9)</b>	(None)	Anti-cancer, anti-inflammatory, anti-viral agent; immunomodulator.
Interleukin-2 (IL2) *	Cetus, GI, Immunex, 7 outside <b>(25+8)</b>	Amgen, Biogen, Chiron, Genentech, Genzyme, XOMA	Highly toxic to cancer tumors. Mediates, stimulates immune response.
Insulin	Amgen, Chiron, Genentech, 4 outside <b>(4+6)</b>	Biogen	Greater efficacy than naturally extracted insulin.
Tissue Plasminogen Activator (tPA)	Biogen, Genentech, 4 outside <b>(8+7)</b>	Chiron, GI, IntG	Activates clot-dissolving enzyme; coronary treatment. Safer, slightly more effective than other drugs.
Epidermal Growth Factor (EGF)	Chiron, 3 outside <b>(1+4)</b>	Amgen	Wound-healing agent; anti-inflammatory drug. May help regenerate nerves, heal tendons.
Fibroblast Growth Factor (FGF)	Synergen, 2 outside <b>(2+2)</b>	Scios, Chiron	Potential for wound healing, esp. large-area skin grafts.
Platelet-derived Growth Factor (PDGF)	1 outside organization <b>(0,5)</b>	Amgen, Chiron	Stimulates tissue growth. Induces collagen synthesis, connective tissue development.
Superoxide Dismutase (SOD)	Biotech. General, 1 outside <b>(3+1)</b>	Chiron	Potential therapy for transplant, coronary, osteoarthritis. Neutralizes toxic free radicals due to inflammation.
Transforming Growth Factor (TGF)	Genentech, 1 outside <b>(3+1)</b>	(None)	Similar to EGF. Produced by tumor cells, cells infected with retrovirus.
Tumor Necrosis Factor (TNF)	Biogen, Cetus, Genentech, 4 outside <b>(10+7)</b>	(None)	Anti-cancer, -inflammatory, -viral agent; immunomodulator. Suspected pathogen for acute shock.

† From "Genetically Engineered Human Therapeutic Drugs," Copsey and Delnatte (1988)

\* Two or more in-sample firms in or past Stage III clinical trials by 1992

**Table A3. Biotechnology Protein Patents noted  
in the *Wall Street Journal* through 1991**

<b>Patent</b>	<b>Firm</b>	<b>Protein</b>	<b>Filed</b>	<b>Granted</b>
4569790	Cetus	Interleukin-2	3/28/84	2/11/86
4677195	Genetics Institute	Erythropoietin (EPO)	1/11/85	6/30/87
4703008	Amgen	EPO	11/30/84	10/27/87
4710463	Biogen	Hepatitis B vaccine	3/31/82	12/1/87
4727138	Genentech	Interferon-gamma	9/11/85	2/23/88
4752603	Genentech	Tissue plasminogen activator (tPA)	5/28/86	6/21/88
4757006	Genetics Institute	Factor VIII	10/28/83	7/12/88
4766106	Cetus	Interleukin-2	1/25/88	8/23/88
4810643	Amgen	Colony stimulating factor (CSF)	3/3/86	3/7/89
4853330	Genentech	TPA	4/21/88	8/1/89
4868112	Genetics Institute	Factor VIII	4/11/86	9/19/89
4879227	Genetics Institute	CSF	5/6/86	11/7/89
4918162	Xoma	Monoclonal antibody for septic shock	10/5/88	4/17/90
5021239	Genetics Institute	CSF	12/8/88	6/4/91
5026839	Synergen	Fibroblast growth factor	4/5/90	6/25/91
5057598	Centocor	Mab for septic shock	2/1/89	10/15/91

The patent sample includes another 9 WSJ patents not associated with any of 17 proteins.