GEOGRAPHICALLY LOCALIZED KNOWLEDGE: SPILLOVERS OR MARKETS?

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Using detailed data on California biotechnology, we find that the positive impact of research universities on nearby firms relates to identifiable market exchange between particular university star scientists and firms and not to generalized knowledge spillovers. Poisson and two-stage Heckman regressions indicate the number of star-firm collaborations powerfully predicts success: for an average firm, five articles coauthored by academic stars and the firm's scientists imply about five more products in development, 3.5 more products on the market, and 860 more employees. Stars collaborating with or employed by firms, or who patent, have significantly higher citation rates than pure academic stars. (*JEL* O31; D62, L65, L66)

I. INTRODUCTION

Knowledge spillovers—positive externalities of scientific discoveries on the productivity of firms which neither made the discovery themselves nor licensed its use from the holder of intellectual property rights—play a central role in the literature as causes of both economic growth and geographic agglomeration.[1] Zvi Griliches [1992] has surveyed the importance of R&D spillovers as a major source of endogenous growth in recent "New Growth Theory" models and the difficult empirical search for their existence. While the search for spillovers has been difficult, there has been considerable success in finding their fingerprints by demonstrating statistically significant effects on a firm's productivity of being near great universities and other sources of scientific discovery—geographically localized knowledge spillovers. (See particularly, Adam B. Jaffe [1989], Jaffe, Manuel Trajtenberg, and Rebecca Henderson [1993],

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1. On the former see, for example, Paul M. Romer [1986; 1990], Gene M. Grossman and Elhanan Helpman [1991], David T. Coe and Helpman [1995], Coe, Helpman, and Alexander W. Hoffmaister [1997], and Jonathan Eaton and Samuel Kortum [1994; 1995].

ABBREVIATION
IMR: Inverse Mills Ratio

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and Edwin Mansfield [1995].)[2] Providing further evidence of the empirical relevance of geographically localized knowledge spillovers in the case of biotechnology, Lynne G. Zucker, Michael R. Darby, and Marilynn B. Brewer [1997] have recently demonstrated that "intellectual human capital," measured operationally by where and when "star" scientists at the leading edge of basic bioscience are active, is a principal determinant of both the location and timing of the entry of new biotechnology enterprises in the United States.[3]

Operationalizing Sherwin Rosen's [1981] superstar concept, Zucker, Darby, and Brewer [1997] relate geographically localized knowledge spillovers in the formative years of the biotech industry to a relatively small number of outstanding scientists (207 of whom ever worked in the U.S.) who combined brilliant scientific productivity with specific knowledge of the new techniques which formed the basis of industrial formation and transformation (see Data Appendix). In this paper, we further explore the technology by which apparent geographically localized knowledge spillovers operate. Case studies and interviews point to the fact that the star scientists are not simply located in the same geographic area with biotech firms, but in fact are frequently deeply involved in their operations as principals, employees, or consultants. We find empirically that what might appear using standard methodology and data sets as geographically localized external economies for enterprises located near university stars turn out to exist only for that much smaller set of enterprises which are linked to particular star professors by contract or ownership—that is, by market exchange. This same subset of firms with explicit ties to star scientists also appear to account for a disproportionately larger share of industry growth, measured here as number of products in development, number of products on the market, and employment growth between 1989 and 1994. Indeed, it seems to us that the source of geographically localized effects on firm performance is the same as the reason that much of the fruits of the biotechnological revolution was much more appropriable by the star scientists than by the universities which (typically) employed them.[4] These star scientists generally retain their university affiliations while involved in commercial applications within easy commuting distance of home or university, thus creating localized effects of university research.

Here we examine the effects of one scientific breakthrough on a relatively small number of industries which experience a technological transformation as a result. If, as we will argue in section V may well be the case, other instances of geographically localized knowledge spillovers are in fact also instances of appropriation and market exchange by discovering scientists, then both interpretation of prior studies and their strong policy implications need to be reexamined. Before drawing these conclusions, we must turn to the concrete analysis which suggested them.

We open the "black box" of the actual working relationships between university star scientists making the discoveries and the firms utilizing them commercially, because we believe that relying on the typically assumed, but unmeasured, pre-publication spillover of new discoveries made in university labs has led to flawed inferences about the processes of technology transfer. We examine the actual transfer by developing a novel empirical indicator (Zucker, Darby, and Armstrong [1994]; Zucker and Darby [1996]; Liebeskind, Oliver, Zucker, and Brewer [1996]; Zucker, Brewer, Oliver, and Liebeskind [1993]): articles written jointly be-

2. Nancy S. Dorfman [1988], Bryan D. Jones and Arnold Vedlitz [1988], Raymond W. Smilor, George Kozmetsky, and David V. Gibson [1988], Neil Bania, Randall Eberts, and Michael Fogarty [1993], and James D. Adams and Jaffe [1994] also indicate geographic localization of knowledge spillovers. There are, of course, other important sources of geographic agglomeration (see, for example, Keith Head, John Ries, and Deborah Swenson [1994]).

3. These firms include both new biotechnology firms formed to exploit the new technologies and divisions, subsidiaries, or other units of incumbent firms which adopt the new biotechnology.

4. Philippe Aghion and Jean Tirole [1994] have begun a complementary research program examining the effects of necessarily incomplete contracts upon the organization of R&D activities where inventing employees may opportunistically appropriate successful discoveries. We note that Stanford and the University of California earned very substantial amounts of money from the Cohen-Boyer patent on the founding discovery of biotechnology, but at least one of the discoverers has realized an order of magnitude higher return on the equity positions obtained with his knowledge of how to actually apply their discovery.

tween university star scientists and firm scientists ("linked") or articles written by university star scientists who become employed full-time by a firm ("affiliated"), with the number of such articles indicating the intensity of the bench level scientific collaboration. The validity of this indicator for the existence of contractual or ownership relationships with firms has been confirmed through extensive interviews conducted with university scientists and administrators, and with firm scientists, CEOs, and corporate board members (for U.S. examples, see Zucker and Darby [1995]; Zucker, Brewer, Oliver, and Liebeskind [1993]).

Our complex, relational data base—to be described in more detail below and in the Data Appendix—provides the basis for linking specific scientists to specific firms, and allows us to construct high validity, high specificity measures without becoming focused on a single innovation case study.[5] By concentrating on genetic sequences and firm-specific products and employment in biotechnology, we are able to combine basic-science data with data from firms in multiple industries from pharmaceuticals to instrumentation, agriculture, food processing, and brewing. This variety of industries is illustrated by such biotech products currently on the market or in development as a hepatitis B vaccine, drugs to combat anemia in kidney dialysis patients, a diagnostic test for testicular cancer, nematodes for control of navel orange worm, modified vegetable oils for improved nutrition and industrial lubrication, improved fermentation processes, and reversible color-change ultraviolet-sensitive ink.[6]

Key to this multi-industry technological revolution was the 1973 discovery by Stanford professor Stanley Cohen and University of California-San Francisco professor Herbert Boyer of the basic technique for recombinant DNA (rDNA).[7] Today biotechnology refers principally to the application of genetic engineering based upon taking a gene from one organism and implanting it in another (rDNA) and production of the outcome of this process.[8] While the production part of biotechnology can be done by many firms, the selection of promising lines and the gene transfer itself require very special skills and talents which were quite rare at least until very recently. Following Harold Demsetz [1988], we argue that mastery of this specialized body of knowledge played a central role in delineating the boundaries of biotechnology firms. Zucker, Darby, and Brewer [1997] showed the key role of leading-edge science in the entry of biotech firms and we show here that role continued in determining the success and failure of these enterprises.

For the empirical work in this paper, California is not only a technically tractable site, given data collection constraints for such a highly detailed relational data base, but indeed nearly an ideal site for the study because of the early entry into both the science and industry of biotechnology, as well as the number of distinct locales where bioscience or both the science and industry have developed. Further, the state's firms exhibit the geographic agglomeration associated with spillovers. Therefore, California is a suitable while still manageable subject for a study that develops techniques for identifying spillovers more precisely by identifying linkages between biotech firms and star scientists affili-

5. See Griliches [1992, S31–S33] on the pitfalls along the path of narrowly focussed research.

6. See Tables A.4 and A.5 in Zucker, Darby, and Armstrong [1994] for more examples.

7. Cohen, Chang, Boyer, and Helling [1973].

8. The other basic technology is cell fusion (also termed monoclonal antibodies, MABs, or hybridomas) in which lymphocytes are fused with myeloma cells to create rapidly proliferating antibody-producing cells. Robert D. Sindelar [1992; 1993] provides a useful introduction to these applications in the pharmaceutical industry. Sindelar [1992, 3-4] notes in reference to pharmaceuticals that modern biotechnological techniques can be divided "into three broad areas...." Recombinant DNA techniques "take identified gene sequences from one organism and place them functionally into another to permit the production of protein medicines such as human insulin, alpha interferon, and colony-stimulating factors. Second, methodologies have been developed for producing monoclonal antibodies, ultrasensitive immune system-derived cells designed to recognize specific substances known as antigens that are uniquely associated with chemicals found in foreign organisms and/or humans. Developments in this field have led to their use as diagnostic agents for laboratory and home use in pregnancy tests and ovulation prediction kits and in the design of site-directed drugs such as OKT-3 for kidney transplant rejection. Finally, the development of technologies to study DND-DNA and DNA-RNA interactions has led to the formation of DNA probes (antisense technology) for a variety of research purposes with potential uses as diagnostics and therapeutics."

ated with universities.[9] Further, as we will discuss in more detail below, the pattern of our results for California at the aggregate level matches the pattern of results found for spillovers in Jaffe's nationwide study [1989].

Section II discusses and presents summary data on California biotechnology firms and their underlying scientific base and relates our methodology and measurements to the literature. Estimation methods are outlined in section III. Section IV presents empirical results on the determinants for California biotech firms of employment growth and numbers of products in development and on the market. Section V analyzes the implications of these results for the concept of geographically localized knowledge spillovers. A Data Appendix concludes the paper.

II. BIOTECHNOLOGY SCIENCE AND INDUSTRY IN CALIFORNIA

California plays a leading role in both the basic science and its commercialization and, if it were a separate country, would tie with Japan in both science and industry for second to the rest of the United States. California boasts 30% of the U.S. universities with biotech-relevant departments receiving the highest ratings in the 1982 National Academy of Sciences reputational survey.[10] California firms such as Amgen, Chiron, and Genentech are world leaders in biotechnology. These firms, along with other California firms, are among early entrants into commercial biotechnology, providing a sufficiently long track record for meaningful analysis of their patterns of performance and growth. To develop our California data base, we build on our U.S. work in which we linked existing publicly available data sets together with published information in ways that have not been done before, allowing us to construct the links between the basic science (using data bases created by and for scientists) and industry (using data bases created by and for firms).

Describing California New Biotechnology Enterprises

For the empirical work in this paper, the existing large scientist-article-citation-university-institute-enterprise-economy data base presented in Zucker, Darby, and Brewer [1994; 1997] was extended for California in five principal ways:[11] (a) a telephone census of California biotech firms verified existing 1989 and added 1994 employment data, (b) data on the numbers of products in development and on the market in 1991 was collected for these firms from *Bioscan*, (c) a second telephone survey of California star scientists was used to illuminate patterns of linkage between firms and stars not affiliated with firms, (d) patterns of coauthorship by stars not affiliated with firms were derived from the existing data base to uncover implicit linkages to firms, and (e) patenting activity by California stars reported in *Entrez* was examined to uncover differences according to the nature of the stars' ties, if any, to local firms.[12] The extended data base was used to examine the determinants of success for California biotech firms with special emphasis on understanding geographically localized knowledge spillovers.

In the May 1994 telephone census, we obtained usable data on 1989 and 1994 employment levels for 110 California biotechnology-using firms.[13] As expected from Zucker, Darby, and Brewer [1997], 109 of these (99.1%) were located in those four of the state's eight functional economic areas (regions) as defined by the Bureau of Economic Analysis where star scientists also worked. Over 40% of the firms are in the San Fran-

9. In California, a relatively small number of star scientists list affiliations with a third category of organizations: research institutes and hospitals. Since these organizations are not generally considered in studies of geographically localized knowledge spillovers and there are no significant linkages between their stars and firms, we focus in this paper exclusively on stars who are located at some time in at least one California university or firm.

10. The survey is reported in Lyle V. Jones, Gardner Lindzey, and Porter E. Coggeshall [1982]. The twenty U.S. universities with top-rated biotech relevant departments included California Institute of Technology, Stanford, and the University of California campuses at Berkeley, Los Angeles, San Diego, and San Francisco.

11. This work was funded by a grant to Zucker and Darby for "Linking California Universities and Scientists to the Biotechnology Industry" from the University of California Systemwide Biotechnology Research and Education Program.

12. For *Entrez*, see U.S. Department of Health and Human Services [1994].

13. Details are described in Zucker, Darby, and Armstrong [1994, 29–30, 55].

cisco Bay region and another third in the San Diego region.[14]

Entry dates for our 110 firms were spread unevenly over time with 35% entering in either 1980 or 1981 compared to 13, 26, and 26% in 1976–1979, 1983–1985, and 1986–1989, respectively. This pattern is similar to that for all U.S. entries into biotechnology: A large number of the firms got their start around the time of the Genentech initial public offering in October 1980, a date considered a financial watershed in biotechnology commercialization (John Elkington [1985, 59–60]). We distinguish between new biotechnology firms founded specifically to exploit the new bioscience technologies (entrants) and preexisting firms (including subsidiaries and other subunits) which adopt these technologies (incumbents). Firm age is measured from date of founding for entrants and date of entry into biotech for incumbents. (Table A.1 lists variable definitions.) Biotech firms in principle also include organizations for which insufficient data exist to establish whether entrant or incumbent and, as in our sample, problematic organizations such as a joint venture between an entrant and an incumbent. In our 110-firm sample, there are 87 entrants and 22 incumbents, which is only slightly higher a ratio of entrants than the national average.

Since many biotech firms are working on pharmaceuticals which typically require about ten years of development and testing prior to FDA approval, revenues and especially profits are generally nonexistent early in those firm's development and cannot provide a reliable indicator of success. Market value of the enterprise would do better, but considerably less than half of the firms are publicly traded. As a result, for performance measures we focus on employment growth from 1989 to 1994 and the numbers of products in development and products on the market in 1991 as measures of enterprise success. At this early stage it is impossible to accurately separate all the winners from the losers in the competitive race, but these indicators seem to do so better than any alternatives.

Interestingly, success is heavily concentrated, particularly in those firms with connections to star scientists by 1989 described in the next sub-section: Firms with star ties had an average increase in employment of 366 workers from 1989 to 1994, compared to only 82 workers for firms without such ties. Firms with tied stars also account for an average of 10.7 products in development and 8.8 on the market compared to 1.2 and 3.5, respectively, for those without ties to star scientists. These star-firm ties, we shall see in section IV, are typically established before the firm, the star, or both achieve success.

California Star Scientists and Their Ties to Enterprises

As indicated by the organizational location given on their publications, 55 star scientists worked in California firms and universities during 1976–1989. Of these, ten gave a California firm at least once as their location during this period; we term these stars "affiliated" with the firm given.[15] It might appear that the other "unaffiliated" stars are pure academic scientists, devoid of commercial concerns and ties, but that conclusion in a number of cases would be misleading. Our telephone survey of California star scientists found that academic stars may simultaneously be linked to specific firms in a number of different ways: exclusive direct employment (often as CEO or other principal), full or part ownership, exclusive and nonexclusive consulting contracts (effectively part-time employment), and chairmanship of or membership on scientific advisory boards. These ties generally establish ownership rights and the star's compensation for the fruits of the collaboration. Given the distinguished achievement of these scientists, most chose to retain their university positions; even when employed full-time by a firm, many retain adjunct professorships. University stars thus tend to be a locally fixed input for commercial applications.

While most academics at major U.S. research universities are aware of colleagues who have become millionaires or billionaires as a result of starting a firm while retaining an university appointment, the picture of explicit contractual linkage to enterprises is at sharp variance with the picture familiar to

14. Most, but not all, of the remainder are located in the Los Angeles region. The Sacramento (Davis) region is the fourth area with star scientists.

15. One of these ten stars was affiliated sequentially with two firms over the period; the other nine stars were each affiliated with only one firm.

economists of how geographically localized spillovers work. The standard economic notion is that by being near the universities where cutting-edge research is being done, employees of local enterprises will hear of important discoveries first and thus be able to utilize them before others are aware of their existence, much less their value. In this paradigm, the information in the discovery is a public good freely available to those who incur the costs of seeking it out in the groves of academe. It is further assumed that scientific discoveries have only fleeting value unless formal intellectual-property-rights mechanisms effectively prevent use of the information by unlicensed parties; i.e., absent patents, trade secrets, or actual secrecy, the value of a discovery erodes quickly as the information diffuses.

Zucker, Darby, and Brewer [1997] have a different view: Scientific discoveries vary in the degree to which others can be excluded from making use of them. Inherent in the discovery itself is its degree of *natural excludability*: if the techniques for replication are not widely known prior to the discovery, then any scientist wishing to build on the new knowledge must first acquire hands-on experience.[16] If he or she cannot gain access to a research team or laboratory setting with that know-how, then working in that area may be very difficult if not impossible. They (and we) argue that a scientific discovery—especially, an "invention of a method of inventing" (Griliches [1957])—can give rise to localized industrial effects where the information is sufficiently costly to transfer due either to its complexity or tacitness (see Richard R. Nelson [1959], Kenneth J. Arrow [1962; 1974], Nelson and Sidney G. Winter [1982], and Nathan Rosenberg [1982]) and the information is embodied in particular individuals tied to particular locales.

The breakthrough discoveries involved in modern biotechnology have fundamentally changed how bioresearch is done. Once a new life form has been created and its use identified and sufficiently demonstrated, then those specific inventions are alienable from their creator through intellectual property mechanisms. However, the new techniques used in their creation have exhibited both high natural excludability and immense commercial value. Therefore, it is not surprising that Zucker, Darby, and Brewer [1997] found that where and when stars were actively publishing were important determinants of where and when enterprises built to use their special knowledge would be formed.

Ultimately, when the knowledge of how to practice a discovery has diffused widely and the information is part of routine science, the intellectual human capital associated with that knowledge will earn only the normal returns to the cost of acquiring it in graduate school.[17] In the early period when new industries are being built and old industries transformed as a result of a major scientific breakthrough, however, the intellectual human capital embodied in the relatively few individuals who possess it will have extraordinary value, particularly so for the early "superstars" (Rosen [1981]) who combine the requisite tacit knowledge of the commercially (or academically) valuable technique with the genius and vision to apply those techniques in the most promising areas of research.[18] Indeed these

16. Indeed natural excludability has created some problems for making the "enabling disclosure" that is required for a valid U.S. patent application. In order to obtain the seventeen-year monopoly granted by a patent the applicant must make a disclosure that will enable the public to practice the innovation once the patent expires. After some litigation and legislation, patents are now obtainable by biotech inventors who disclose their invention by placing a culture in a recognized public depositary. (See Rebecca S. Eisenberg [1987] for a discussion of this history.) Disclosure by deposit eliminates the inherent difficulty in disclosing the art used to obtain the invention so that it can be readily replicated.

17. Where natural excludability is entirely absent and the discovery can be easily incorporated into the human capital of any competent scientist, the discoverer(s) cannot earn any personal returns—as opposed to returns to intellectual property such as patents or trade secrets. In the case of biotechnology, it may be empirically difficult to separate intellectual human capital from the conceptually distinct value of cell cultures created and controlled by a scientist who used his or her nonpublic information to create the cell culture.

18. Clearly the extent to which access to particular localized individuals shapes the evolution of an industry is positively related to both the importance of the breakthrough and the degree of natural excludability. First, there must be the defining technological opportunity for commercialization but there must also be sufficient natural excludability to provide appropriability to individuals personally rather than through mechanisms of intellectual property. Thus precisely the same factors that drive technical progress for industries (Nelson and Edward N. Wolff [1992], Alvin K. Klevorick, Richard C. Levin, Nelson, and Winter [1995]) appear to be crucial at another level to endowing individuals with the opportunity to exert geographically localized influence.

stars can be the key determinant of the geographic agglomeration of the new industries (Zucker, Darby, Brewer [1997]). As we will show below, firms with most access to this intellectual human capital are most likely to be the winners in the new and transformed industries.

Since star scientists in biotechnology could simultaneously provide immense value to both great research universities and biotech firms, many chose to do both. Scientists in academe and firms agree in interviews that an effective way to identify those scientists wearing two hats is to examine the coauthorship pattern of stars unaffiliated with firms. A star is locally "linked" to a biotech firm if the star publishes an article with one or more scientists in the firm while he or she is located at a university in the same region as the firm. We hypothesize that such locally linked stars are the main channel by which university star scientists have influenced the success of biotech firms.[19]

They do so in two primary ways. First, linked star scientists provide access to and information about discoveries with potential commercial value made in their own and other university-based labs, transmitting complex, tacit knowledge by bench-level collaboration. Zucker, Darby, Brewer, and Yusheng Peng [1996] have shown that organizational boundaries serve as informational envelopes within which valuable information characterized by natural excludability is much more likely to be diffused than to those outside the organization. So, by being in both the university and the firm, the linked star is able to convey knowledge of processes and techniques which is not otherwise available to the firm.

Second, the linked university stars are able to maintain both university and firm relationships because of the very high quality of their input. Central to understanding how these dual affiliations work is the case study finding that bioscientists act as individual actors, as opposed to acting as agents of their primary ties, whether to the university or the firm (Zucker, Brewer, Oliver, and Liebeskind [1993]). These bioscientists can exercise their expertise independently primarily because they are recognized as having excellent "scientific taste" in the selection of research problems and using exceptional care and expertise in executing that research.[20] By exercising their "scientific taste" these linked stars judge the likely payoff of different lines of bioscience research and advise the firm concerning their relative merit. As noted above, we expect that the scientific advisory boards play a similar role, and plan to investigate them in later research. Linked stars, while they generally have a significant financial interest in the firm, also often have the advantage of being part of a broad external "network for evaluation," providing the basis for high quality input in product development decisions (Zucker [1991]).[21]

As described in the Data Appendix, we examined every article through 1989 reporting a gene-sequence discovery written by a star located in a California university or firm. We classified for each star whether he or she was affiliated with a firm on that article or, if not, whether any scientists from a firm in the local region were coauthors on the article. Accordingly, for each article the star was classified as affiliated with or unaffiliated with a specific firm. Unaffiliated stars were further subdivided into those who were locally linked to a specific firm or untied to any firm.[22]

19. Coauthorship serves here as a proxy for a variety of more complex relationships including ownership, employment, consulting, and serving on a board of directors or scientific advisers. In future research, we plan to examine some of these other relationships separately using data from IPO prospectuses for those firms that have gone public (see Lerner [1995]). This will require expanding the data set to cover the entire U.S.

20. Dual affiliations of bioscientists are a specific instance of a very general phenomenon in which individuals with exceptional quality of performance and productivity compared to others with similar kinds of skills come to have more than one simultaneous organizational affiliation (Zucker [1991]). For example, top ranked physicians tend to have multiple affiliations with hospitals and top producers and directors are much more likely to have multiple contracts with independent film companies while others have none (R. R. Faulkner and A. B. Anderson [1987, Tables 2–4]).

21. For similar internal firm use of external evaluative information, see Robert Eccles and Dwight Crane [1988, 152–154] on the use of customer surveys to determine salary increases, bonuses, and promotion in investment banking.

22. The linked and untied distinction for our university stars may suggest James D. Thompson's [1967] distinction between boundary-spanning and core personnel. However, this analogy could prove misleading since nearly all the university stars have extensive contacts with organizations other than their own university and those stars who are actively involved in collaborations with firms typically do so for their own gain and not as part of their role in the university.

TABLE I
Commercial Involvement and Citations of California Star Scientists

	Genetic Sequence Patents		
	No Patents	Some Patents	Total (both)
		Numbers of Stars	
Ever firm affiliated	5	5	10
Local firm linked	6	2	8
Untied (never linked or affiliated)	32	5	37
Total distinct stars	43	12	55

Test for independence in a 3×2 contingency table: $\chi^2(2) = 6.20\, (p \leq 0.05)$

		Average Annual Citations[a]	
Ever firm affiliated	138.0	615.3	376.6
Local firm linked	147.6	303.2	186.5
Untied (never linked or affiliated)	95.1	188.7	107.8
Total distinct stars	107.4	385.5	168.1

[a]This table gives for each class the total number of citations in the *Science Citation Index* per scientist per year for the years 1982, 1987, and 1992 for all genetic-sequence discovery articles authored or coauthored by each of the 55 California star scientists.

For the empirical work reported in section IV below, we use counts of these classified articles, but first consider a simpler breakdown of the 55 individual California stars as affiliated (if ever affiliated with a California firm), linked (if ever linked to a California firm but never affiliated), and untied (otherwise) as reported in Table I.

As discussed above, while natural excludability leads to the embodiment of certain knowledge and techniques in individuals, there is also a role for formal intellectual property rights. When the knowledge is implemented to create alienable, potentially commercially valuable discoveries, patents offer an important mechanism for appropriating returns. Thus, the patenting of discoveries by stars is an indication of expected commercial value of their discoveries. The data presented in the upper panel of Table I show that those stars affiliated with firms are very different in their patenting activity compared to unaffiliated university stars: half have patented discoveries versus only 15.6% of the university stars. Among the university stars, a quarter of those linked to specific firms in the same region have patented discoveries compared to 13.5% of those not tied to such firms. Although the numbers are small, the standard $\chi^2(2)$ test rejects the hypothesis of independence.

Comments on earlier versions of this paper suggest that it is commonly thought—especially among academics—that the very best scientists are unlikely to be involved with firms or to patent their discoveries. This presumption may rest on the idea that scientific norms of openness and disinterestedness in fact contribute to the advance of science and are most likely to be observed by the best scientists.[23] Commercialization of high science is presumed to be done by lesser scientists, perhaps in the role of bridge-builders between science and technology (Lieberman [1978]).

23. In the literature, the norms of science are said to dictate open disclosure to all other scientists, in an "invisible college" model of the flow of scientific information (Diana Crane [1972]; Robert M. Merton [1970, 80-111]). However, as noted in Zucker, Darby, Brewer, and Peng [1996], whenever the discoveries have significant value, whether as pure science or as a commercial product, behavior has often systematically excluded potential competitors from access to that information (James D. Watson [1980]; G. Taubes [1986]). There is considerable evidence that this has occurred in bioscience, perhaps because of a divergence between the norms and the reward structure (Eisenberg [1987, especially 197–205, 214–216, and 229–231]).

However, as seen in the lower part of Table I, patented scientists are generally more widely cited than unpatented scientists and affiliated scientists are more cited than linked scientists who in turn are more cited than untied scientists. To take the extreme cases, affiliated scientists with patents are cited 6.5 times as frequently as untied scientists without patents. Citation frequency is the standard indicator of scientific eminence in quantitative work.[24] It appears that work done either in or in collaboration with firms is quite productive in terms of influence on future research. Zucker and Darby [1996] report for the U.S. as a whole that this apparent positive effect of commercial ties on scientific productivity of the stars partially reflects the fact that stars with commercial ties publish at a higher rate (before, during, and after those ties) than those who do not ever have them. The largest part of the explanation, however, comes from a much higher average rate of citation to articles written by stars with or as employees of firms than before or afterwards. When we put these results together with the strong positive effects of stars on firm productivity, as we report here, the relationship between scientists and firms appears to be truly symbiotic contributing to the success of both science and commercial ends.

Relation to Other Empirical Work

In describing the general features of our data base, we have raised questions concerning prior models and related empirical measures of innovative inputs, the knowledge generation process, and outputs of that process. Innovative inputs have generally been treated as measured by the resources invested in them, most often R&D expenditures. The underlying assumption that equal investment in R&D produces equal innovative returns is easily falsifiable and recently patents have been seen as a better measure of inputs than output of the innovative process.[25] We know that most scientists have very low productivity, with most of the scientific output typically produced by the top 1% or 2% of all scientists working in a specific area (Harriet Zuckerman [1967], Crane [1972], Paul D. Allison, J. Scott Long, and Tad K. Krauze [1982]). Thus, we are concerned with identifying and locating the most productive, star scientists (all of whom were located in universities initially), their explicit linkages to firms, and actual measures of their productivity in the firm linkage. The latter is measured here by the number of articles reporting genetic-sequence discoveries that are published either with the firm listed explicitly as the star's affiliation or which include firm scientists as coauthors.

As an alternative to patents as a measure of innovative output, we separately measure three different aspects of the economic impact of inventive activity: the number of products in development (generally close to the inventive activity), the number of products on the market (indicating successful development), and net growth in employment (indicating successful development and marketing of products). Each can be seen as a successive step in moving from the initial invention to the impact on economic performance of the firm. Although we use only cross-sectional data in the work reported here, we are proposing in future work to exploit available information to develop time series on the first two measures for 1987–1994, as well as less complete data on employment changes at the firm level over the same period.

III. ESTIMATION METHODS

Because of the nature of the processes which we will be estimating, we use two approaches to estimation: (a) poisson regressions are used for products in development and on the market and (b) a modified Type II Tobit procedure following Takeshi Amemiya [1985] is used for change in employment. The procedures used are outlined here and explained more fully in Zucker, Darby, and Armstrong [1994].

Products in development and on the market are count variables (0, 1, 2, ...) with a considerable number of 0 observations and other values tailing off in frequency as they increase numerically. Accordingly, the regressions were estimated in the poisson form appropriate for count variables with numerous zeroes using LIMDEP (William Greene [1992, 539–549]), with the Wooldridge regression-based

24. See, for example, Mark Blaug [1985, vii-ix], David Colander [1989], H. P. F. Peters and A. F. J. van Raan [1994], and R. Plomp [1994].

25. See Griliches [1990] for a review of the use of patent statistics as economic indicators.

correction for the variance-covariance matrix estimates.[26] The poisson regressions estimate the logarithm of the expected number of firm births; so the signs and significance of coefficients have the usual interpretation.

It would seem that employment growth is appropriately estimated by OLS, but we again run into a problem of too many zeroes—although in this case only one eighth of the observations (see Table A.3). We suspect that these reports of no change in employment are most often due to response-bias in which firms for which there has been little change report no change rather than bother to look up the exact figures. An observationally equivalent interpretation (which is closer to most of the econometric literature) is that there are fixed costs of change so it will be undertaken only where the gains to doing so are significant. In this case a modified Type II Tobit following James Heckman [1976] two-stage procedure is appropriate. The first stage is an ordered probit which predicts whether the firm reports decreased, unchanged, or increased employment. The second stage (a) estimates the size of a change using only the observations reporting changes, (b) corrects for sample-selection bias by including as a regressor the Inverse Mills Ratio (IMR) computed in the first stage, and (c) calculates a consistent and unbiased estimate of the variance-covariance matrix due to the work of Keunkwan Ryu [1993] and Woon Gyu Choi [1993]. Inclusion of the IMR results in unbiased estimates of the coefficients of other explanatory variables; a significant coefficient on the IMR confirms the presence of selection bias.

IV. EMPIRICAL RESULTS

In this section we report results on three different measures of biotech-using firm performance: the number of products the firm has in development as of 1991, the number of products it has on the market at that time, and the net change in its employment over the five years following 1989. None of these measures are by any means perfect substitutes for changes in value of the enterprise as measures of success. However, many biotechnology firms are small start-up ventures which are not yet publicly traded and other firms are subunits of much larger enterprises not primarily involved in biotechnology. Thus, the sample size would be unacceptably reduced from the 76 firms for which we have data if we restricted ourselves to those for which enterprise value was also available.[27] Nonetheless, these three indicators are interesting in and of themselves from organizational, economic, and policy perspectives and are likely to reflect spillover effects if they exist.

As indicated above, in these estimates we use a set of variables built by counting the number of articles reporting genetic sequence discoveries and written by each star located in California universities or firms, according to whether for each article the star was affiliated with, locally linked to (by being in the same region as their coauthors affiliated with the firm), or not tied to each of the 110 firms in the data set. Using an article count to "weight" the stars' publications was important because there was considerable variation in the authorship and coauthorship histories (though the star tie, unweighted by articles, produces qualitatively the same results). The count also served to capture the strength and/or productivity of the relationship between the star scientists and enterprises.

In using these variables to explain biotech firm performance, obvious concerns about the direction of cause-and-effect had to be addressed. For example, firms could have established ties to star scientists as a signalling device or because firms which became successful ex post absorbed scientists as part of their expansion. These concerns were not supported

26. As discussed in Jerry Hausman, Bronwyn H. Hall, and Griliches [1984], the poisson process is the most appropriate statistical model for count data such as ours. In practice, overdispersion (possibly due to unobserved heterogeneity) frequently occurs. Given the problems with resort to the negative binomial discussed by A. Colin Cameron and Pravin K. Trivedi [1990], Jeffrey M. Wooldridge [1991] developed a flexible and consistent method (his "Procedure 2.1") for correcting the poisson variance-covariance matrix estimates regardless of the underlying relationship between the mean and variance. We are indebted to Wooldridge and Greene for advice in implementing the procedure in LIMDEP subsequent to Zucker, Darby, and Armstrong [1994].

27. From an organizational sociology perspective, products in development is the preferred measure because it is conceptually most closely related to the R&D function of intellectual human capital. The extent to which scientific entrepreneurs are able to transfer intellectual human capital value to the firm and the accuracy with which that capital is priced in the financial markets is the subject of future research.

in the data because tied stars typically were either with the firm when or very soon after it was founded, or became part of the firm's production and innovation process shortly after the star had first published (Zucker and Darby [1996]).[28] In the first case, with a ten-plus year product cycle the timing argues that these scientists were the cause—not the result—of the success of the firm. In the second case, the scientists are too young to be any sort of signalling device, and again it is more plausible that they are working with the firm because they are productive, not famous. We also constructed an analogous set of measures by which individual stars were counted as affiliated, linked, or untied without regard to article weighting. The model results using these variables, while qualitatively similar to the weighted model results, performed less well in terms of goodness of fit.[29] If star recruitment was a signalling effect motivated by the desire to list individual stars on the company roster, then the weighted model results should not have been superior to the unweighted results.

Products in Development

The number of products the firm has in development as of 1991 is taken from the firm's listing in *Bioscan* (see Data Appendix). Generally, these products are in various stages of clinical trials or field testing, although in some cases the listed products may be at earlier stages of development or have received F.D.A. market approval but not yet be marketed. Among the three indicators examined, this measure appears to be most closely related to success in application of the new biotechnologies and least affected either by use of other technologies or by differences in business strategy (e.g., in-house production and/or marketing vs. joint agreements with established pharmaceutical firms).

We first examine the results of a poisson regression in the spirit of Jaffe [1989]. Model a in Table II explains products in development by the number of gene-sequence-discovery articles written by stars from within a local university who were not affiliated with any firm ("unaffiliated articles"), by whether or not the firm is a entrant (as opposed to a biotech subunit of a pre-existing firm), by the firm's age, and by whether or not the firm utilizes the rDNA technology. Model b broadens model a by also including the number of gene-sequence-discovery articles written by stars affiliated with the firm ("affiliated articles"). Consider first model a: As expected, the firm's age and its use of the rDNA technology both contribute significantly and positively to the number of products in development. Interestingly, the new dedicated biotech firms are significantly more likely to be developing new products than incumbent firms. Finally, we see that the stars concept which was used by Zucker, Darby, and Brewer [1997] to identify the scientists around which entrants and incumbents would be built also appears to work here to uncover important, positive, significant geographically localized spillover effects of local universities on the success of nearby-enterprise R&D efforts in the manner of Jaffe [1989]. These results all persist in model b, although the addition to the poisson regression of the significantly positive number of affiliated articles for the firm generally reduces both the magnitude and t-statistics for the other explanatory variables.

Models c and d are identical to models a and b, respectively, except that the number of articles written by university stars is broken down into those written in collaboration with scientists from the firm ("linked articles") and the remaining ("untied articles"). The explanatory power of the regressions are substantially and significantly improved by relaxing the implicit constraint that research done in the university has the same effect on enterprise R&D productivity whether or not it is done in collaboration with the enterprise's scientists. In fact, the coefficient on articles written by local university stars not in collaboration with the firm loses its significance and nearly vanishes in magnitude. What had appeared to be an undifferentiated geographically localized knowledge spillover seems to have resulted from a specification error: If we

28. For scientists who began publishing by the year the firm entered, the average lag between its entry and the first tied publication by the star was 3.0 years—small given the time to establish a new laboratory and given the prevalence of listing affiliation where the work was done rather than where one is employed at time of publication. For star scientists who began publishing after the firm was founded, the average lag from the star's first publication to the first publication affiliated or linked with the firm was 2.1 years.

29. These results will be made available upon request to any of the authors at least through 1999.

TABLE II
Estimates for Products in Development Poisson Regressions, Dependent Variable: Products in Development

Variables	Coefficients (standard errors)			
	model a	model b	model c	model d
Constant	−3.3850*** (0.1875)	−2.4341*** (0.2576)	−1.9838*** (0.2102)	−1.9324*** (0.2796)
Local Star Authorships of:				
Unaffiliated articles	0.0017*** (0.0002)	0.0013*** (0.0003)	—	—
Untied articles	—	—	0.0001 (0.0003)	0.0001 (0.0003)
Linked articles	—	—	0.3222*** (0.0190)	0.3197*** (0.0161)
Affiliated articles	—	0.0083*** (0.0011)	—	0.0006 (0.0010)
Other Firm Characteristics:				
Dummy-entrant	1.6232*** (0.1201)	1.4363*** (0.1379)	1.3504*** (0.1396)	1.3417*** (0.1455)
Firm Age	0.2088*** (0.0098)	0.1395*** (0.0150)	0.1256*** (0.0116)	0.1209*** (0.0191)
Dummy-use rDNA	0.9038*** (0.0785)	0.6082*** (0.1099)	0.2974*** (0.1114)	0.2845*** (0.1278)
Log-likelihood	−196.06	−190.48	−169.48	−169.46
Log-likelihood (coefficients = 0) = −255.28				
Significance levels: * ≤ 0.10, ** ≤ 0.05, *** ≤ 0.01				

Note: Unaffiliated articles = Untied articles + Linked articles
Standard errors (adjusted by Wooldridge's [1991] Procedure 2.1) are in parentheses below coefficients.

did not have the data set required to identify which university stars were linked to which enterprises, then this study would have confirmed the previous findings. Instead we find that no such indiscriminate spillovers are apparent for biotechnology products in development.

It is interesting that when linked articles is admitted to the regression separately, the coefficients of both affiliated articles and Dummy-use rDNA are cut sharply in magnitude, and only the latter retains its significance. We believe that the insignificance of affiliated articles in this regression should not be taken to mean that having stars affiliated with an enterprise is irrelevant for developing new products. For example, enterprises with affiliated stars are most likely to attract university stars to collaborate with them.[30] The enterprises with links to university stars are able to most effectively acquire and use the results of ongoing university research; linked stars become the conduits for the information and for evaluation of different lines of research related to potential product development. Furthermore, we will see that affiliated articles have a significant, positive effect when products on the market is substituted as the dependent variable.

Products on the Market

The number of products each biotech firm has on the market as of 1991 also is taken from the firm's listing in *Bioscan*. Although some of these products result from the application of the new biotechnologies, by and large, given the typical decade-long FDA approval process for human therapeutics, the products on the market include a higher proportion than those in development of reagents and instruments used in applying the technol-

30. The number of linked articles is positively and significantly correlated with the number of affiliated articles, and neither of these variables are significantly correlated with untied articles.

TABLE III
Estimates for Products on the Market and Change in Employment

Dependent Variable:	Products on Market[a]		Change in Employment[b]	
	model c	model d	model c	model d
Independent Variables	Coefficients (standard errors)			
Constant	1.4615*** (0.1035)	1.4953*** (0.1085)	89.417 (250.37)	51.022 (252.53)
Local Star Authorships of:				
Untied articles	−0.0006*** (0.0002)	−0.0006*** (0.0002)	−0.7164 (0.4282)	−0.7130 (0.4256)
Linked articles	0.1378*** (0.0120)	0.1143*** (0.0140)	130.74** (63.875)	172.17** (78.157)
Affiliated articles	—	0.0024*** (0.0006)	—	−4.3847 (4.7782)
Other Firm Characteristics:				
Dummy-entrant	−0.3398*** (0.0721)	−0.3512*** (0.0733)	−235.18 (164.25)	−225.45 (163.82)
Firm Age	0.0673*** (0.0083)	0.0643*** (0.0088)	32.604 (22.448)	36.439 (22.719)
Dummy-use rDNA	−0.5778*** (0.0551)	−0.5880*** (0.0567)	259.67* (132.02)	267.78** (131.56)
Inverse Mills ratio	n/a	n/a	162.17** (74.530)	166.33** (74.189)
Log-likelihood	−296.42	−296.20	n/a	n/a
Log-likelihood (coeffts.=0)	−323.14	−323.14	n/a	n/a
Adjusted R^2	n/a	n/a	0.1659	0.1623
Significance levels: * ≤ 0.10, ** ≤ 0.05, *** ≤ 0.01				

Notes: Standard errors are in parentheses below coefficients.

[a]Poisson regressions, standard errors adjusted by Wooldridge's [1991] Procedure 2.1.

[b]Second-stage Heckman estimates with consistent variance-covariance matrix. The dependent variable is employment growth for the nonzero observations.

ogy rather than the result of the new biotechnologies themselves.

For products on the market (and also employment growth) there is no evidence of geographically localized knowledge spillovers, so models a and b are not reported in either case in Table III to conserve space.[31] The differences between products on the market and products in development rationalize most of the differences between the results reported in Tables II and the first two columns of Table III. In Table III, the coefficients on Dummy-entrant and Dummy-use rDNA are both negative and significant which we believe reflects the fact that firms which are engaged primarily in applying the new technologies are likely to have fewer products than their suppliers. Nonetheless, firm age (measured from the date of entry into biotech), affiliated articles (in model d) and especially linked articles have a positive effect on the number of products on the market. As to the latter effects, the positive coefficients reflect the fact that the most successful firms using the new biotechnologies are the ones most likely to have products which reached the market.

A more surprising result is the very small but statistically significant coefficients found for publications by local university star scientists not linked to the firm (untied articles). We do not think that this represents any sort of negative spillover from the unlinked university stars but may reflect the fact that areas with many stars have many firms competing

31. These models are reported in Zucker, Darby, and Armstrong [1994] but without the Wooldridge correction for the standard errors.

for local resources so that we detect a slight congestion effect in these coefficients. This would be consistent with the result found in Zucker, Darby, and Brewer [1997] that the number of stars in a region has a positive but diminishing effect on firm births.

Changes in Employment

The first-stage ordered probit estimates (useful primarily as a basis for correction for selectivity bias) are not reported here but is available in Zucker, Darby, and Armstrong [1994]. In sum, those estimates indicate that an enterprise is more likely to increase employment and less likely to decrease employment if it uses rDNA technology to produce human therapeutics and if it is younger. We will see below, however, that firm age is (insignificantly) positive in determining the size of the firm's employment increase. What we have identified in the first-stage estimates appears to be a sorting phenomenon in which as the enterprise matures, it either begins to grow more rapidly or else to shrink according to whether or not its strategy is proving successful. This increasing probability of decline or failure is in contrast to the findings for U.S. manufacturing plants generally reported by Timothy Dunne, Mark J. Roberts, and Larry Samuelson [1989], perhaps because it is so difficult to tell whether or not a young biotech enterprise is or is not achieving success.

The last two columns of Table III report selectivity-corrected second-stage OLS estimates for change in the number of employees analogous to those reported for products in Tables II and III. Following Ryu [1993], the variance-covariance matrix has been corrected for the non-spherical error structure inherent in the two-stage estimation of the Type II Tobit procedure as noted in section III.[32] The linked stars are seen to have a significant positive effect as with the other performance variables. The untied university stars do not enter significantly nor (in model d) do the affiliated stars as was the case for products in development. Of the other variables, the only significant effects are a positive coefficient on the use of the rDNA technology and another on the Inverse Mills ratio which signifies the importance of the selectivity bias correction.

Summary of Empirical Results

For all three measures of firm performance, the collaborative research evidenced by publications written by university stars and employees of particular firms has a significant positive effect on the firm's performance whenever these linked articles are in the regression. Publications by stars affiliated with a firm have a positive impact on performance whenever they are significant, but their effect is not robust. While affiliated stars then do not have a robust direct effect on firm performance, it should be noted that firms with affiliated stars are more likely to have linked stars and that this significant correlation between the linked- and affiliated-articles variables makes it difficult to separately identify their effects.

Local university stars in general, as well as those specifically not linked to the firm, display inconsistent impacts—inconsistent both across models and performance measures and with the predictions of the geographically localized knowledge spillover literature. For the variable most directly related to innovative activity, the number of products in development, there appears to be a significant classic geographically localized knowledge spillover effect from the number of local university stars. However, this disappears when university stars are broken down into those which have direct links to the specific firm and all others. For the other performance variables, local university stars not linked to the enterprise are estimated to have, if anything, a negative effect, although where statistically significant this effect is tiny in magnitude. Such negative effects—if they are taken seriously—are consistent with congestion effects to the extent they are associated with more local firms, but not with geographically localized knowledge spillovers.

An interesting issue of interpretation arises with respect to the differential performance of entrants and incumbents. The entrants appear to have significantly more products in development and less on the market and insignifi-

32. Recall that these regressions are run only for the subset of firms for which employment changes were reported. We also tried percentage changes in employment with no significant differences in the qualitative results. We believe the level changes are easier to interpret and conform more closely to a Type II Tobit model and so report them here.

cantly less employment growth in comparison to incumbents. We related the differences in significant coefficients to the comparative emphases on therapeutics by entrants and reagents and instruments among incumbents. However, in a case study of a large pharmaceutical firm (Zucker and Darby [1995]), two other plausible explanations were suggested by (the not disinterested) scientists at that incumbent: Pharmaceutical firms are more experienced and hence better at choosing winning research projects which get to market and less inclined to keep pursuing projects which look like dead ends because they are one of the few things going on at the firm. The incentive system and policy at this incumbent, at least, also discourages announcements of products in development until they are proven in humans (late Phase II of clinicals) while many entrants have to tout their nascent projects to the financial markets to obtain initial or additional financing. Clearly it would be premature to attempt a definitive performance comparison between entrants and incumbents on the basis of these results.

For the biotechnology industry, we have provided strong evidence that apparent geographically localized knowledge spillovers in fact represent specific market exchange. Informal discussions with many of the linked scientists indicates that this exchange often takes place through equity sharing. With even a small degree of non-salvageability among the transacting parties—as when a firm's product development becomes uniquely dependent on a particular star scientist—coupled with a high degree of uncertainty, it is not surprising to observe such "vertical integration" as described by Benjamin Klein, Robert Crawford, and Armen Alchian [1978]. While we await other researchers' results for additional industries and technologies, we hypothesize that apparent local spillovers generally may confound strong effects from university scientists directly involved with local firms and weak or nonexistent effects from all other university scientists.

V. CONCLUSIONS

Paul M. Romer [1990] shows that knowledge spillovers have substantial macroeconomic implications for growth and international trade. These implications result because investments in R&D produce an output (characterized by Romer as a set of instructions) which is both nonrivalrous and at least partially excludable.[33] Our empirical results suggest that what have been termed geographically localized knowledge spillovers do not seem to fit this definition of spillovers, at least in the case of biotechnology. In particular, because discoveries in this area are characterized by natural excludability and embodied in human capital and because transmitting the discovery to others requires the active participation of those with the knowledge, the technology cannot be characterized as a nonrivalrous set of instructions.[34] Thus to the extent that our results generalize to other cases of apparent geographically localized knowledge spillovers, the inefficiencies derived in Romer's analysis are not present.

The standard notion of geographically localized knowledge spillovers is based on the idea that university scientists are pursuing disinterested basic research, the results of which can be most quickly put to commercial use by those enterprises located nearby who can most readily learn novel results from social ties between employees and university scientists or by attending informal seminars at the university.

Our picture of how the process in fact has worked in biotechnology is quite different. We find that all the parties involved (government and other funding agencies, universities, professors, and enterprises) are or can be connected by contractual and/or ownership ties in competitive markets. The most productive scientists generally are either employees of or collaborators with the enterprises. The government grants patent rights to universities (with a proviso for minimum royalty rates for discovering scientists) and rights of exploitation to scientists who embody any intellectual human capital resulting from their work. As a result, the prices paid by government funding agencies are reduced both directly due to any expected patent royalties to universities and

33. Nonrivalry implies that use by one person or enterprise does not reduce the amount available for use by others. Excludability, which refers to the ability of the owner of a good to prevent others from using it, can derive from technology, law, or both.

34. See Romer's careful discussion [1990, S74-S75] of the key distinction between his technology and human capital.

indirectly because competitive university salaries are lower, other things equal, in areas where faculty expect the possibility of receiving substantial outside income or wealth as a result of skills developed doing research at the university. Since these discoveries are characterized by natural excludability, the discovering scientists do not give away to enterprises the fruits of their intellectual human capital but instead enter into contractual arrangements with existing firms or start their own firm in order to extract the supranormal returns available to those fortunate and talented enough to acquire that capital. The scientists work with or create firms within commuting distance of home or university—where they nearly always retain affiliation—thus creating localized effects of university research. In this way, we see that what appeared to others as a case of knowledge spillovers with resulting inefficiencies is in fact a standard case of market exchange of rivalrous and excludable goods. We believe that this geographically localized impact, like extraordinary returns to intellectual human capital itself, is a transitory phenomenon during the important initial period of industry development resulting from a major, commercially valuable scientific breakthrough characterized by natural excludability.

The quantitative estimates of the effects of the collaborations between academic stars and firm scientists are interesting in themselves, providing direct evidence of a large, significant impact of academic research on local industrial development. For an otherwise average firm, the full models d in Tables II and III imply that just two such collaborative articles translate into one more product in development, one more product on the market, and 344 more employees.[35] Since the product relations are nonlinear, we should note that five such collaborative articles imply 4.7 more products in development, 3.5 more products on the market, and 861 more employees.

The empirical results in this paper are restricted to evidence on geographically localized knowledge spillovers in the California biotechnology industry. However, we believe that the analytical technology we are developing and many of our central findings will prove generalizable to other cases of major scientific breakthroughs which lead to important commercial applications. As observed by Alvin Klevorick, Richard Levin, Nelson, and Sydney Winter [1995], economists have recently explained an industry's R&D intensity "by two key factors—*technological opportunity* and *the ability to appropriate returns from new developments*." [their emphasis] While relatively few mature industries are driven by technological opportunity in the form of basic scientific breakthroughs, the emergence phase of important industries frequently is so driven. The most important lessons are to be drawn not for analysis of past breakthroughs which have formed or transformed industries, but for those yet to come in sciences we can only guess. Nonetheless, we are pleased that other researchers are beginning to apply our earlier work to the analysis of technologies such as semiconductors and high-temperature superconductors. We are encouraged in our belief that our results will be generalizable to other technologies by extended discussions with those familiar with those technologies and by some fragmentary evidence in the literature.

For example, Bruce Kogut, Gordon Walker, Weijian Shan, and Dong-Jae Kim [1994] find broadly similar patterns of interfirm relationships for large and small enterprises within and across national boundaries for semiconductors and biotechnology, although they argue and point to some corroborating evidence that embodiment of technology in individual scientists is even more important for semiconductors than for biotechnology. Levin [1982] notes that [as with products of recombinant DNA] integrated circuits were initially nearly impossible to patent. More generally, David Balkin and Luis Gomez-Mejia [1985] report on the distinctive emphasis on incentive pay and equity participation for technical employees in (largely non-biotech) high-tech firms, especially for the "few key individuals in research and development ... viewed as essential to the company...." Success in high-technology, espe-

35. The antilog of the regressions in Table II and III (first two columns) give the expected numbers of products in development and on the market respectively. The numbers quoted in the text are calculated by substituting the mean values for the other independent variables from Table A.2 and comparing the antilog for linked articles = 0, 2, and 5. The regressions in the last two columns of Table III are linear in linked articles, so a similar procedure is not required to predict the employment effects.

cially in formative years, we believe comes down to motivated services of a small number of extraordinary scientists with vision and mastery of the breakthrough technology.

The results reported here, if they are confirmed for additional industries and locations, have great significance for the interpretation of geographically localized knowledge spillovers: First, the welfare losses normally associated with uncompensated externalities are not present.[36] Second, the question of why some apparent knowledge spillovers—as in biotechnology—are geographically localized while others—as in high-temperature superconductivity—are not appears to be intimately related to what Zucker, Darby, and Brewer [1997] termed intellectual human capital, in particular whether the discovery in question is characterized by natural excludability. Third, university policies which limit professors' ability to contract freely with and to establish ownership positions in firms may protect norms of disinterested science at the cost of limiting technology transfer and local development in scientific areas characterized by natural excludability.

DATA APPENDIX

A detailed description of the basic data sets developed for the Project on "Intellectual Capital, Technology Transfer, and the Organization of Leading-Edge Industries: The Case of Biotechnology" (Lynne G. Zucker, Marilynn B. Brewer, and Michael R. Darby, Principal Investigators) is presented in Zucker, Darby, and Brewer [1994] and Zucker, Darby, and Armstrong [1994]. These data will be archived upon completion of the project in the Data Archives Library at the UCLA Institute for Social Science Research.

Summary definitions of the variables are provided in Table A.1. Table A.2 provides summary statistics for the variables. Table A.3 provides summary statistics for key variables broken down by regions and by whether employment is reported as increased, unchanged, or decreased.

Our basic source for employment growth from 1989 to the winter or spring of 1994 is a telephone census conducted in May 1994. We attempted to conduct telephone interviews for all 182 California biotech firms in the Zucker, Darby, and Brewer [1994] data base and obtained 110 useable observations for employment (1994) as detailed in Zucker, Darby, and Armstrong [1994, 29–30, 55]. For 78 of these firms, we were able to count how many products were in development and on the market using 1991 issues of *Bioscan* (1992 or 1990 issues in a few cases). Two more cases were lost due to missing data on whether the firm reported using the recombinant DNA technology (indicated by Dummy-use rDNA = 1). The missing cases are generally for small firms, marginally in the industry and are not believed to distort the results reported (see Zucker, Darby, and Armstrong [1994] for further discussion).

Zucker, Darby, and Brewer [1994] defined star scientists based on the universe of all articles reporting genetic sequence discoveries up to 1990.[37] Worldwide 327 leading researchers (the "stars") were identified on the basis of the number of genetic sequence discoveries and articles reporting them up to 1990 for which they were an author. These 327 stars were listed as authors on 4,061 distinct articles in major journals. These articles were hand collected and used to identify and locate institutional affiliations at the time of publication for each of our stars and their coauthors who were either other stars or "collaborators" (6,082 scientists worldwide).

"Affiliated articles" counts the number of articles by stars where the firm is given as the affiliation. The summed number of articles written by stars listing universities located in the region ("unaffiliated articles") is the same for each firm in a given region. This total is disaggregated into two firm-specific variables: "Linked articles" counts the number of articles by a university star coauthoring with a scientist affiliated with the firm (either a collaborator or another star scientist); "untied articles" counts the number of articles by university stars that were not linked to the firm. For each firm, the sum of its linked and untied articles equals its unaffiliated articles count.

36. It should not be entirely surprising that where the holders of the valuable knowledge are few in number, contracts can be negotiated which eliminate the effects of potential externalities; see Ronald H. Coase [1960]. Coase [1974] also observed that economists are overly prone to assume externalities, as in lighthouses, where market contracts can in fact exist. Steven N.S. Cheung [1987, 456] notes that Coase objected to the term The Coase Theorem since "what he did was to specify the conditions under which the traditional theorem of exchange becomes operative." This paper aims to show that those conditions may also apply in the case of what has been considered to be geographically localized spillovers.

37. See also Zucker, Brewer, Oliver, and Liebeskind [1993]. The rDNA technology devolved from high to routine science in the late 1980s; so 1990 was a good year to end the literature base for identifying scientists possessing intellectual human capital.

TABLE A.1

Variables List

All observations are taken from the Zucker, Darby, and Brewer [1994] data base and defined for the 110 usable California-firm observations in the 1994 telephone census except as noted.

Variable Name	Description
Category-emp. growth	Categorical variable: –1, 0, or 1 as employment growth is less than, equal to, or greater than 0, respectively.
Dummy-any products	Categorical variable: 1 if the firm has any products in development or on the market; 0 otherwise[a]
Dummy-human diagnostics	Categorical variable: 1 if the firm is involved in human diagnostics; 0 otherwise[a]
Dummy-human therapeutics	Categorical variable: 1 if the firm is involved in human therapeutics; 0 otherwise[a]
Dummy-entrant	Categorical variable: 1 if the firm is a entrant; 0 otherwise
Dummy-use rDNA	Categorical variable: 1 if the firm uses the recombinant DNA technology; 0 otherwise[c]
Employment growth	The change in the firm's employment from 1989 to 1993: employment(1994)—employment(1989)
Employment(1989)	Employment levels in 1989 from the Zucker, Darby, and Brewer [1994] data base[b]
Employment(1994)	Employment levels in winter-spring 1994 from the telephone census
Firm age	Age of firm in 1989; 1990—date of founding
Inverse Mills ratio	Inverse–Mills ratio as defined in Section III
N	Number of observations for a variable or regression after excluding missing observations
Products in development	Number of products in development by firm[a]
Products on market	Number of products on the market by firm[a]
Local Star Authorships of:	
Affiliated articles	Sum over all stars of the number of articles written by each star while affiliated with the firm at any time 1976–1989[d]
Linked articles	Sum over all stars of the number of articles written by each star during 1976–1989 which (a) lists the star at a university located in the firm's region, and (b) is coauthored with one or more other scientists who is (are) listed as affiliated with the firm
Unaffiliated articles	Sum over all stars of the number of articles written by each star during 1976–1989 which (a) does not list the star as affiliated with any firm and (b) does list the star as affiliated with a university located in the firm's region[e]
Untied articles	Sum over all stars of the number of articles written by each star during 1976–1989 which (a) lists the star at a university located in the firm's region, and (b) is not coauthored with any other scientists who is (are) listed as affiliated with the firm. Note: untied articles = unaffiliated articles—linked articles.

Notes:

[a]*Source*: *Bioscan*, 1991 [1992 or 1990 in a few cases] (N = 78, 32 missing observations)

[b]The telephone census described above confirmed these numbers closely in every case where they could be obtained; with two exceptions (see note a to Table A.3), the original data base numbers were retained to maintain time consistency.

[c]Excludes those observations in the Zucker, Darby, and Brewer [1994] data base which have no technologies reported unless the firm has licensed the Cohen-Boyer patent. (N = 103, 7 missing observations)

[d]In addition to any earlier articles, each of the stars affiliated with a firm was so identified in at least one article published in 1988 or 1989.

[e]By definition, this variable will have the same value for each firm located in a given region.

TABLE A.2
Sample Statistics for Variables

Variable	N	Mean	Std. Dev.	Minimum	Maximum
Category-emp. growth	110	0.1818	0.9205	–1	1
Dummy-any products	78	0.7564	0.4320	0	1
Dummy-human diagnostics	78	0.5769	0.4972	0	1
Dummy-human therapeutics	78	0.5897	0.4951	0	1
Dummy-entrant	110	0.7909	0.4085	0	1
Dummy-use rDNA	103	0.5437	0.5005	0	1
Employment growth	110	100.21	456.82	–383	3766
Employment(1989)	110	120.67	276.47	1	1800
Employment(1994)	110	220.88	661.36	0	5400
Firm age	110	7.3091	3.1789	1	14
Products in development	78	1.9615	4.2194	0	22
Products on market	78	3.8846	5.3500	0	29
Local Star Authorships of:					
Affiliated articles	110	1.5818	13.375	0	139
Linked articles	110	0.1545	0.8587	0	7
Unaffiliated articles	110	204.02	153.72	0	376
Untied articles	110	203.86	153.54	0	376

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TABLE A.3

Means and Standard Deviations of New Biotechnology Enterprise Characteristics by BEA-Defined Region and Enterprise Employment Growth

Variable	Region			Category-emp. growth		
	N	Mean	St. Dev.	N	Mean	Std. Dev.
	San Francisco Region			Employment Decreased		
Category-emp. growth	48	0.12	0.91	38	−1.00	0.00
Employment growth	48	46.21	269.70	38	−47.13	69.61
Dummy-any products	33	0.76	0.44	27	0.77	0.42
Products in development	33	2.73	5.62	27	1.30	2.32
Products on market	33	3.76	4.34	27	3.15	5.03
Firm age	48	7.44	3.21	38	8.18	2.56
	San Diego Region			Employment Unchanged		
Category-emp. growth	37	0.49	0.83	14	0.00	0.00
Employment growth	37	71.22	128.26	14	0.00	0.00
Dummy-any products	29	0.79	0.41	9	0.89	0.33
Products in development	29	1.03	1.61	9	0.78	1.30
Products on market	29	5.10	7.12	9	5.22	5.67
Firm age	37	6.24	3.22	14	9.29	3.10
	Other California Regions			Employment Increased		
Category-emp. growth	25	−0.16	0.94	58	1.00	0.00
Employment growth	25	246.80	866.68	58	220.93	603.93
Dummy-any products	16	0.69	0.48	42	0.71	0.46
Products in development	16	2.06	4.02	42	2.64	5.35
Products on market	16	1.94	2.26	42	4.07	5.54
Firm age	25	8.64	2.56	58	6.26	3.21
	Full Sample					
Category-emp. growth	110	0.18	0.92			
Employment growth	110	100.21	456.82			
Dummy-any products	78	0.76	0.43			
Products in development	78	1.96	4.22			
Products on market	78	3.88	5.35			
Firm age	110	7.31	3.18			

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