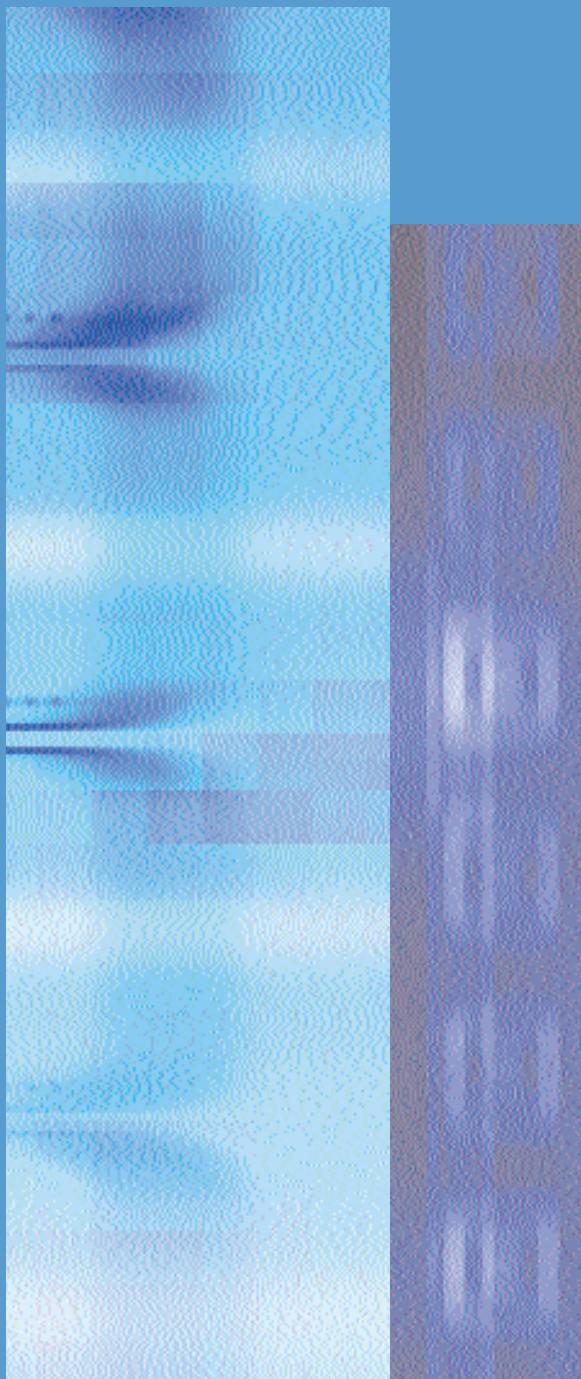


Signs of Life:

The Growth of Biotechnology Centers in the U.S.

JOSEPH CORTRIGHT
AND HEIKE MAYER

THE BROOKINGS INSTITUTION
CENTER ON URBAN AND
METROPOLITAN POLICY



Joseph Cortright is an economist with IMPRESA, Inc., and principal investigator for the New Economy Observatory of Portland State University's Institute for Portland Metropolitan Studies. **Heike Mayer** is a graduate research assistant with the Observatory and a Ph.D. candidate in the university's College of Urban and Public Affairs. Cortright and Mayer also wrote "*High Tech Specialization: A Comparison of High Technology Centers*," published by The Brookings Institution Center on Urban and Metropolitan Policy in January 2001.

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Executive Summary

The biotechnology industry is built on fundamental breakthroughs in the understanding of genetic and biological processes to develop new means of diagnosing and treating disease. Biotechnology is at the heart of an important and fast-growing new sector of the U.S. economy, and as the industry expands, it has become a focal point of many local, regional, and state economic development strategies. The present report is a survey of biotechnology research and commercialization in the 51 largest U.S. metropolitan areas. By providing an examination of the industry, its location, and the key ingredients needed to foster its development, the report may help to inform regions across the country that are hoping to capture a share of biotechnology growth. Several important insights have emerged from the analysis.

The biotechnology industry is concentrated within nine of the nation's 51 largest metropolitan areas.

These nine areas account for three-fourths of the nation's largest biotechnology firms and for three-fourths of the biotech firms formed in the past decade. Two of the nine metropolitan areas, Boston and San Francisco, established themselves as the research leaders in biotechnology in the early days after the industry's founding in the 1970s and continue today to be the dominant centers of the biotech industry. Two other metropolitan areas, Philadelphia and New York, have substantial concentrations of biotech activity, related chiefly to the historical presence of the headquarters of the nation's largest pharmaceutical manufacturers. Since the 1970s, three other metropolitan areas have emerged as significant centers of biotech industry—San Diego, Seattle, and Raleigh-Durham—each of which has built upon a well-recognized and well-funded medical research establishment and has been the site of many start-up firms.

Two additional metropolitan areas, Washington/Baltimore and Los Angeles, also have a concentration of biotech activity. Washington, D.C., has a significant biomedical research establishment and is home to the National Institutes of Health (NIH); in addition, several firms related to the exploration and

mapping of the human genome are located in the Washington/Baltimore area. Los Angeles is home to the nation's largest biotech firm, Amgen, located in Thousand Oaks.

These nine biotech regions are leaders because they have two necessary elements for industry growth: strong research capacity and the ability to convert research into successful commercial activity.

The present analysis suggests that the critical factor in the development of a biotechnology industry is not only the availability of pre-commercial medical research but also the availability of continuing private-sector investment in product development. Most biotech firms operate at a loss, spending large amounts on research and development for several years in advance of earning any sales revenue. These money-losing biotech research firms depend on venture capital investments, on research contracts and equity investments from large pharmaceutical companies (usually in exchange for marketing rights), and on sales of their company stock in public markets.

Biomedical research activity is now relatively widespread, but thus far only a few of the country's 51 largest metropolitan areas have demonstrated the entrepreneurial and financial capacity required for consistently generating

significant numbers of new biotechnology-related businesses. Five of the nine top biotechnology metropolitan areas—the leaders (Boston and San Francisco) and three other areas in which biotech is growing rapidly (San Diego, Seattle, and Raleigh-Durham)—account for the bulk of the growth of new biotechnology firms. Together these five areas have accounted for 75 percent of the new venture capital in biopharmaceuticals in the past 6 years, for 74 percent of the value of research contracts from pharmaceutical firms, and for 56 percent of the new biotech businesses formed during the 1990s.

Thus far none of the other 42 largest metropolitan areas in the United States has developed a significant concentration of biotechnology activity.

These other 42 metropolitan areas are divided into three groups, as follows:

- Four metropolitan areas (Chicago, Detroit, Houston, and St. Louis) can be classified as research centers with limited commercial activity because they rank above average in research activity but below average in commercialization.
- Twenty-eight metropolitan areas have some biotechnology research and commercialization but at levels well below the average of the 51 metro areas in the sample. These may be regarded as median metropolitan areas.
- Ten metropolitan areas (Charlotte, Grand Rapids, Jacksonville, Las Vegas, Louisville, Norfolk, Orlando, Phoenix, San Juan, and West Palm Beach) have no significant biotech research or commercialization, with levels of both research and commercialization at less than 10 percent of the average of the 51 metropolitan areas in the sample.

Biomedical research activity is now relatively widespread, but thus far only a few of the country's 51 largest metropolitan areas have demonstrated the entrepreneurial and financial capacity required for consistently generating significant numbers of new biotechnology-related businesses.

The historically low odds of success and the extended stretch of time associated with developing and securing regulatory approval for commercial biotechnology products mean that metropolitan areas seeking to develop a biotech industry will need to invest a significant amount of time and resources.

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Development of a successful biotechnology cluster requires a considerable amount of time and investment.

Although growing rapidly, the biotechnology industry is still a small portion of most metropolitan economies.

Established concentrations of medical researchers and research institutions change slowly. It often takes a decade or more to develop biotechnology-based products, and perhaps one in 1,000 patented biotech innovations produces a successful commercial product. The historically low odds of success and the extended stretch of time associated with developing and securing regulatory approval for commercial biotechnology products mean that metropolitan areas seeking to develop a biotech industry will need to invest a significant amount of time and resources.

To date, even successful biotechnology industry clusters have produced only modest returns to their regional economies. Most biotechnology firms are quite small: nationally only 44 have more than 1,000 employees. (Institute for Biotechnology Information 2001) Biotech firms typically contract with global pharmaceutical firms to produce, market, and distribute successful products rather than attempting to create their own capacity to do so. In the two largest concentrations of biotech activity in the nation (Boston and San Francisco), none of the largest biotech firms is among either region's 25 largest private employers.

Introduction

Biotechnology, an industry built on fundamental breakthroughs in the understanding of genetic processes, is barely three decades old. Biotech is widely perceived to be the next great frontier of scientific advancement that will bring with it whole new industries. The potential economic impacts of new technologies, though unknown, seem to be huge.

Clearly, the competition to be a biotech center will be keen. Who will triumph? For those metropolitan areas that do not already have a strong biotechnology industry cluster, what will it take to develop one?

The relevance of biotechnology breakthroughs to people's daily lives has become increasingly clear. In June 2000 an international team of researchers announced that they had completed mapping the human genome, an accomplishment compared to Isaac Newton's physics observations. This biotech advancement is predicted to lead to a new era of medicine in which scientists develop treatments and vaccines that target the molecular underpinnings of disease. In recent months, attacks using Anthrax spores have heightened public awareness of the potential of bioterrorism and have also triggered demand for the antibiotic Cipro.

The interest in biotechnology is especially strong among those involved in promoting economic development. A survey of 77 local and 36 state economic development agencies reported that 83 percent have listed biotechnology as one of their top two targets for industrial development (Grudkova 2001). Some 41 states have undertaken programs or activities to stimulate the development of biotechnology (Battelle Memorial Institute, State Science and Technology Institute, *et al.* 2001). Clearly, the competition to be a biotech center will be keen. Who will triumph? For those metropolitan areas that do not already have a strong biotechnology industry cluster, what will it take to develop one?

The present survey examines the location and intensity of biotechnology activity in the 51 U.S. metropolitan areas with populations of a million or more. It offers a systematic assessment of various measures of biomedical research and biotech commercialization, the two primary components of a strong and successful industry. There exists no single universally agreed-upon definition of biotechnology, but the range of data sources presented in the survey offers a variety of complementary perspectives on the varying facets of the biotechnology industry. The analysis is based on the composite picture provided by these various data sources.

The unit of analysis is the census-defined Metropolitan Statistical Area (MSA), with the Bureau of the Census list used for ranking metropolitan areas by population. Census combines adjacent metropolitan areas having strong commuting ties into consolidated metropolitan statistical areas; the report follows that same convention in grouping and ranking metropolitan areas. For brevity, these metropolitan areas are referred to by the name of the principal or largest city (or in some cases, cities) in the metropolitan area, even though all of the data are tabulated for the entire metropolitan area. Our sample includes the 51 metropolitan areas in the continental United States and San Juan -Caguas-Arecibo, in the Commonwealth of Puerto Rico.

Overview of the Biotechnology Industry

Biotechnology is the application of biological knowledge and techniques pertaining to molecular, cellular, and genetic processes to develop products and services. The biotechnology industry, as it defines itself, consists of firms established to develop this knowledge and to exploit it commercially. Biotechnology has potential applications in a wide variety of industries. It is already used in agriculture (genetic engineering of plants and animals for food and fiber), in manufacturing (food processing and chemical engineering), and even in computing (bio-computers)—all of them important although often related more closely to nonmedical uses of biotechnology. The largest category of biotechnology applications is in health and medicine: diagnosing, treating, and in some cases preventing disease. Standard and Poors estimates that human diagnostics and therapeutics account for 95 percent of biotechnology revenues (Standard and Poors 2000). Because diagnostics and therapeutics constitute the largest segment of the biotech industry, the report focuses on these applications of biotechnology. (A fuller description of the report's industry definition is contained in the appendix.)

Biotechnology is not synonymous with medical technology or even with high-tech medicine. Many medical technologies and disciplines are unconnected to genetic and cellular manipulation. A wide variety of medical-device manufacturers produce everything from diagnostic instruments to surgical tools to physical prostheses, but these producers are considered to be largely outside of the area of biotechnology, as are firms developing software or information technology for medical records, epidemiology, and other such purposes. These are all important technologies, but they are generally unconnected to the genetic and cellular

techniques that are the hallmark of biotechnology. (An important exception is the production of software and tools for gene sequencing and analysis.)

Biotechnology firms are not separately classified as such in either the Standard Industrial Classification System or in its successor, the North American Industry Classification System (NAICS). Instead, most biotechnology firms are assigned to one of two broader industry categories encompassing research and development and drug manufacturing—namely, NAICS five-digit industry 54171 (Research and Development in the Physical, Engineering, and Life Sciences) or NAICS industry group 3254 (Pharmaceutical and Medicine Manufacturing). For the purposes of gathering statistical data, the present report focuses on these two classifications.

Structure of the Pharmaceutical and Biotechnology Industries

The pharmaceutical industry and the biotechnology industry have a number of important characteristics that distinguish them from each other and from other industries. There follows a brief overview of the history and development of these two industrial sectors, their current structures, and some of the important aspects of the regulatory and competitive environment surrounding firms in each one of them.

The 1997 Economic Census provides data on the number of firms, employment, and sales by firms in the pharmaceutical and life science industries (**table 1**). (As noted earlier, these industry categories include a broader set of activities than simply biotechnology.) In 1997 the pharmaceutical and biotechnology industries represented by these industry classifications had total sales of nearly \$105 billion and employed about 300,000 persons in the United States. The industry has added about 100,000 jobs in the last 15 years, although year-to-year employment

growth has been uneven, declining in the mid-1990s but rebounding and growing rapidly in the final years of the decade.

The industry classifications shown in **table 1** comprise many different types of firms, including pharmaceutical manufacturers and makers of a wide variety of related products including vitamins, herbs, blood derivatives, anesthetics, antiseptics, and medical mouthwashes. The bulk of employment and sales is accounted for by large vertically integrated pharmaceutical manufacturers. No separate category exists for biotechnology firms, which are defined not by their products but by the technologies they use. Biotechnology firms are generally defined as those firms founded for the purpose of applying biological knowledge and techniques to develop products and services. The present survey adopts the common definition of biotechnology used by firms in the industry, by the industry's leading trade association, and by investment analysts and adopted by the majority of comprehensive academic studies of the industry.

Biotechnology research firms tend to be small and fairly recently established and to devote most of their resources to research and development. Pharmaceutical firms are much larger and much

older and have well-developed manufacturing and marketing operations, often worldwide in scale. The world's pharmaceutical industry is led by U.S.-based giants like Merck and Bristol-Myers-Squibb and by European-based firms like Bayer and Novartis. **Tables 2 and 3** provide a list of the ten top-grossing biotech and pharmaceutical firms in the United States.

Firms tend not to move between these two categories—small biotech firms, even extraordinarily successful ones, do not grow into large pharmaceutical firms. Instead, biotech research firms tend to sell or license their technologies to larger pharmaceutical firms, or to form joint ventures with them, or to sell them their entire companies. The different business skills required and the high cost of scaling up to global-scale manufacturing and distribution usually discourage small research firms from growing internally.

The result is huge differences in the apparent optimal scale of biotech research firms and that of pharmaceutical firms, appropriately referred to as "Davids" and "Goliaths." The typical pharmaceutical corporation is four decades older than the typical biotech research firm and a hundred times larger (measured by employment or sales) (Dibner 1999). For instance, according

TABLE 1: PHARMACEUTICAL AND BIOTECHNOLOGY INDUSTRY EMPLOYMENT AND SALES (UNITED STATES, 1997)

NAICS	Industry	Companies	Employment	Sales (in \$ thousands)
325411	Medicinals/Botanicals	312	23,378	11,920,571
325412	Pharmaceuticals	710	115,781	67,520,044
325413	Diagnostic Substances	202	36,502	8,145,884
325414	Biological Products, except Diagnostic	268	23,285	5,685,943
5417102	Research and Development in the Life Sciences	4,044	98,279	11,722,721
Total		5,536	297,225	104,995,163

Source: Census Bureau, 1997 Economic Census.

TABLE 2: SALES RANK OF TEN LARGEST U.S. BIOTECH COMPANIES, 1999

Rank	Biotech Company	Headquarters	Sales (\$)
1	Amgen Inc.	Los Angeles	3,340,100,000
2	Biogen Inc.	Boston	794,435,000
3	Genzyme Corp	Boston, MA	772,288,000
4	Immunex Corp	Seattle	541,718,000
5	Life Technologies Inc.	Basel, Switzerland	409,609,000
6	Medimmune Inc.	Washington, D.C.	383,375,000
7	Nabi	Boca Raton	233,603,000
8	Charles River Laboratories Inc.	Boston	219,276,000
9	Gilead Sciences Inc.	San Francisco	168,979,000
10	Serologicals Corp	Atlanta	129,744,000
Total			6,993,127,000

Source: PriceWaterhouseCoopers Edgarscan (2001).

TABLE 3: SALES RANK OF TEN LARGEST U.S. PHARMACEUTICAL COMPANIES, 1999

Rank	Pharmaceutical Company	Headquarters	Sales (\$)
1	Merck & Co., Inc..	New York City	32,714,000,000
2	Bristol-Myers-Squibb Co.	New York City	20,222,000,000
3	Columbia Laboratories Inc.	Miami	18,921,074,000
4	Pfizer Inc.	New York City	16,204,000,000
5	American Home Products Corp.	New York City	13,550,176,000
6	Abbott Laboratories	Chicago	13,177,625,000
7	Warner Lambert Co.	New York City	12,928,900,000
8	Eli Lilly & Co.	Indianapolis	10,002,900,000
9	Schering Plough Corp.	New York City	9,176,000,000
10	Pharmacia & Upjohn Inc.	New York City	7,253,000,000
Total			154,149,675,000

Source: PriceWaterhouseCoopers Edgarscan (2001).

to revenue rankings of publicly traded U.S.-based firms, Amgen, the largest U.S. biotech company, would be smaller than each of the ten largest pharmaceutical firms. The tenth-largest U.S. pharmaceutical firm has sales (\$7.25 billion) in excess of the combined sales of the ten largest biotech firms (\$6.99 billion).

The geography of the pharmaceutical and biotech firms tends to differ as well. The United States has the largest

concentration of biotechnology research firms, but many of the world's largest pharmaceutical firms are located in other nations, particularly in Europe. Global leaders in pharmaceuticals include Novartis (Switzerland), Hoffman-LaRoche (Switzerland), Glaxo-Wellcome (Great Britain), and Bayer (Germany). Not only do these firms sell their products in the United States but also many of them have U.S. subsidiaries or joint ventures with U.S. firms. Six of the nation's ten largest pharmaceutical firms

are headquartered in the New York-Philadelphia corridor, but none of the ten largest biotech firms is found in that area (PriceWaterhouseCoopers Edgarscan data, based on 1999 sales).

There also exists a great difference in profitability between biotechnology firms and pharmaceutical firms. Most small biotech firms are losing money. According to Ernst and Young, the typical biotech firm spent \$8.4 million on research and development and earned revenues of \$2.5 million in 1998. In contrast, pharmaceutical firms tend to be extremely profitable. Merck & Company, one of the largest pharmaceutical houses, had net income of \$4.6 billion that same year, an amount greater than the collective \$3.4 billion loss of all of the biotech research firms combined.

Differences in size are reflected also in differences in industry volatility.

Biotechnology firms regularly rise and fall, according to industry observers: Dibner (2000) estimated that half of the biotech firms formed since the 1970s had folded or were merged into other companies. Pharmaceutical firms tend to be much more long-lived, despite the recent wave of mergers among the pharmaceutical industry leaders (which has produced even larger firms).

The pharmaceutical sector and the biotech sector are characterized by very widespread intersectoral ties between firms. These ties take the form of cross-ownership, licensing, joint ventures, and research agreements. Large pharmaceutical firms often invest in promising research at smaller biotech firms. Small firms obtain access to the pharmaceutical firms' regulatory expertise and manufacturing and marketing capability. Firms frequently share technology: Recombinant Capital (2001), a research firm specializing in the biotechnology industry, reports more than 10,000 industry alliances during the 1990s.

Economics of Biotechnology

The distinctive economics of biotechnology greatly shapes the development of the industry. The process of developing new biopharmaceutical products is uncertain, time consuming, and expensive.

Biotechnology is a risky business. Improved understanding of genetics has led to some novel and successful therapies, but relatively few research projects lead directly to new products. In a given year, the National Institutes of Health (NIH) will fund about 25,000 research projects. Researchers and private companies get an average of 5,500 patents for new biotechnology in a given year. Around 400 biotech medicines are in development, but only about 100 biotech-related drugs have reached the market in the past 30 years, with the top ten accounting for nearly all of the sales (Standard and Poors 2000).

The process of developing new biotechnology projects is time consuming. Not only is there considerable work in research before a drug is developed but also any promising products must endure lengthy testing and clinical trials to prove their safety and efficacy. Development of a new drug typically takes between five and twelve years (Dibner 1999).

The high level of uncertainty of success and the great length of time required to develop biotech products make biotech development a costly proposition. Biotech firms need to pay for expensive medical research, laboratory facilities, and legal fees many years in advance of any likely sales revenue and with uncertain prospects of success. This reality makes large amounts of patient, up-front capital an essential ingredient for successful biotechnology firms.

Role of Government Policy

In many respects, biotechnology is the quintessential knowledge-based industry. Genetic material is analogous to encoded information. Many of the advances in biotechnology stem from applying information technology to developing a better understanding of how genetic processes work and what genes are responsible for which traits and diseases.

It is no surprise then that intellectual property is a defining feature of the biotechnology industry. Biotechnology involves the creation of new ideas through research, the development of new products and processes embodying these ideas, the testing of the efficacy of these products, and the communication of this information to physicians and patients.

Government policy plays an important role in almost every stage of the biotechnology industry. Government support for basic and applied research provides much of the knowledge on which new products are based. The government heavily subsidizes the training of medical researchers. Patents on drugs, on diagnostic products, and most recently on gene sequences codify the ownership of particular kinds of knowledge. The country's patent policy is set by Congress and administered by the U.S. Patent and Trademark Office. Most biotechnology products cannot be offered for sale unless their safety and efficacy have been approved by the Food and Drug Administration. The FDA also regulates the conditions for manufacturing pharmaceuticals and for advertising them to consumers. Finally, government policies on health care, particularly the decision of whether to include coverage for particular drugs or therapies in national health care programs like Medicare and Medicaid, influence the demand for drugs.

It is difficult to overstate the importance of these governmental decisions to the performance of this industry. Everything from fundamental questions of policy—can a gene sequence be patented?—to mundane administrative trivia has a profound effect on industry development. For instance, at one point the patent office had accumulated a backlog of more than 11,000 biotechnology-related patent applications, producing enormous uncertainty over property rights and product development (Dibner 1999).

Methods

The study aims to identify the top biotechnology clusters in the United States, using data gathered on various aspects of biomedical research and commercialization in order to ascertain the relative amount of biotechnology activity in 51 metropolitan areas. Biomedical research capacity and activity were examined first, as measured by employment and education, NIH funding levels, and the number of biotechnology patents issued in each metropolitan area. Biotechnology commercialization activity was then assessed by looking at the level of venture capital funding, the value of research contracts with pharmaceutical companies, the level of initial stock market offerings, the number of biotechnology firms with 100 or more employees, the number of new biotechnology firms established during the 1990s, firms' market capitalization, and firms' membership in industry associations.

The composite measures were constructed as follows. For each variable, such as NIH funding, the average level of activity was computed for the 51 metropolitan areas in the sample, and the level of activity in each metropolitan area was indexed to this overall average. For each metropolitan area, a composite measure of activity was then computed as the average of its index scores on each of the variables.

Findings

Findings from the analysis include the following, each of which will be discussed in some detail:

- The biotechnology industry is highly concentrated.
- Biotechnology centers flourish for varying reasons.
- Research and commercialization are key elements in growing a successful biotechnology industry cluster.

The biotechnology industry is highly concentrated.

Four general groupings of the 51 metropolitan areas can be defined by the relative amount of biotechnology activity in each. Nine metropolitan areas stand out as biotechnology centers because they have above-average levels of biotechnology research activity and biotechnology commercialization. Four metro areas can be characterized as biotech research centers with limited commercial activity. Twenty-eight metro areas have median levels of biotech research and commercialization. Ten metro areas have no significant biotech activities taking place. **Table 4** provides a list of the metro areas and their classifications.

The U.S. biotechnology industry is concentrated largely within nine metropolitan areas: Boston, Los Angeles, New York, Philadelphia, Raleigh-Durham, San Diego, San Francisco, Seattle, and Washington/Baltimore. These nine areas account for more than three-fifths of all NIH spending on research and for slightly less than two-thirds of all biotechnology-related patents. Biotechnology commercialization is even more concentrated within these areas: more than three-fourths of all biotech firms with 100 or more employees and those firms founded in the past decade are in one of these nine areas; the same areas account for eight of every nine dollars in venture capital for biopharmaceuticals and for 95 percent of the dollars in research alliances.

Table 5 compares the average level of research and commercial activity in these nine biotechnology centers with the other 42 metropolitan areas in the sample analyzed. The activity gap between the nine biotechnology centers and the other metropolitan areas is quite wide. The typical biotechnology center has about eight times as much research activity as other metropolitan areas, about ten times as many large

TABLE 4: METROPOLITAN AREA CLASSIFICATIONS

Metropolitan Area

Biotechnology Centers

Boston—Worcester—Lawrence, MA—NH—ME—CT CMSA
 San Francisco—Oakland—San Jose, CA CMSA
 San Diego, CA MSA
 Raleigh—Durham—Chapel Hill, NC MSA
 Seattle—Tacoma—Bremerton, WA CMSA
 New York—Northern New Jersey—Long Island, NY—NJ—CT—PA CMSA
 Philadelphia—Wilmington—Atlantic City, PA—NJ—DE—MD CMSA
 Los Angeles—Riverside—Orange County, CA CMSA
 Washington—Baltimore, DC—MD—VA—WV CMSA

Research Centers

Chicago—Gary—Kenosha, IL—IN—WI CMSA
 Detroit—Ann Arbor—Flint, MI CMSA
 Houston—Galveston—Brazoria, TX CMSA
 St. Louis, MO—IL MSA

Median Metropolitan Areas

Atlanta, GA MSA
 Austin—San Marcos, TX MSA
 Buffalo—Niagara Falls, NY MSA
 Cincinnati—Hamilton, OH—KY—IN CMSA
 Cleveland—Akron, OH CMSA
 Columbus, OH MSA
 Dallas—Fort Worth, TX CMSA
 Denver—Boulder—Greeley, CO CMSA
 Greensboro—Winston-Salem—High Point, NC MSA
 Hartford, CT MSA
 Indianapolis, IN MSA
 Kansas City, MO—KS MSA
 Memphis, TN—AR—MS MSA
 Miami—Fort Lauderdale, FL CMSA
 Milwaukee—Racine, WI CMSA
 Minneapolis—St. Paul, MN—WI MSA
 Nashville, TN MSA
 New Orleans, LA MSA
 Oklahoma City, OK MSA
 Pittsburgh, PA MSA
 Portland—Salem, OR—WA CMSA
 Providence—Fall River—Warwick, RI—MA MSA
 Richmond—Petersburg, VA MSA
 Rochester, NY MSA
 Sacramento—Yolo, CA CMSA
 Salt Lake City—Ogden, UT MSA
 San Antonio, TX MSA
 Tampa—St. Petersburg—Clearwater, FL MSA

No Significant Biotech Research or Commercialization

Charlotte—Gastonia—Rock Hill, NC—SC MSA
 Grand Rapids—Muskegon—Holland, MI MSA
 Jacksonville, FL MSA
 Las Vegas, NV—AZ MSA
 Louisville, KY—IN MSA
 Norfolk—Virginia Beach—Newport News, VA—NC MSA
 Orlando, FL MSA
 Phoenix—Mesa, AZ MSA
 San Juan—Caguas—Arecibo, PR CMSA
 West Palm Beach—Boca Raton, FL MSA

**TABLE 5: SUMMARY MEASURES OF BIOTECHNOLOGY ACTIVITY
IN METROPOLITAN AREAS**

Measures of Biotechnology	Average Values for		
	All 51 Metro Areas	Top 9 Metro Areas	Other 42 Metro Areas
Biomedical Research Capacity and Activity			
NIH Research Funding, 2000, millions	\$229	\$812	\$104
Biotechnology-related Patents, 1990–1999	683	2,641	263
Index of Biomedical Research	1.0	3.7	0.4
Biotechnology Commercialization			
Venture Capital Investments in Biopharmaceuticals, 1995–2001, millions	\$191	\$957	\$27
Value of Biotech Research Alliances 1996–2001, millions	\$201	\$1,089	\$11
New Biotech Firms Established, 1991–1999	8	35	3
Biotechnology Firms with 100+ Employees, 2001	6	24	2
Index of Biotechnology Commercialization	1.0	4.8	0.2

Biotechnology Centers: Boston, Los Angeles, New York, Philadelphia, Raleigh-Durham, San Diego, San Francisco, Seattle, and Washington/Baltimore.

Source: See text.

and newly established biotech firms, and about 30 times more venture capital funding. On average, a top biotechnology center has about nine times as much biotech research activity and about twenty times as much biotech commercialization activity as any of the 42 metropolitan areas that are not biotech centers.

Four metropolitan areas (Chicago, Detroit, Houston, and St. Louis) rank above average in research activity but below average in commercialization. These areas may be classified as research centers with limited commercial activity. Although these four metropolitan areas have significant research activity—an average of more than \$500 million in NIH funding in 2000 and more than 1,100 biotechnology-related patents during the 1990s—they have modest levels of biotechnology commercialization, with only about \$80 million in biotechnology-related venture capital between 1995 and 2001, about \$23 million in research contracts from technology

alliances, and five new biotech firms founded during the 1990s. These four metropolitan areas have on average as much research activity as Seattle, San Diego, and Raleigh Durham, but they have only one-sixth as much related commercial activity.

Twenty-eight metropolitan areas have some amount of biotechnology research and commercialization, but at levels well below the mean of the 51 metropolitan areas in the sample. These areas can be regarded as median metropolitan areas, because their levels of biomedical research and commercialization are clustered at about the median values for the analyzed sample. Most metropolitan areas with a population of one million or more are home to at least one medical school and (thanks to widespread and growing federal support for biomedical research) to a noticeable level of research and patenting as well. Each of these 28 median areas receives about \$100 million in NIH-funded biotechnology research on average per year—a

substantial sum, but only an eighth of the \$800 million average level of NIH research spending in each of the nine major biotechnology metro centers. To date, none of the 28 median metro areas has developed more than modest levels of commercial biotechnology.

Only one (Denver) has garnered more than \$100 million in biotechnology-related venture capital investment, and only three (Denver, Minneapolis, and Salt Lake City) have recorded any biotechnology research alliances out of the nearly 500 recorded nationally. The typical median metropolitan area has had three new biotechnology firms start locally in the past five years and contains one and one-half biotech firms with more than 100 employees. On average the level of commercialization in these areas is one-twentieth as large as in the nine biotechnology centers.

Ten metropolitan areas (Charlotte, Grand Rapids, Jacksonville, Las Vegas, Louisville, Norfolk, Orlando, Phoenix, San Juan, and West Palm Beach) all have levels of both research and commercialization below 10 percent of the average of the 51 metropolitan areas in the sample. These areas can be classified as having no significant biotech research or commercialization. None of these metropolitan areas has a major medical school or other medical research institution, greatly limiting their access to NIH research funding. Only one of these ten cities (San Juan) appears on the NIH list of the 100 cities receiving the most NIH funding in 2000. Through 2000, eight of these ten cities have attracted no biotech-related venture capital, nine of the ten have no biotech research alliances, and seven of the ten have seen no new biotech start-ups in the last ten years. The small scope of their research infrastructure and activities and their minimal levels of commercial biotechnology suggest that these areas face the greatest challenge in trying to develop a new biotechnology industry.

Biotechnology centers flourish for varying reasons.

As a group, the nine metropolitan areas classified here as biotechnology centers have a substantial lead on other metropolitan areas in the development of commercial biotechnology. The characteristics of biotechnology activity in each of these nine areas differ substantially. Underlying these differences are varying reasons for the success of biotechnology centers: some had “first-mover” advantages by establishing an early lead in the technology; others built on a base of local pharmaceutical industry leadership; others have been exceptionally entrepreneurial in the past ten to fifteen years; and special conditions have enabled others to succeed. Based on the varying strengths that appear to have driven biotech development in each of these metropolitan areas, biotech centers can be classified into four distinct groups (pharmaceutical centers, biotech leaders, biotech challengers, and other biotech centers), as summarized in **table 6**.

[There] are varying reasons for the success of biotechnology centers: some had “first-mover” advantages by establishing an early lead in the technology; others built on a base of local pharmaceutical industry leadership; others have been exceptionally entrepreneurial in the past ten to fifteen years...

Pharmaceutical Centers

New York and Philadelphia are the traditional centers of the U.S. pharmaceutical industry. These two regions are relatively stronger in research than they are in commercialization (an interesting contrast with Boston and San Francisco, which have much higher indices of commercialization than of research). New York's research activity is about eight times the U.S. mean, and its commercialization about six times the U.S. mean. Similarly, Philadelphia has nearly four times the U.S. mean level of research

activity and about double the U.S. mean level of commercialization. Strikingly, although both regions have important concentrations of biotech firms (36 such firms with 100 or more employees in New York and ten in Philadelphia), both have actually lost share of commercial biotechnology activity as measured by new-firm formation vis-à-vis their performance during the 1980s.

**TABLE 6: SUMMARY MEASURES OF BIOTECHNOLOGY ACTIVITY IN BIOTECHNOLOGY CENTERS
GROUP AVERAGES**

Group of Metropolitan Areas	Pharmaceutical Centers	Biotech Leaders	Biotech Challengers	Other Biotech Centers
	New York, Philadelphia	Boston, San Francisco	San Diego, Raleigh-Durham, Seattle	Washington, Los Angeles
Biomedical Research Capacity and Activity				
NIH Funding 1999*	989	1,063	551	774
Patents 1990–1999	5,007	3,499	1,066	1,781
Index of Research Activity	5.8	4.9	2.0	3.0
Biotechnology Commercialization				
Venture Capital 1995–2001*	548	2,472	769	133
Alliances 1996–2001*	928	2,564	795	214
New Firms 1991–1999	27	68	32	17
Firms with 100+ Workers	23	40	17	21
Index of Commercialization	3.7	10.3	3.7	1.9

*Dollars in millions

Source: See text.

Biotech Leaders

By almost all measures, Boston and San Francisco stand out as the strongest biotech regions in the United States. Both were home to pioneering firms in the biotechnology industry in the 1970s and have continued to build on their first-mover advantages and on their solid research base. Both of these metropolitan areas are strong in biotechnology research but truly excel in commercialization. These regions have about five times as much research activity as the U.S. mean but about ten times as much biotech commercialization. Boston gets more NIH funding (about \$1.4 billion in 2000) than any other metropolitan area in the country, San Francisco and Boston each have three of the nation's 20 top-ranked medical research institutions, and each region accounts for more than 3,000 biotechnology-related patents in the past decade. These two regions also account for a majority of the venture capital investment made in biotechnology and also for a majority of the value of research alliances, and each has generated more than 60 new biotech companies in the past decade.

Biotech Challengers

Raleigh-Durham, Seattle, and especially San Diego have seen rapid growth in commercial biotechnology activity in the past decade. These regions have been particularly successful in generating new firms and in securing venture capital and research contracts with pharmaceutical firms. Each has an above-average level of research activity (1.6 times to 2.7 times the U.S. mean), but all are relatively stronger in

commercialization than in research. San Diego is clearly the strongest of the three, having attracted \$1.5 billion in venture capital and \$1.6 billion in alliance funding and having created 38 new firms in the past decade; San Diego now has 31 biotech firms with 100 or more employees. Seattle and Raleigh-Durham have garnered about \$400 million each in venture capital during the decade, resulting in 11 new firms in Seattle and 46 new firms in Raleigh-Durham.

Other Biotechnology Centers

Two other regions—Washington/Baltimore and Los Angeles—represent special cases. Each of these regions has a formidable concentration of research institutions and some particularly strong firms, and each region draws on special advantages. The Washington-Baltimore metropolitan area has an important concentration of biotechnology firms and is aided by the local presence of the NIH and the FDA. Research institutions in metropolitan Washington/Baltimore receive nearly a billion dollars in NIH research funding annually (ranking the area third after Boston and New York). In addition, the region is home to a number of important organizations serving the biotech industry, including the industry trade organization BIO and providers of legal and professional services. Los Angeles is the second-largest metropolitan area in the United States (after New York) and is the location of the headquarters of Amgen, the nation's largest biotech firm. Both regions have substantially stronger bases in research (almost four

times the U.S. mean for Washington/Baltimore and more than double the U.S. mean for Los Angeles) than they have in commercialization (slightly more than double the U.S. mean for Washington/Baltimore and about one and a half times the U.S. mean for Los Angeles). Both regions have a relatively large base of biotechnology activity, but neither has attracted as much venture capital financing as have the three biotech challengers.

Research and commercialization are key elements in growing a successful biotechnology industry cluster.

Biotechnology is highly concentrated within those metropolitan areas that combine a strong research capacity with the ability to convert research into substantial commercial activity. The geographic distribution of research activities and the contrasting distribution of private investment and new-firm formation illustrate how both these ingredients need to be combined in order to generate a thriving industry cluster.

Biotechnology Research

Almost every discussion of the biotechnology industry begins with reference to the fundamental role of biomedical research. Breakthroughs in the understanding of genetics, cellular processes, the functioning of the immune system, and the inner workings of viruses and bacteria have made it possible to pursue new and promising means of diagnosing and treating disease. Much of this research has been undertaken at medical schools and other medical research institutions with the substantial assistance of public funding from the National Institutes of Health. The insights from such research are the basis of this industry, and thus the initial step in understanding the geography of biotechnology is to examine the location of research institutions and research scientists.

Biotechnology is highly concentrated within those metropolitan areas that combine a strong research capacity with the ability to convert research into substantial commercial activity.

Research institutions are repositories of knowledge and expertise about the fundamental science behind biological processes. These institutions, staffed by biological scientists and other trained professionals and supported principally by publicly financed grant funding, undertake an enormous amount of fundamental research. They also train new generations of biological scientists. Most biotech companies can trace their intellectual roots and their human capital to these research institutions.

BIOLOGICAL-SCIENCE WORK FORCE AND EDUCATION: As a knowledge-based industry, biotechnology is highly dependent on the availability of specially trained professionals, particularly research scientists and technicians. One survey of biotech firms indicates that a majority of such firms' activities involve research and development, making access to highly skilled personnel a critical location factor (Dibner 2000). Highly skilled persons are more concentrated in some metropolitan areas than others. Occupational data compiled by the U.S. Bureau of Labor Statistics illustrate the patterns of concentrations of life scientists (Bureau of Labor Statistics 2000). (These data are not strictly comparable across metropolitan areas, since data for some occupational categories are suppressed for particular metropolitan areas because there are so few persons in those occupations or because a single firm employs a large portion of such persons.) **Table 7** shows that with the exception of Raleigh-Durham, the number of life scientists in 1998 is considerably higher in the biotechnology centers than in the other metropolitan areas. The particularly large number of scientists working in Washington/Baltimore, New York, and Boston is not surprising, given the relatively high number of medical research institutions in these areas.

Biotechnology employees are highly educated; many have doctoral degrees. A good indicator of the relative supply of highly trained individuals is the number of life sciences PhD degrees conferred annually in a metropolitan area. In addition, because PhD students are typically engaged in ongoing academic research as part of their degree programs, the number of life sciences PhD degrees conferred annually in a metropolitan area is also an indirect measure of research capacity. The National Science Foundation annually tabulates the number of life science PhDs issued by each of the universities in the United States (Hill 2000). In **table 7** this information has been aggregated by metropolitan area. The New York metropolitan area granted the most life sciences PhDs (519) in 1999, followed by Boston (355). Washington/Baltimore, Los Angeles, and San Francisco each conferred more than 200 life sciences PhD degrees that same year.

The quality of medical research and education is also likely to have a bearing on the development of a biotechnology industry. In particular, medical schools with the best reputations may be relatively more effective in recruiting the best faculty and students and in attracting funding for research activities. Surveys conducted by the National Science Foundation periodically assess the relative reputation of graduate educational institutions in a variety of disciplines (Hill 2000). The number of institutions ranked among the top 20 nationally in 1982 in each metropolitan area is shown in **table 7**. In all, eighteen of the top twenty institutions were located in the 51 metropolitan areas in the sample; all but two of those eighteen were located in the nine biotechnology centers.

RESEARCH FUNDING BY THE NATIONAL INSTITUTES OF HEALTH: Scientific advancement is the driving force behind the growth of the biotechnology industry. The federal government's generous and growing support for medical and biological research helps seed the creation of new ideas and not incidentally supports the education and training of new research scientists.

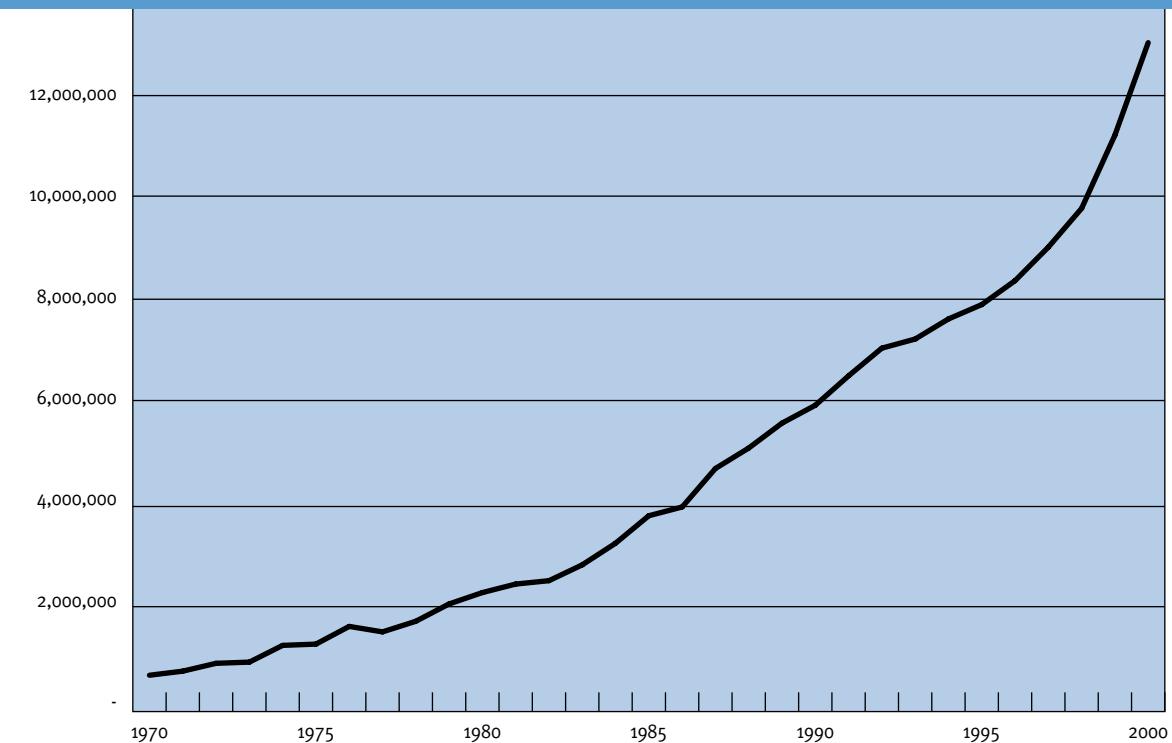
A wide variety of federal agencies provide funding for research and training related to medicine, health, and biotechnology and to related fields like agriculture, but the largest single funder of such research is the National Institutes of Health (NIH). During the past decade the growth rate of spending for NIH extramural research has been 7.8 percent annually. Total NIH spending for research has more than doubled during the 1990s, from about \$6.5 billion in 1991 to more than \$13 billion in 2000. Enthusiasm for continuing support for medical research shows no signs of waning: in December 2001 Congress approved a total fiscal-year 2002 budget of more than \$23.3 billion for NIH, an increase of 14.7 percent over the previous fiscal year. Through NIH, the government provides funding for research activities of universities, medical schools, research institutions, and in some cases private firms. In 2000 NIH disbursed a total of \$13.3 billion for research activities (National Institutes of Health 2001) (**figure 1**). Public support for biomedical research is large relative to the scale of the biotech industry. In 1998 the research and development budgets of biopharmaceutical firms totaled \$6.6 billion (Dibner 1999).

TABLE 7: BIOMEDICAL RESEARCH INFRASTRUCTURE

Metropolitan Area	Life Scientists 1998	Biological Science PhDs			Top-Ranked Research Universities 1982	NIH Funding to Top 100 Cities, 2000	
		Institutions Granting PhDs 1999	Number of PhDs Granted 1999	Amount		Share	
Biotechnology Centers							
Boston—Worcester—Lawrence, MA—NH—ME—CT CMSA	4,980	13	355	3	1,422,875,474	12.2%	
San Francisco—Oakland—San Jose, CA CMSA	3,090	3	215	3	703,529,044	6.0%	
San Diego, CA MSA	1,430	3	82	1	680,954,889	5.8%	
Raleigh—Durham—Chapel Hill, NC MSA	910	3	166	1	469,119,754	4.0%	
Seattle—Tacoma—Bremerton, WA CMSA	1,810	1	68	1	504,375,867	4.3%	
New York—Northern New Jersey—Long Island, NY—NJ—CT—PA CMSA	4,790	20	519	3	1,382,530,715	11.8%	
Philadelphia—Wilmington—Atlantic City, PA—NJ—DE—MD CMSA	1,410	7	139	1	596,195,344	5.1%	
Los Angeles—Riverside—Orange County, CA CMSA	2,450	7	218	2	594,666,368	5.1%	
Washington—Baltimore, DC—MD—VA—WV CMSA	6,670	12	241	1	952,835,848	8.1%	
Research Centers							
Chicago—Gary—Kenosha, IL—IN—WI CMSA	n.a.	7	177	1	416,777,457	3.6%	
Detroit—Ann Arbor—Flint, MI CMSA	150	3	105	-	349,064,265	3.0%	
Houston—Galveston—Brazoria, TX CMSA	750	6	135	-	420,810,647	3.6%	
St. Louis, MO—IL MSA	430	3	73	-	324,015,608	2.8%	
Median Metropolitan Areas							
Atlanta, GA MSA	860	4	47	-	183,862,069	1.6%	
Austin—San Marcos, TX MSA	610	1	58	-	28,091,551	0.2%	
Buffalo—Niagara Falls, NY MSA	1,100	1	45	-	61,504,692	0.5%	
Cincinnati—Hamilton, OH—KY—IN CMSA	n.a.	1	42	-	105,990,581	0.9%	
Cleveland—Akron, OH CMSA	n.a.	3	47	-	195,978,256	1.7%	
Columbus, OH MSA	140	1	99	-	105,040,196	0.9%	
Dallas—Fort Worth, TX CMSA	560	7	77	-	130,625,561	1.1%	
Denver—Boulder—Greeley, CO CMSA	640	1	52	1	208,884,942	1.8%	
Greensboro—Winston-Salem—High Point, NC MSA	190	1	25	-	76,990,609	0.7%	
Hartford, CT MSA	n.a.	2	56	-	34,352,802	0.3%	
Indianapolis, IN MSA	360	1	1	-	82,159,529	0.7%	
Kansas City, MO—KS MSA	220	1	11	-	27,921,183	0.2%	
Memphis, TN—AR—MS MSA	90	2	14	-	78,984,525	0.7%	
Miami—Fort Lauderdale, FL CMSA	n.a.	2	43	-	79,170,511	0.7%	
Milwaukee—Racine, WI CMSA	170	3	24	-	76,730,979	0.7%	
Minneapolis—St. Paul, MN—WI MSA	690	1	89	-	178,428,711	1.5%	
Nashville, TN MSA	380	2	58	-	140,546,951	1.2%	
New Orleans, LA MSA	n.a.	1	28	-	52,288,186	0.4%	
Oklahoma City, OK MSA	n.a.	1	23	-	35,789,408	0.3%	
Pittsburgh, PA MSA	240	4	63	-	281,542,496	2.4%	
Portland—Salem, OR—WA CMSA	780	3	28	-	125,520,699	1.1%	
Providence—Fall River—Warwick, RI—MA MSA	250	2	20	-	65,555,741	0.6%	
Richmond—Petersburg, VA MSA	290	1	45	-	50,052,818	0.4%	
Rochester, NY MSA	140	1	51	-	106,262,273	0.9%	
Sacramento—Yolo, CA CMSA	560	1	129	-	79,715,427	0.7%	
Salt Lake City—Ogden, UT MSA	370	1	32	-	105,325,621	0.9%	
San Antonio, TX MSA	320	1	20	-	123,381,414	1.1%	
Tampa—St. Petersburg—Clearwater, FL MSA	n.a.	-	-	-	25,372,505	0.2%	
No Significant Biotech Research or Commercialization							
Charlotte—Gastonia—Rock Hill, NC—SC MSA	100	-	-	-	-	0.0%	
Grand Rapids—Muskegon—Holland, MI MSA	n.a.	-	-	-	-	0.0%	
Jacksonville, FL MSA	360	-	-	-	-	0.0%	
Las Vegas, NV—AZ MSA	230	1	1	-	-	0.0%	
Louisville, KY—IN MSA	60	1	20	-	-	0.0%	
Norfolk—Virginia Beach—Newport News, VA—NC MSA	420	-	-	-	-	0.0%	
Orlando, FL MSA	170	-	-	-	-	0.0%	
Phoenix—Mesa, AZ MSA	420	1	20	-	-	0.0%	
San Juan—Caguas—Arecibo, PR CMSA	190	-	-	-	27,999,514	0.2%	
West Palm Beach—Boca Raton, FL MSA	200	1	1	-	-	0.0%	

Sources: National Institutes of Health 2001; National Science Foundation 2001.

FIGURE 1: NIH FUNDING FOR RESEARCH AND TRAINING, 1970–2000



Source: National Institutes of Health.

Funding by NIH is disbursed to research programs throughout the nation, but it goes disproportionately to areas with a large, well-established research infrastructure. **Table 7** illustrates the distribution of overall NIH research funding by metropolitan area for 2000. The greatest shares go to Boston (12.2 percent) and New York (11.8 percent).

The largest share of NIH funding goes to support research activities carried out at the nation's medical colleges and universities. **Table 8** shows the amount of NIH funding received by medical schools in each of the nation's 51 largest metropolitan areas in 1985, 1990, 1995, and 2000.

Federal support for biomedical research has increased in a steady and sustained manner. Total federal research funding for medical schools in these metropolitan areas more than tripled during the past decade and a half, growing from \$2.4 billion in 1985 to \$7.6 billion in

2000. Nearly every metropolitan area shared in this increase, which was distributed among metropolitan areas in a proportion very similar to their share of research activity during 1985. In this 15-year period only three metropolitan areas (Boston, New York, and San Francisco) saw their share of federal research funding decline by more than 1 percentage point; no metropolitan area saw its share of federal funding increase by more than 1 percentage point. Thus the volume of NIH support for medical schools increased rapidly and became slightly less concentrated, but the overall distribution pattern changed very little. The distribution of NIH funding is remarkably unvarying through time, with 92 percent of the variation in funding levels in 2000 being explainable by the level of 1970 funding.

BIOTECHNOLOGY PATENTS: Which metropolitan areas are the most successful at creating new ideas? Measures of research capacity such as the number of bioscientists or the amount of NIH funding reflect only the inputs into the knowledge creation process, not the outputs. Patent data, although far from perfect, can provide an illuminating view of the biotech industry. Because the industry is predicated on knowledge creation and intellectual property, firms and researchers generally seek to patent new products and processes. Patenting is particularly important in the structure of the industry, because small firms develop their intellectual property and sell it to larger firms for manufacture and distribution.

Patent data are classified according to product or technology characteristics (U.S. Patent and Trademark Office 1999). Many patent classifications (including database technologies for epidemiological research and genetic

TABLE 8: NIH FUNDING FOR MEDICAL SCHOOLS AND RESEARCH INSTITUTIONS

Metropolitan Area	NIH Research Funding for Medical Schools and Research Institutions (Dollars in Thousands)								Change in Share, 1985-2000
	1985	1990	1995	2000	Share to Top 50 Metros		1985	1990	
					1985	1990	1995	2000	
Biotechnology Centers									
Boston—Worcester—Lawrence, MA—NH—ME—CT CMSA	185,980	234,956	315,396	499,825	7.9%	6.5%	6.5%	6.6%	-1.3%
San Francisco—Oakland—San Jose, CA CMSA	175,333	279,852	309,574	473,463	7.5%	7.8%	6.4%	6.2%	-1.2%
San Diego, CA MSA	113,463	181,844	237,912	379,150	4.8%	5.0%	4.9%	5.0%	0.2%
Raleigh—Durham—Chapel Hill, NC MSA	105,435	177,666	254,458	367,211	4.5%	4.9%	5.2%	4.8%	0.3%
Seattle—Tacoma—Bremerton, WA CMSA	97,482	167,608	254,828	379,163	4.1%	4.6%	5.3%	5.0%	0.9%
New York—Northern New Jersey—Long Island, NY—NJ—CT—PA CMSA	308,357	413,455	465,912	763,492	13.1%	11.5%	9.7%	10.1%	-3.0%
Philadelphia—Wilmington—Atlantic City, PA—NJ—DE—MD CMSA	128,800	186,666	280,058	432,414	5.5%	5.2%	5.8%	5.7%	0.2%
Los Angeles—Riverside—Orange County, CA CMSA	124,553	194,901	241,715	433,093	5.3%	5.4%	5.0%	5.7%	0.4%
Washington—Baltimore, DC—MD—VA—WV CMSA	230,969	365,016	504,357	678,905	9.8%	10.1%	10.5%	8.9%	-0.9%
Research Centers									
Chicago—Gary—Kenosha, IL—IN—WI CMSA	99,119	129,880	181,547	307,946	4.2%	3.6%	3.8%	4.1%	-0.2%
Detroit—Ann Arbor—Flint, MI CMSA	63,422	111,046	149,253	223,950	2.7%	3.1%	3.1%	2.9%	0.3%
Houston—Galveston—Brazoria, TX CMSA	77,277	111,139	152,983	293,711	3.3%	3.1%	3.2%	3.8%	0.6%
St. Louis, MO—IL MSA	70,029	121,870	170,791	283,466	3.0%	3.4%	3.5%	3.7%	0.8%
Median Metropolitan Areas									
Atlanta, GA MSA	17,825	39,183	61,495	126,762	0.8%	1.1%	1.3%	1.7%	0.9%
Austin—San Marcos, TX MSA	-	-	-	-	0.0%	0.0%	0.0%	0.0%	0.0%
Buffalo—Niagara Falls, NY MSA	10,270	17,381	15,971	17,449	0.4%	0.5%	0.3%	0.2%	-0.2%
Cincinnati—Hamilton, OH—KY—IN CMSA	429	455	1,951	-	0.0%	0.0%	0.0%	0.0%	0.0%
Cleveland—Akron, OH CMSA	41,669	62,891	126,936	197,905	1.8%	1.7%	2.6%	2.6%	0.8%
Columbus, OH MSA	20,655	24,702	36,511	83,018	0.9%	0.7%	0.8%	1.1%	0.2%
Dallas—Fort Worth, TX CMSA	38,882	53,141	77,359	124,325	1.7%	1.5%	1.6%	1.6%	0.0%
Denver—Boulder—Greeley, CO CMSA	29,698	52,780	84,321	134,378	1.3%	1.5%	1.7%	1.8%	0.5%
Greensboro—Winston-Salem—High Point, NC MSA	15,454	27,949	48,231	73,743	0.7%	0.8%	1.0%	1.0%	0.3%
Hartford, CT MSA	16,009	20,097	23,635	32,096	0.7%	0.6%	0.5%	0.4%	-0.3%
Indianapolis, IN MSA	15,195	27,720	47,099	70,413	0.6%	0.8%	1.0%	0.9%	0.3%
Kansas City, MO—KS MSA	6,024	13,219	19,981	28,402	0.3%	0.4%	0.4%	0.4%	0.1%
Memphis, TN—AR—MS MSA	12,213	17,117	22,718	38,557	0.5%	0.5%	0.5%	0.5%	0.0%
Miami—Fort Lauderdale, FL CMSA	23,123	47,849	52,142	71,051	1.0%	1.3%	1.1%	0.9%	0.0%
Milwaukee—Racine, WI CMSA	14,183	24,134	32,019	70,287	0.6%	0.7%	0.7%	0.9%	0.3%
Minneapolis—St. Paul, MN—WI MSA	41,829	61,760	83,521	103,930	1.8%	1.7%	1.7%	1.4%	-0.4%
Nashville, TN MSA	33,818	64,172	77,219	118,482	1.4%	1.8%	1.6%	1.6%	0.1%
New Orleans, LA MSA	23,209	30,738	32,910	47,614	1.0%	0.9%	0.7%	0.6%	-0.4%
Oklahoma City, OK MSA	10,855	11,851	18,611	32,796	0.5%	0.3%	0.4%	0.4%	0.0%
Pittsburgh, PA MSA	34,095	64,225	111,057	177,423	1.4%	1.8%	2.3%	2.3%	0.9%
Portland—Salem, OR—WA CMSA	23,018	39,423	53,941	113,557	1.0%	1.1%	1.1%	1.5%	0.5%
Providence—Fall River—Warwick, RI—MA MSA	6,493	10,963	14,189	27,434	0.3%	0.3%	0.3%	0.4%	0.1%
Richmond—Petersburg, VA MSA	24,013	36,374	38,269	42,219	1.0%	1.0%	0.8%	0.6%	-0.5%
Rochester, NY MSA	41,228	66,134	61,277	90,760	1.8%	1.8%	1.3%	1.2%	-0.6%
Sacramento—Yolo, CA CMSA	10,523	19,003	27,431	39,634	0.4%	0.5%	0.6%	0.5%	0.1%
Salt Lake City—Ogden, UT MSA	24,322	32,902	47,978	75,047	1.0%	0.9%	1.0%	1.0%	0.0%
San Antonio, TX MSA	27,775	41,581	53,698	74,874	1.2%	1.2%	1.1%	1.0%	-0.2%
Tampa—St. Petersburg—Clearwater, FL MSA	3,523	6,702	7,223	21,530	0.1%	0.2%	0.1%	0.3%	0.1%
No Significant Biotech Research or Commercialization									
Charlotte—Gastonia—Rock Hill, NC—SC MSA	-	-	-	-	0.0%	0.0%	0.0%	0.0%	0.0%
Grand Rapids—Muskegon—Holland, MI MSA	-	-	-	-	0.0%	0.0%	0.0%	0.0%	0.0%
Jacksonville, FL MSA	-	-	-	-	0.0%	0.0%	0.0%	0.0%	0.0%
Las Vegas, NV—AZ MSA	-	-	-	-	0.0%	0.0%	0.0%	0.0%	0.0%
Louisville, KY—IN MSA	1,433	4,069	5,535	14,630	0.1%	0.1%	0.1%	0.2%	0.1%
Norfolk—Virginia Beach—Newport News, VA—NC MSA	1,187	2,811	2,484	4,944	0.1%	0.1%	0.1%	0.1%	0.0%
Orlando, FL MSA	-	-	-	-	0.0%	0.0%	0.0%	0.0%	0.0%
Phoenix—Mesa, AZ MSA	470	751	515	1,069	0.0%	0.0%	0.0%	0.0%	0.0%
San Juan—Caguas—Arecibo, PR CMSA	3,201	10,353	14,467	21,431	0.1%	0.3%	0.3%	0.3%	0.1%
West Palm Beach—Boca Raton, FL MSA	-	-	-	-	0.0%	0.0%	0.0%	0.0%	0.0%

Source: National Institutes of Health 2001.

**TABLE 9: NUMBER OF PATENTS IN THE
PRINCIPAL BIOTECHNOLOGY/PHARMACEUTICAL PATENT CLASSIFICATIONS
(UNITED STATES, 1995–1999)**

Patent Classification	Description	Patents Issued 1995–1999
Class 424	Drug, Bio-Affecting and Body-Treating Compositions	6,962
Class 435	Chemistry: Molecular Biology and Microbiology	9,777
Class 514	Drug, Bio-Affecting and Body-Treating Compositions	9,546
Class 800	Multicellular Living Organisms and Unmodified Parts Thereof and Related Processes	1,246
Total Biotech Patenting in the United States		27,531

Source: U.S. Patent and Trademark Office.

studies as well as a variety of instruments used in medical and genetic research) overlap with the biotechnology industry, but most biotechnology patents fall into relatively few categories. Four classes account for more than 27,000 biotechnology/pharmaceutical patents issued between 1995 and 1999. Three biotechnology classes (classes 424, 435, and 514) represent the three patent classes with the most patents issued during the 1995–1999 period. (table 9).

These biotech-related patent classifications represent a large and growing fraction of all of the patents issued in the United States—about 5.6 percent of the patents issued in the country in 1995 and about 8.8 percent by 1999. The four classifications are not an exhaustive list of all of the possible categories into which biotech-related innovations might fall, but they are likely to encompass most of the patented biotechnology innovation, and therefore they serve as a representative indicator of regional variations in biotech activity.

Most patents are owned by private firms. Universities and government agencies also own large numbers of patents because they sponsor a considerable amount of research. The nation's leading pharmaceutical and biotechnology companies appear frequently in the list of the most prolific biotech patentees, but none accounts for more than a small share of all patents. Procter and Gamble, for example, the largest holder of drug patents (class 424), accounted for less than 5 percent of the patents issued in that category.

The amount of biotech patenting varies substantially across regions. Table 10 illustrates the number of patents issued to each of the 51 metropolitan areas between 1975 and 1999. The table shows a substantial jump in patent activity during this 25-year period. With nearly 12,000 biotech-related patents, New York was clearly the leader, followed by San Francisco and Philadelphia, with more than 5,000 patents each. Only ten other metropolitan areas captured more than 1,000 biotechnology-related patents each during this period.

Biotechnology Commercialization

Which metropolitan areas are leading in translating biomedical research into commercial biotechnology activity as measured by investment, new-product development, and the formation and success of biotechnology businesses? To answer this question, a series of measures was developed that focuses on capital investment in biotechnology and on the number and size of biotechnology firms.

The availability of capital plays an important role in the development of the biotech industry. Not only does biotechnology require expensive and time-consuming research but also the resultant promising diagnostics and therapeutics must undergo a long process of testing and regulatory approval. Many research projects and promising product ideas fail to produce revenue. Even those firms that ultimately succeed record many years of losses during research, development, and regulatory review. Consequently, large amounts of patient capital are required in order to develop and sustain the biotech industry. Each of the three measures of capital flows to the biotech industry—venture capital, research alliances, and initial public offerings—reflects different phases in the life cycle of firms and in the development of products.

Start-up firms typically depend on venture capital investment to underwrite their initial costs. Small biotech firms with more ideas than money will form research alliances with larger pharmaceutical firms, trading equity or future marketing rights for up-front cash. Once some promising products are developed, venture capitalists and other early-stage investors seek to recoup their investment (or a portion of it) by having the firm issue stock to the public in an “initial public offering” (IPO). IPO financing is shaped both by the maturity of the firm and its product and by the general state of the capital

TABLE 10: BIOTECHNOLOGY RELATED PATENTS

Metropolitan Area	Number of Patents			
	1975-79	1980-89	1990-99	1975-99
Biotechnology Centers				
Boston—Worcester—Lawrence, MA—NH—ME—CT CMSA	126	592	3,007	3,725
San Francisco—Oakland—San Jose, CA CMSA	414	1,173	3,991	5,578
San Diego, CA MSA	23	210	1,632	1,865
Raleigh—Durham—Chapel Hill, NC MSA	27	204	796	1,027
Seattle—Tacoma—Bremerton, WA CMSA	9	93	770	872
New York—Northern New Jersey—Long Island, NY—NJ—CT—PA CMSA	1,420	3,590	6,800	11,810
Philadelphia—Wilmington—Atlantic City, PA—NJ—DE—MD CMSA	679	1,309	3,214	5,202
Los Angeles—Riverside—Orange County, CA CMSA	106	330	1,399	1,835
Washington—Baltimore, DC—MD—VA—WV CMSA	121	470	2,162	2,753
Research Centers				
Chicago—Gary—Kenosha, IL—IN—WI CMSA	215	575	1,444	2,234
Detroit—Ann Arbor—Flint, MI CMSA	51	342	655	1,048
Houston—Galveston—Brazoria, TX CMSA	18	144	634	796
St. Louis, MO—IL MSA	79	156	780	1,015
Median Metropolitan Areas				
Atlanta, GA MSA	11	33	323	367
Austin—San Marcos, TX MSA	4	10	110	124
Buffalo—Niagara Falls, NY MSA	17	58	129	204
Cincinnati—Hamilton, OH—KY—IN CMSA	141	282	972	1,395
Cleveland—Akron, OH CMSA	40	56	147	243
Columbus, OH MSA	13	63	183	259
Dallas—Fort Worth, TX CMSA	26	84	434	544
Denver—Boulder—Greeley, CO CMSA	11	54	389	454
Greensboro—Winston-Salem—High Point, NC MSA	12	10	64	86
Hartford, CT MSA	6	23	206	235
Indianapolis, IN MSA	177	472	1,036	1,685
Kansas City, MO—KS MSA	22	58	103	183
Memphis, TN—AR—MS MSA	14	74	191	279
Miami—Fort Lauderdale, FL CMSA	18	149	229	396
Milwaukee—Racine, WI CMSA	15	43	118	176
Nashville, TN MSA	3	9	71	83
Minneapolis—St. Paul, MN—WI MSA	89	187	554	830
New Orleans, LA MSA	22	56	109	187
Oklahoma City, OK MSA	-	13	118	131
Pittsburgh, PA MSA	19	45	180	244
Portland—Salem, OR—WA CMSA	9	32	164	205
Providence—Fall River—Warwick, RI—MA MSA	3	28	77	108
Richmond—Petersburg, VA MSA	44	89	116	249
Rochester, NY MSA	62	175	379	616
Sacramento—Yolo, CA CMSA	1	58	282	341
Salt Lake City—Ogden, UT MSA	11	31	252	294
San Antonio, TX MSA	4	29	172	205
Tampa—St. Petersburg—Clearwater, FL MSA	6	17	103	126
No Significant Biotech Research or Commercialization				
Charlotte—Gastonia—Rock Hill, NC—SC MSA	2	4	23	29
Grand Rapids—Muskegon—Holland, MI MSA	4	25	38	67
Jacksonville, FL MSA	4	5	25	34
Las Vegas, NV—AZ MSA	2	5	18	25
Louisville, KY—IN MSA	3	6	36	45
Norfolk—Virginia Beach—Newport News, VA—NC MSA	4	11	39	54
Orlando, FL MSA	5	8	19	32
Phoenix—Mesa, AZ MSA	2	40	92	134
San Juan—Caguas—Arecibo, PR CMSA	-	-	-	-
West Palm Beach—Boca Raton, FL MSA	7	12	37	56

Source: U.S. Patent & Trademark Office 2001.

markets (enthusiasm for IPOs waxes and wanes with fluctuations in the overall stock market).

VENTURE CAPITAL INVESTMENT: Pre-venture financing for the creation of new biotech knowledge comes substantially from the federal government through its support of health-related research. In addition there is a small role for self-financed firms and for so-called angel investment (individual private investors underwriting the finances of start-up firms). But by far the most important source of start-up capital for the biotech industry is organized venture capital: private investments made by professional fund managers, typically specializing in a related set of technologies. Venture capital investment finances most biotech firms from their inception and usually through the years of research and product development needed to prove the potential of a promising idea. A firm may get one or several rounds of venture capital financing as it develops its products. Because of the considerable expense and long lead times associated with developing and proving novel diagnostic and therapeutic products, patient venture capital is essential to the start-up of firms that may go several years before generating revenues.

Venture capital is a good leading indicator of the development of ideas into potential businesses. In 2000 during the midst of a capital market boom, biotech firms attracted more than \$3 billion in venture capital investments. Biotech investments, which averaged less than \$300 million per quarter between 1995 and 1998, were greater than \$800 million per quarter in 2000. Still, biotech was not as popular as other investments: biotech accounted for about 10 percent of all venture capital invested in 1995 and about 5 percent in 2000 (PriceWaterhouseCoopers 2001).

Between 1995 and the second quarter of 2001, the PriceWaterhouseCoopers database reported 1,109 venture capital investments in biopharmaceutical firms (a category that closely parallels the earlier-described definition of *biotechnology*) with an aggregate total amount of \$10.1 billion (PriceWaterhouseCoopers 2001). These investments were then geo-coded by the present analysis on the basis of the location of the firm receiving the venture capital investment. About \$9.7 billion, or 97 percent of this investment, went to the 51 largest metropolitan areas in the United States (**table 11**).

Venture capital investment in biopharmaceutical firms is concentrated within just a few metropolitan areas. Boston and San Francisco account for a majority of all venture capital investment in the 51 largest metropolitan areas: \$4.9 billion of the \$9.7 billion invested between 1995 and 2001. Another one-fourth of all biotech investment was made in three other metropolitan areas: San Diego, Seattle, and Raleigh-Durham.

The availability of venture capital is contingent in part on the presence of local venture capital firms. Because venture capital investing requires making risky judgments about the likelihood of commercial success of particular research ideas, venture capitalists must have particular technical expertise in appraising biotech business plans. In addition, venture capital investment firms attempt to minimize their risks and to increase the proba-

bility of success of their investments by playing an active role in the management of the firms in which they invest. Typically, venture capitalists take seats on the investee corporation's board and offer advice on marketing, product development, personnel, finance, and other issues. They are also particularly active in brokering alliances with other firms having complementary skills or interests. Because these tasks tend to be time consuming, venture capitalists strongly prefer to invest in and work with firms located near their offices. For these same reasons, venture capital firms tend to specialize in particular markets or technologies.

Data on venture capital investing patterns illustrate the degree of industry specialization by venture capital firms. Fewer than one in ten venture capital firms invests frequently in biotechnology companies. According to PriceWaterhouseCoopers, between 1995 and 2001, some 178 venture capital firms made investments in biopharmaceutical companies at least once, a number equal to less than a third of the 621 venture capital firms active in 2001 (PriceWaterhouseCoopers 2001). Some 51 of the firms that made any biotech investment were very active, making investments in biopharmaceuticals firms in at least eight of the 26 calendar quarters during this six-year period. **Table 11** presents the geo-coded locations of these very active biotechnology venture capitalists, based on information in the PriceWaterhouseCoopers Moneytree database.

[B]y far the most important source of start-up capital for the biotech industry is organized venture capital: private investments made by professional fund managers, typically specializing in a related set of technologies.

TABLE 11: VENTURE CAPITAL FOR BIOPHARMACEUTICALS

Metropolitan Area	Number	Venture Capital Investments			Highly Active	Initial
		1995–2001 Amount	Share	1995–2001 Firms	1998–2001 Public Offerings	
Biotechnology Centers						
Boston—Worcester—Lawrence, MA—NH—ME—CT CMSA	211	1,915,654,300	19.7%	10	3	
San Francisco—Oakland—San Jose, CA CMSA	261	3,028,917,500	31.1%	21	31	
San Diego, CA MSA	169	1,505,896,000	15.4%	4	10	
Raleigh—Durham—Chapel Hill, NC MSA	54	379,687,000	3.9%	2	1	
Seattle—Tacoma—Bremerton, WA CMSA	44	419,954,000	4.3%	1	8	
New York—Northern New Jersey—Long Island, NY—NJ—CT—PA CMSA	63	639,099,000	6.6%	5	5	
Philadelphia—Wilmington—Atlantic City, PA—NJ—DE—MD CMSA	51	457,550,000	4.7%	3	2	
Los Angeles—Riverside—Orange County, CA CMSA	26	180,761,000	1.9%	1	1	
Washington—Baltimore, DC—MD—VA—WV CMSA	20	85,150,000	0.9%	0	2	
Research Centers						
Chicago—Gary—Kenosha, IL—IN—WI CMSA	7	61,837,000	0.6%	3	0	
Detroit—Ann Arbor—Flint, MI CMSA	15	95,100,000	1.0%	0	1	
Houston—Galveston—Brazoria, TX CMSA	10	72,617,000	0.7%	0	3	
St. Louis, MO—IL MSA	3	8,800,000	0.1%	0	0	
Median Metropolitan Areas						
Atlanta, GA MSA	6	57,300,000	0.6%	0	0	
Austin—San Marcos, TX MSA	4	58,400,000	0.6%	0	1	
Buffalo—Niagara Falls, NY MSA	0	-	0.0%	0	0	
Cincinnati—Hamilton, OH—KY—IN CMSA	1	1,500,000	0.0%	0	0	
Cleveland—Akron, OH CMSA	9	83,317,000	0.9%	0	2	
Columbus, OH MSA	1	200,000	0.0%	0	0	
Dallas—Fort Worth, TX CMSA	0	-	0.0%	0	0	
Denver—Boulder—Greeley, CO CMSA	16	156,162,000	1.6%	0	1	
Greensboro—Winston-Salem—High Point, NC MSA	3	38,900,000	0.4%	0	0	
Hartford, CT MSA	0	-	0.0%	0	0	
Indianapolis, IN MSA	2	15,500,000	0.2%	0	0	
Kansas City, MO—KS MSA	1	12,000,000	0.1%	0	0	
Memphis, TN—AR—MS MSA	0	-	0.0%	0	0	
Miami—Fort Lauderdale, FL CMSA	0	-	0.0%	0	2	
Milwaukee—Racine, WI CMSA	0	-	0.0%	0	0	
Minneapolis—St. Paul, MN—WI MSA	19	81,600,000	0.8%	1	1	
Nashville, TN MSA	4	11,520,000	0.1%	0	0	
New Orleans, LA MSA	2	3,700,000	0.0%	0	0	
Oklahoma City, OK MSA	4	34,750,000	0.4%	0	0	
Pittsburgh, PA MSA	3	47,030,000	0.5%	0	0	
Portland—Salem, OR—WA CMSA	1	4,300,000	0.0%	0	0	
Providence—Fall River—Warwick, RI—MA MSA	1	13,000,000	0.1%	0	0	
Richmond—Petersburg, VA MSA	8	83,330,000	0.9%	0	0	
Rochester, NY MSA	0	-	0.0%	0	0	
Sacramento—Yolo, CA CMSA	3	26,000,000	0.3%	0	1	
Salt Lake City—Ogden, UT MSA	8	60,500,000	0.6%	0	1	
San Antonio, TX MSA	12	90,440,000	0.9%	0	1	
Tampa—St. Petersburg—Clearwater, FL MSA	2	3,800,000	0.0%	0	0	
No Significant Biotech Research or Commercialization						
Charlotte—Gastonia—Rock Hill, NC—SC MSA	0	-	0.0%	0	0	
Grand Rapids—Muskegon—Holland, MI MSA	0	-	0.0%	0	0	
Jacksonville, FL MSA	1	5,500,000	0.1%	0	0	
Las Vegas, NV—AZ MSA	0	-	0.0%	0	0	
Louisville, KY—IN MSA	5	8,895,000	0.1%	0	0	
Norfolk—Virginia Beach—Newport News, VA—NC MSA	0	-	0.0%	0	0	
Orlando, FL MSA	0	-	0.0%	0	0	
Phoenix—Mesa, AZ MSA	0	-	0.0%	0	0	
San Juan—Caguas—Arecibo, PR CMSA	0	-	0.0%	0	0	
West Palm Beach—Boca Raton, FL MSA	0	-	0.0%	0	0	

Sources: PriceWaterhouseCoopers Moneytree; IPO.com.

Very active biotech investors tend to be most heavily concentrated within relatively few metropolitan areas. Two metropolitan areas, San Francisco and Boston, are home to a majority of the very active investment firms (31 of the 51). New York and Philadelphia, leading centers of the pharmaceutical industry, are home to eight of the very active venture capital investors in biotechnology. San Diego has four such firms, Chicago has three, and Raleigh-Durham has two. No other metropolitan area has more than one very active venture capital firm investing in biotechnology.

ALLIANCES AND RESEARCH CONTRACTS: A major source of funding for biotech firms developing new products consists of research and development contracts and equity funding arrangements with major pharmaceutical companies. Such arrangements take many forms, but commonly they involve exchanging a financial interest in the biotech company or marketing rights to its products or to its technology in exchange for funds to be used for research and development. This is a key source of funding for small biotech companies: Recombinant Capital, a private analyst of the biotechnology industry, reports that pharmaceutical companies entered into research and development agreements worth \$17.3 billion with biotechnology companies between 1980 and 2001 (Recombinant Capital 2001). The dollar value of these research agreements has grown rapidly from about \$846 million prior to 1990, to \$5.2 billion between 1990 and 1995, and \$11.2 billion since 1996. (Typically, agreements involve several years of funding for research activities, so precise annual spending amounts are not available. In addition, payments are often tied to researchers' successful attainment of designated milestones; the actual amounts ultimately disbursed are less than these reported totals because some research reaches a dead end.)

The flow of research contracts from pharmaceutical funds to biotechnology firms is a strong indicator of the location of commercially promising research activities.

The flow of research contracts from pharmaceutical funds to biotechnology firms is a strong indicator of the location of commercially promising research activities. The Recombinant Capital database reports the dollar amount of 493 such contracts between 1980 and 2001. Of these, 29 contracts worth approximately \$1 billion were with biotech companies located outside the United States, four could not be geo-coded, and six were with biotech firms located outside the 51 largest metropolitan areas in the United States. Thus 460 contracts worth \$16.1 billion were placed with biotech firms in the 51 largest metropolitan areas in the country. **Table 12** illustrates the distribution of the value of research and development contracts among these metropolitan areas by the year in which the contract was initiated.

Research contracts extended to biotechnology companies by pharmaceutical companies are very highly concentrated within just a few metropolitan areas. Four metropolitan areas account for more than four-fifths of the value of all research contracts: Boston (\$5.1 billion), San Francisco (\$2.8 billion), San Diego (\$2.7 billion), and New York (\$2.6 billion). Only two other metropolitan areas attracted more than half a billion dollars in such contracts: Washington/Baltimore (\$600 million) and Seattle (\$700 million).

INITIAL PUBLIC OFFERINGS: In addition to venture capital and research contracts with pharmaceutical firms, biotechnology firms can also raise money to

finance research and development activities by selling stock in public markets. For privately held firms, going public requires undertaking an initial public offering (IPO) prior to which the firm must undergo a rigorous process of review and disclosure. The costs of undertaking an IPO mean that only those firms with a relatively large scale and/or sufficiently well-developed intellectual property or products can raise funds in this fashion. The attractiveness of an initial public offering as a source of funds is also contingent on the stock market: if the price of biotechnology stocks is perceived to be high, the managers of a biotech firm may be able to raise a relatively large amount of funds for the company by selling a portion of its ownership to the public.

IPO.com, an investment research firm, tracks initial public offerings (IPO.com 2001). Between 1998 and 2001, some 89 biotechnology firms made the initial filings to undertake an initial public offering. Five of these firms were located outside the United States. The location of 80 of the 84 U.S.-based initial public offerings was geo-coded; 77 of these were located in the 51 largest metropolitan areas in the United States. The geography of filings of initial public offering during this period shows which metropolitan areas had promising new biotechnology companies. Established biotechnology centers accounted for the bulk of these initial public offerings. Three metro areas—San Francisco, San Diego, and Seattle—accounted for more than 60 percent of the initial public offerings (**table 11**).

TABLE 12: PHARMACEUTICAL/BIOTECHNOLOGY ALLIANCES

Metropolitan Area	Value of Research and Development Alliances (millions)			
	Before 1980	1990–1995	1996–2001	Total
Biotechnology Centers				
Boston—Worcester—Lawrence, MA—NH—ME—CT CMSA	254	882	3,924	5,060
San Francisco—Oakland—San Jose, CA CMSA	230	1,357	1,205	2,792
San Diego, CA MSA	46	1,022	1,615	2,684
Raleigh—Durham—Chapel Hill, NC MSA	-	33	192	225
Seattle—Tacoma—Bremerton, WA CMSA	68	45	579	692
New York—Northern New Jersey—Long Island, NY—NJ—CT—PA CMSA	149	724	1,729	2,602
Philadelphia—Wilmington—Atlantic City, PA—NJ—DE—MD CMSA	5	85	127	216
Los Angeles—Riverside—Orange County, CA CMSA	0	73	69	143
Washington—Baltimore, DC—MD—VA—WV CMSA	17	260	358	634
Research Centers				
Chicago—Gary—Kenosha, IL—IN—WI CMSA	-	0	9	9
Detroit—Ann Arbor—Flint, MI CMSA	-	25	-	25
Houston—Galveston—Brazoria, TX CMSA	11	55	53	119
St. Louis, MO—IL MSA	-	-	7	7
Median Metropolitan Areas				
Atlanta, GA MSA	-	-	-	-
Austin—San Marcos, TX MSA	-	50	-	50
Buffalo—Niagara Falls, NY MSA	-	-	-	-
Cincinnati—Hamilton, OH—KY—IN CMSA	-	-	-	-
Cleveland—Akron, OH CMSA	-	23	-	23
Columbus, OH MSA	-	-	-	-
Dallas—Fort Worth, TX CMSA	-	-	-	-
Denver—Boulder—Greeley, CO CMSA	19	16	133	169
Greensboro—Winston-Salem—High Point, NC MSA	-	-	-	-
Hartford, CT MSA	-	-	-	-
Indianapolis, IN MSA	-	-	-	-
Kansas City, MO—KS MSA	-	-	-	-
Memphis, TN—AR—MS MSA	-	-	-	-
Miami—Fort Lauderdale, FL CMSA	0	100	-	100
Milwaukee—Racine, WI CMSA	-	-	-	-
Minneapolis—St. Paul, MN—WI MSA	19	-	10	29
Nashville, TN MSA	-	-	-	-
New Orleans, LA MSA	-	-	-	-
Oklahoma City, OK MSA	-	-	-	-
Pittsburgh, PA MSA	-	-	-	-
Portland—Salem, OR—WA CMSA	2	-	-	2
Providence—Fall River—Warwick, RI—MA MSA	-	-	-	-
Richmond—Petersburg, VA MSA	-	-	-	-
Rochester, NY MSA	-	-	-	-
Sacramento—Yolo, CA CMSA	-	-	-	-
Salt Lake City—Ogden, UT MSA	9	276	185	470
San Antonio, TX MSA	-	-	-	-
Tampa—St. Petersburg—Clearwater, FL MSA	-	-	-	-
No Significant Biotech Research or Commercialization				
Charlotte—Gastonia—Rock Hill, NC—SC MSA	-	-	60	60
Grand Rapids—Muskegon—Holland, MI MSA	-	-	-	-
Jacksonville, FL MSA	-	-	-	-
Las Vegas, NV—AZ MSA	-	-	-	-
Louisville, KY—IN MSA	-	-	-	-
Norfolk—Virginia Beach—Newport News, VA—NC MSA	-	-	-	-
Orlando, FL MSA	-	-	-	-
Phoenix—Mesa, AZ MSA	-	-	-	-
San Juan—Caguas—Arecibo, PR CMSA	-	-	-	-
West Palm Beach—Boca Raton, FL MSA	-	-	-	-

Source: Biospace.com.

BIOTECHNOLOGY FIRMS WITH MORE THAN 100 EMPLOYEES: The formation and flourishing of biotechnology firms ought ultimately to be the objectives of biotechnology development strategies and the result of an effective combination of research capability, knowledge creation activity, and investment capital. The present analysis provides several different measures of the location of the biotech industry, and to illustrate the geographic distribution of industry activity it examines employment data from the economic census and company level data from a widely used biotechnology industry directory.

Published government statistics, including the Census Bureau's Economic Census, are somewhat poorly suited to assessing the biotechnology industry. No separate industry classification code exists for the biotechnology industry, even under the recently adopted North American Industry Classification System. Most biotechnology firms are classified under one of two industry categories: (1) pharmaceutical and medicine manufacturing and (2) life sciences research and development. Although these industry categories overlap substantially with most biotech firms, they are not a perfect fit. Some biotech firms may be classified in other industry categories. Furthermore, many firms that are not biotechnology firms are included in these categories; for instance, pharmaceutical and medicine industries include manufacturers of vitamins and non-biotech drugs, and life science research can include a variety of disciplines other than biotechnology.

Table 13 shows the 1997 employment level for the 51 largest metropolitan areas in the United States for these two industrial categories. Approximately 132,000 persons worked in the pharmaceutical industry (NAICS 3254) and 83,000 in the life sciences research and development industry (NAICS 5417102) in these metropolitan areas (Bureau of the Census 2000). The largest concentrations of pharmaceutical employment are found in the nation's largest metropolitan areas: New York, Los Angeles, Chicago, Philadelphia, and Boston. Most of the nation's largest pharmaceutical firms are headquartered in the New York or Philadelphia metropolitan area. The life science research industries are concentrated within the nine biotech centers. Only three areas outside of the centers—Chicago, Denver, and San Antonio—have more than 1,000 people employed in the sector.

Private analysts and public-sector agencies compile and maintain directories and other lists of businesses that illustrate the location and size of biotechnology businesses in the United States. Two information sources were used in the present study to identify the location of biotech firms.

One of the sources, the Institute for Biotechnology Information (IBI), a private research firm, maintains a directory of businesses in biotechnology, pharmaceuticals, and related fields (Institute for Biotechnology Information 2001). The IBI directory for 2001 contains listings for 1,762 firms, with 1,291 of these firms being classified as "biotechnology" firms. The location of these firms was geo-coded on the basis of the address information contained in the IBI database. Some 73 firms either were located outside the United States or could not be geo-coded, leaving 1,238 geo-coded U.S. biotech firms. Of the latter group, some 1,080 were located in the 51 largest metropolitan areas in the United States and 138 in smaller metropolitan areas or in nonmetropolitan areas.

Data contained in the IBI database permitted the classification of firms by number of employees and by the year of founding. According to the IBI database, about 25 percent of all biotechnology firms have 100 or more employees. Some 282 of these firms are located in the 51 largest metropolitan areas in the United States. **Table 14** illustrates the distribution of these larger biotech firms, which are concentrated within just a few metropolitan areas, half of them located in only four metros: San Francisco has 46 large biotechnology firms, and three other metropolitan areas (Boston, New York, and San Diego) have more than 30.

The formation and flourishing of biotechnology firms ought ultimately to be the objectives of biotechnology development strategies and the result of an effective combination of research capability, knowledge creation activity, and investment capital.

TABLE 13: PHARMACEUTICAL AND LIFE SCIENCES RESEARCH EMPLOYMENT

Metropolitan Area	NAICS 3254: Pharmaceuticals		NAICS 541702: Life Sciences R&D	
	Establishments	Number of Employees (estimated)	Establishments	Number of Employees (estimated)
Biotechnology Centers				
Boston—Worcester—Lawrence, MA—NH—ME—CT CMSA	67	6,945	284	11,249
San Francisco—Oakland—San Jose, CA CMSA	77	11,302	353	9,674
San Diego, CA MSA	58	3,547	181	7,487
Raleigh—Durham—Chapel Hill, NC MSA	19	3,679	90	3,356
Seattle—Tacoma—Bremerton, WA CMSA	16	758	102	5,499
New York—Northern New Jersey—Long Island, NY—NJ—CT—PA CMSA	130	22,578	382	14,328
Philadelphia—Wilmington—Atlantic City, PA—NJ—DE—MD CMSA	54	8,961	129	4,539
Los Angeles—Riverside—Orange County, CA CMSA	134	11,885	204	4,522
Washington—Baltimore, DC—MD—VA—WV CMSA	25	1,750	284	7,499
Research Centers				
Chicago—Gary—Kenosha, IL—IN—WI CMSA	37	18,753	91	1,499
Detroit—Ann Arbor—Flint, MI CMSA	23	1,382	23	263
Houston—Galveston—Brazoria, TX CMSA	17	405	56	943
St. Louis, MO—IL MSA	35	4,581	35	320
Median Metropolitan Areas				
Atlanta, GA MSA	18	674	30	375
Austin—San Marcos, TX MSA	12	1,517	20	890
Buffalo—Niagara Falls, NY MSA	8	1,398	14	750
Cincinnati—Hamilton, OH—KY—IN CMSA	9	994	37	749
Cleveland—Akron, OH CMSA	7	542	14	126
Columbus, OH MSA	6	1,019	na	na
Dallas—Fort Worth, TX CMSA	na	na	40	633
Denver—Boulder—Greeley, CO CMSA	34	2,125	81	1,501
Greensboro—Winston-Salem—High Point, NC MSA	8	1,195	na	na
Hartford, CT MSA	na	na	12	175
Indianapolis, IN MSA	10	3,750	16	750
Kansas City, MO—KS MSA	24	2,477	7	375
Memphis, TN—AR—MS MSA	9	2,240	na	na
Miami—Fort Lauderdale, FL CMSA	16	1,443	50	382
Milwaukee—Racine, WI CMSA	14	915	na	na
Minneapolis—St. Paul, MN—WI MSA	32	1,429	70	930
Nashville, TN MSA	na	na	9	175
New Orleans, LA MSA	na	na	na	na
Oklahoma City, OK MSA	6	375	na	na
Pittsburgh, PA MSA	na	na	12	740
Portland—Salem, OR—WA CMSA	18	703	42	583
Providence—Fall River—Warwick, RI—MA MSA	na	na	7	375
Richmond—Petersburg, VA MSA	2	1,750	10	195
Rochester, NY MSA	2	1,750	na	na
Sacramento—Yolo, CA CMSA	7	503	23	549
San Antonio, TX MSA	14	492	34	1,124
Salt Lake City—Ogden, UT MSA	19	1,538	36	621
Tampa—St. Petersburg—Clearwater, FL MSA	13	1,479	21	175
No Significant Biotech Research or Commercialization				
Charlotte—Gastonia—Rock Hill, NC—SC MSA	8	452	na	na
Grand Rapids—Muskegon—Holland, MI MSA	8	3,019	na	na
Jacksonville, FL MSA	na	na	na	na
Las Vegas, NV—AZ MSA	na	na	na	na
Louisville, KY—IN MSA	na	na	na	na
Norfolk—Virginia Beach—Newport News, VA—NC MSA	na	na	na	na
Orlando, FL MSA	na	na	na	na
Phoenix—Mesa, AZ MSA	18	1,162	na	na
San Juan—Caguas—Arecibo, PR CMSA	na	na	na	na
West Palm Beach—Boca Raton, FL MSA	8	412	na	na

Source: Bureau of the Census, 1997 Economic Census.

TABLE 14: BIOTECHNOLOGY COMPANIES WITH 100 OR MORE EMPLOYEES

Metropolitan Area	Biotechnology Companies with 100 or More Employees	
	Number	Share
Biotechnology Centers		
Boston—Worcester—Lawrence, MA—NH—ME—CT CMSA	33	11.7%
San Francisco—Oakland—San Jose, CA CMSA	46	16.3%
San Diego, CA MSA	31	11.0%
Raleigh—Durham—Chapel Hill, NC MSA	13	4.6%
Seattle—Tacoma—Bremerton, WA CMSA	7	2.5%
New York—Northern New Jersey—Long Island, NY—NJ—CT—PA CMSA	36	12.8%
Philadelphia—Wilmington—Atlantic City, PA—NJ—DE—MD CMSA	10	3.5%
Los Angeles—Riverside—Orange County, CA CMSA	18	6.4%
Washington—Baltimore, DC—MD—VA—WV CMSA	23	8.2%
Research Centers		
Chicago—Gary—Kenosha, IL—IN—WI CMSA	12	4.3%
Detroit—Ann Arbor—Flint, MI CMSA	1	0.4%
Houston—Galveston—Brazoria, TX CMSA	5	1.8%
St. Louis, MO—IL MSA	3	1.1%
Median Metropolitan Areas		
Atlanta, GA MSA	4	1.4%
Austin—San Marcos, TX MSA	-	0.0%
Buffalo—Niagara Falls, NY MSA	-	0.0%
Cincinnati—Hamilton, OH—KY—IN CMSA	1	0.4%
Cleveland—Akron, OH CMSA	1	0.4%
Columbus, OH MSA	-	0.0%
Dallas—Fort Worth, TX CMSA	1	0.4%
Denver—Boulder—Greeley, CO CMSA	4	1.4%
Greensboro—Winston-Salem—High Point, NC MSA	2	0.7%
Hartford, CT MSA	-	0.0%
Indianapolis, IN MSA	4	1.4%
Kansas City, MO—KS MSA	2	0.7%
Memphis, TN—AR—MS MSA	-	0.0%
Miami—Fort Lauderdale, FL CMSA	3	1.1%
Milwaukee—Racine, WI CMSA	-	0.0%
Minneapolis—St. Paul, MN—WI MSA	9	3.2%
Nashville, TN MSA	-	0.0%
New Orleans, LA MSA	-	0.0%
Oklahoma City, OK MSA	1	0.4%
Pittsburgh, PA MSA	1	0.4%
Portland—Salem, OR—WA CMSA	-	0.0%
Providence—Fall River—Warwick, RI—MA MSA	-	0.0%
Richmond—Petersburg, VA MSA	-	0.0%
Rochester, NY MSA	1	0.4%
Sacramento—Yolo, CA CMSA	1	0.4%
Salt Lake City—Ogden, UT MSA	3	1.1%
San Antonio, TX MSA	1	0.4%
Tampa—St. Petersburg—Clearwater, FL MSA	-	0.0%
No Significant Biotech Research or Commercialization		
Charlotte—Gastonia—Rock Hill, NC—SC MSA	-	0.0%
Grand Rapids—Muskegon—Holland, MI MSA	1	0.4%
Jacksonville, FL MSA	-	0.0%
Las Vegas, NV—AZ MSA	1	0.4%
Louisville, KY—IN MSA	1	0.4%
Norfolk—Virginia Beach—Newport News, VA—NC MSA	-	0.0%
Orlando, FL MSA	-	0.0%
Phoenix—Mesa, AZ MSA	1	0.4%
San Juan—Caguas—Arecibo, PR CMSA	-	0.0%
West Palm Beach—Boca Raton, FL MSA	1	0.4%

Source: Institute for Biotechnology Information 2001.

FIRMS FOUNDED DURING THE 1990S: **Table 15** classifies biotech firms, regardless of number of employees, by the decade in which they were founded. Information on founding dates was not available for 25 of the 1,081 biotech firms. These data reflect only those firms surviving as independent entities in 2001 and so do not reflect firms that were started in some earlier year and that subsequently went out of business or were acquired by another firm. Fewer than 200 biotechnology firms were more than 20 years old, 471 date from the 1980s, and 414 such firms have been founded during the past ten years.

The largest concentrations of biotechnology firms are in San Francisco (151) and Boston (141). Other significant centers of activity are New York (127), San Diego (94), Washington/Baltimore (83), and Raleigh-Durham (72). No other areas have more than 50 biotech firms.

Significant shifts have occurred during the past three decades in the pattern of biotechnology firm formation. San Francisco and Boston accounted for fewer than 20 percent of biotech firms founded prior to the 1980s but about one-third of those founded in the 1990s. San Diego, Raleigh-Durham, and Seattle accounted for fewer than 10 percent of the firms founded prior to 1980 but nearly one-fourth of the firms founded in the 1990s. During the past two decades the founding of biotech firms appears to have become more concentrated into relatively fewer metropolitan areas. These five metropolitan areas accounted for a little more than 25 percent of biotech firms founded prior to 1980 but about 56 percent of the firms founded in the 1990s.

During the past two decades the founding of biotech firms appears to have become more concentrated into relatively fewer metropolitan areas. [F]ive metropolitan areas accounted for... about 56 percent of the firms founded in the 1990s.

MARKET CAPITALIZATION OF FIRMS: Another way of examining the geography of the biotechnology industry is to look at the market value of biotechnology firms. Stock analysts frequently use the market capitalization of a company (a firm's share price multiplied by the number of shares outstanding) to describe the relative value the stock market places on different corporations. Biospace, Inc., a private research firm following the biotechnology industry, maintains a database with information on the stocks of 460 publicly traded companies that it classifies as being in the biotechnology industry (Biospace Inc. 2001).

A few large firms account for the bulk of the market capitalization of the biotechnology industry. The location of the headquarters of each of these firms was identified, and the total market capitalization of publicly traded biotechnology firms by metropolitan area was tabulated. **Table 16** shows the distribution of public firms and market capitalization by metropolitan area. Four metropolitan areas (Boston, San Francisco, New York, and Los Angeles) account for 65 percent of all market capitalization of biotechnology companies.

INDUSTRY ASSOCIATION MEMBERSHIP: Another indicator of the relative presence of biotechnology firms in different metropolitan areas is membership in industry and trade associations. Nationally, the largest trade association for biotech firms is BIO, the Biotechnology Industry Organization, based in Washington, D.C. The BIO membership directory was analyzed in order to identify the number of member companies in each of the 51 largest metropolitan areas in the United States (Biotechnology Industry Organization 2001).

In 2001, there were 799 members of BIO with addresses in the United States; 695 of these members were located in the 51 largest metropolitan areas. **Table 17** shows the number of BIO members in each of the 51 largest metropolitan areas. More than 60 percent of BIO members were located in five metropolitan areas. The largest concentrations of members were in San Francisco (114), New York (106), and Boston (101). San Diego and Washington/Baltimore each had 61 members, Philadelphia 42, and Raleigh-Durham 35. No other metropolitan area had more than 25 members.

TABLE 15: BIOTECHNOLOGY COMPANIES BY FOUNDING DATE

Metropolitan Area	through 1980	Companies by Decade of Founding				All Firms	Share of Firms by Decade of Founding			
		1981- 1990	1991- 2001	Not Available	1981- 1990	1991- 2001	All Firms	1981- 1990	1991- 2001	All Firms
Biotechnology Centers										
Boston—Worcester—Lawrence, MA—NH—ME—CT CMSA	15	57	65	4	141	8.8%	12.1%	15.7%	13.0%	
San Francisco—Oakland—San Jose, CA CMSA	16	64	71	1	152	9.4%	13.6%	17.1%	14.1%	
San Diego, CA MSA	7	46	38	3	94	4.1%	9.8%	9.2%	8.7%	
Raleigh—Durham—Chapel Hill, NC MSA	7	18	46	1	72	4.1%	3.8%	11.1%	6.7%	
Seattle—Tacoma—Bremerton, WA CMSA	1	17	11	1	30	0.6%	3.6%	2.7%	2.8%	
New York—Northern New Jersey— Long Island, NY—NJ—CT—PA CMSA	25	59	38	5	127	14.6%	12.5%	9.2%	11.7%	
Philadelphia—Wilmington— Atlantic City, PA—NJ—DE—MD CMSA	8	20	16	2	46	4.7%	4.2%	3.9%	4.3%	
Los Angeles—Riverside—Orange County, CA CMSA	13	24	10	0	47	7.6%	5.1%	2.4%	4.3%	
Washington—Baltimore, DC—MD—VA—WV CMSA	13	45	23	2	83	7.6%	9.6%	5.6%	7.7%	
Research Centers										
Chicago—Gary—Kenosha, IL—IN—WI CMSA	10	10	6	2	28	5.8%	2.1%	1.4%	2.6%	
Detroit—Ann Arbor—Flint, MI CMSA	0	8	2	0	10	0.0%	1.7%	0.5%	0.9%	
Houston—Galveston—Brazoria, TX CMSA	2	9	4	0	15	1.2%	1.9%	1.0%	1.4%	
St. Louis, MO—IL MSA	4	2	2	0	8	2.3%	0.4%	0.5%	0.7%	
Median Metropolitan Areas										
Atlanta, GA MSA	2	5	4	2	13	1.2%	1.1%	1.0%	1.2%	
Austin—San Marcos, TX MSA	0	3	3	0	6	0.0%	0.6%	0.7%	0.6%	
Buffalo—Niagara Falls, NY MSA	2	1	2	0	5	1.2%	0.2%	0.5%	0.5%	
Cincinnati—Hamilton, OH—KY—IN CMSA	1	1	0	0	2	0.6%	0.2%	0.0%	0.2%	
Cleveland—Akron, OH CMSA	3	4	2	0	9	1.8%	0.8%	0.5%	0.8%	
Columbus, OH MSA	0	3	1	0	4	0.0%	0.6%	0.2%	0.4%	
Dallas—Fort Worth, TX CMSA	4	4	3	0	11	2.3%	0.8%	0.7%	1.0%	
Denver—Boulder—Greeley, CO CMSA	2	9	8	0	19	1.2%	1.9%	1.9%	1.8%	
Greensboro—Winston-Salem—High Point, NC MSA	1	1	7	0	9	0.6%	0.2%	1.7%	0.8%	
Hartford, CT MSA	0	0	0	0	0	0.0%	0.0%	0.0%	0.0%	
Indianapolis, IN MSA	2	3	1	0	6	1.2%	0.6%	0.2%	0.6%	
Kansas City, MO—KS MSA	2	2	1	0	5	1.2%	0.4%	0.2%	0.5%	
Memphis, TN—AR—MS MSA	1	1	0	0	2	0.6%	0.2%	0.0%	0.2%	
Miami—Fort Lauderdale, FL CMSA	3	6	4	0	13	1.8%	1.3%	1.0%	1.2%	
Milwaukee—Racine, WI CMSA	3	6	2	0	11	1.8%	1.3%	0.5%	1.0%	
Minneapolis—St. Paul, MN—WI MSA	7	11	5	0	23	4.1%	2.3%	1.2%	2.1%	
Nashville, TN MSA	0	1	1	0	2	0.0%	0.2%	0.2%	0.2%	
New Orleans, LA MSA	0	1	0	0	1	0.0%	0.2%	0.0%	0.1%	
Oklahoma City, OK MSA	1	1	1	0	3	0.6%	0.2%	0.2%	0.3%	
Pittsburgh, PA MSA	2	1	8	0	11	1.2%	0.2%	1.9%	1.0%	
Portland—Salem, OR—WA CMSA	2	6	7	0	15	1.2%	1.3%	1.7%	1.4%	
Providence—Fall River—Warwick, RI—MA MSA	0	3	1	0	4	0.0%	0.6%	0.2%	0.4%	
Richmond—Petersburg, VA MSA	0	3	3	1	7	0.0%	0.6%	0.7%	0.6%	
Rochester, NY MSA	0	1	1	0	2	0.0%	0.2%	0.2%	0.2%	
Sacramento—Yolo, CA CMSA	3	1	3	0	7	1.8%	0.2%	0.7%	0.6%	
Salt Lake City—Ogden, UT MSA	3	4	4	0	11	1.8%	0.8%	1.0%	1.0%	
San Antonio, TX MSA	0	2	4	0	6	0.0%	0.4%	1.0%	0.6%	
Tampa—St. Petersburg—Clearwater, FL MSA	2	3	2	0	7	1.2%	0.6%	0.5%	0.6%	
No Significant Biotech Research or Commercialization										
Charlotte—Gastonia—Rock Hill, NC—SC MSA	0	0	0	0	0	0.0%	0.0%	0.0%	0.0%	
Grand Rapids—Muskegon—Holland, MI MSA	1	0	0	0	1	0.6%	0.0%	0.0%	0.1%	
Jacksonville, FL MSA	0	1	0	0	1	0.0%	0.2%	0.0%	0.1%	
Las Vegas, NV—AZ MSA	0	0	1	0	1	0.0%	0.0%	0.2%	0.1%	
Louisville, KY—IN MSA	1	1	0	0	2	0.6%	0.2%	0.0%	0.2%	
Norfolk—Virginia Beach—Newport News, VA—NC MSA	0	0	2	0	2	0.0%	0.0%	0.5%	0.2%	
Orlando, FL MSA	0	0	0	0	0	0.0%	0.0%	0.0%	0.0%	
Phoenix—Mesa, AZ MSA	0	2	1	1	4	0.0%	0.4%	0.2%	0.4%	
San Juan—Caguas—Arecibo, PR CMSA	0	1	0	0	1	0.0%	0.2%	0.0%	0.1%	
West Palm Beach—Boca Raton, FL MSA	2	0	0	0	2	1.2%	0.0%	0.0%	0.2%	

Source: Institute for Biotechnology Information 2001.

TABLE 16: MARKET CAPITALIZATION OF U.S. BIOTECHNOLOGY COMPANIES

Metropolitan Area	Publicly Traded Biotechnology Companies		
	Number	Capitalization (millions)	Share of Capitalization
Biotechnology Centers			
Boston—Worcester—Lawrence, MA—NH—ME—CT CMSA	58	52,756	12.9%
San Francisco—Oakland—San Jose, CA CMSA	90	82,731	20.2%
San Diego, CA MSA	33	24,764	6.0%
Raleigh—Durham—Chapel Hill, NC MSA	10	9,949	2.4%
Seattle—Tacoma—Bremerton, WA CMSA	15	14,600	3.6%
New York—Northern New Jersey—Long Island, NY—NJ—CT—PA CMSA	77	52,520	12.8%
Philadelphia—Wilmington—Atlantic City, PA—NJ—DE—MD CMSA	19	6,052	1.5%
Los Angeles—Riverside—Orange County, CA CMSA	33	82,992	20.2%
Washington—Baltimore, DC—MD—VA—WV CMSA	23	23,062	5.6%
Research Centers			
Chicago—Gary—Kenosha, IL—IN—WI CMSA	8	2,877	0.7%
Detroit—Ann Arbor—Flint, MI CMSA	3	338	0.1%
Houston—Galveston—Brazoria, TX CMSA	5	1,145	0.3%
St. Louis, MO—IL MSA	1	127	0.0%
Median Metropolitan Areas			
Atlanta, GA MSA	10	1,076	0.3%
Austin—San Marcos, TX MSA	3	627	0.2%
Buffalo—Niagara Falls, NY MSA	-	-	0.0%
Cincinnati—Hamilton, OH—KY—IN CMSA	2	2,564	0.6%
Cleveland—Akron, OH CMSA	2	41	0.0%
Columbus, OH MSA	-	-	0.0%
Dallas—Fort Worth, TX CMSA	4	167	0.0%
Denver—Boulder—Greeley, CO CMSA	8	896	0.2%
Greensboro—Winston-Salem—High Point, NC MSA	2	6,481	1.6%
Hartford, CT MSA	-	-	0.0%
Indianapolis, IN MSA	1	9,860	2.4%
Kansas City, MO—KS MSA	2	1,868	0.5%
Memphis, TN—AR—MS MSA	-	-	0.0%
Miami—Fort Lauderdale, FL CMSA	8	14,236	3.5%
Milwaukee—Racine, WI CMSA	-	-	0.0%
Minneapolis—St. Paul, MN—WI MSA	12	7,835	1.9%
Nashville, TN MSA	1	5	0.0%
New Orleans, LA MSA	1	5	0.0%
Oklahoma City, OK MSA	2	170	0.0%
Pittsburgh, PA MSA	4	5,261	1.3%
Portland—Salem, OR—WA CMSA	3	284	0.1%
Providence—Fall River—Warwick, RI—MA MSA	1	0	0.0%
Richmond—Petersburg, VA MSA	4	950	0.2%
Rochester, NY MSA	-	-	0.0%
Sacramento—Yolo, CA CMSA	2	77	0.0%
Salt Lake City—Ogden, UT MSA	5	1,962	0.5%
San Antonio, TX MSA	1	3	0.0%
Tampa—St. Petersburg—Clearwater, FL MSA	2	87	0.0%
No Significant Biotech Research or Commercialization			
Charlotte—Gastonia—Rock Hill, NC—SC MSA	-	-	0.0%
Grand Rapids—Muskegon—Holland, MI MSA	-	-	0.0%
Jacksonville, FL MSA	-	-	0.0%
Las Vegas, NV—AZ MSA	-	-	0.0%
Louisville, KY—IN MSA	-	-	0.0%
Norfolk—Virginia Beach—Newport News, VA—NC MSA	-	-	0.0%
Orlando, FL MSA	-	-	0.0%
Phoenix—Mesa, AZ MSA	4	1,633	0.4%
San Juan—Caguas—Arecibo, PR CMSA	-	-	0.0%
West Palm Beach—Boca Raton, FL MSA	1	267	0.1%

Source: Biospace.Com 2001.

TABLE 17: MEMBERSHIP IN BIOTECHNOLOGY INDUSTRY ASSOCIATION

Metropolitan Area	Members of BIO	Share
Biotechnology Centers		
Boston—Worcester—Lawrence, MA—NH—ME—CT CMSA	101	14.5%
San Francisco—Oakland—San Jose, CA CMSA	114	16.4%
San Diego, CA MSA	61	8.8%
Raleigh—Durham—Chapel Hill, NC MSA	35	5.0%
Seattle—Tacoma—Bremerton, WA CMSA	19	2.7%
New York—Northern New Jersey—Long Island, NY—NJ—CT—PA CMSA	106	15.3%
Philadelphia—Wilmington—Atlantic City, PA—NJ—DE—MD CMSA	42	6.0%
Los Angeles—Riverside—Orange County, CA CMSA	24	3.5%
Washington—Baltimore, DC—MD—VA—WV CMSA	61	8.8%
Research Centers		
Chicago—Gary—Kenosha, IL—IN—WI CMSA	21	3.0%
Detroit—Ann Arbor—Flint, MI CMSA	2	0.3%
Houston—Galveston—Brazoria, TX CMSA	10	1.4%
St. Louis, MO—IL MSA	9	1.3%
Median Metropolitan Areas		
Atlanta, GA MSA	9	1.3%
Austin—San Marcos, TX MSA	2	0.3%
Buffalo—Niagara Falls, NY MSA	0	0.0%
Cincinnati—Hamilton, OH—KY—IN CMSA	1	0.1%
Cleveland—Akron, OH CMSA	4	0.6%
Columbus, OH MSA	1	0.1%
Dallas—Fort Worth, TX CMSA	3	0.4%
Denver—Boulder—Greeley, CO CMSA	13	1.9%
Greensboro—Winston-Salem—High Point, NC MSA	1	0.1%
Hartford, CT MSA	2	0.3%
Indianapolis, IN MSA	3	0.4%
Kansas City, MO—KS MSA	1	0.1%
Memphis, TN—AR—MS MSA	0	0.0%
Miami—Fort Lauderdale, FL CMSA	3	0.4%
Milwaukee—Racine, WI CMSA	2	0.3%
Minneapolis—St. Paul, MN—WI MSA	10	1.4%
Nashville, TN MSA	2	0.3%
New Orleans, LA MSA	0	0.0%
Oklahoma City, OK MSA	2	0.3%
Pittsburgh, PA MSA	4	0.6%
Portland—Salem, OR—WA CMSA	1	0.1%
Providence—Fall River—Warwick, RI—MA MSA	0	0.0%
Richmond—Petersburg, VA MSA	2	0.3%
Rochester, NY MSA	4	0.6%
Sacramento—Yolo, CA CMSA	4	0.6%
Salt Lake City—Ogden, UT MSA	9	1.3%
San Antonio, TX MSA	3	0.4%
Tampa—St. Petersburg—Clearwater, FL MSA	0	0.0%
No Significant Biotech Research or Commercialization		
Charlotte—Gastonia—Rock Hill, NC—SC MSA	1	0.1%
Grand Rapids—Muskegon—Holland, MI MSA	0	0.0%
Jacksonville, FL MSA	2	0.3%
Las Vegas, NV—AZ MSA	0	0.0%
Louisville, KY—IN MSA	0	0.0%
Norfolk—Virginia Beach—Newport News, VA—NC MSA	0	0.0%
Orlando, FL MSA	0	0.0%
Phoenix—Mesa, AZ MSA	0	0.0%
San Juan—Caguas—Arecibo, PR CMSA	0	0.0%
West Palm Beach—Boca Raton, FL MSA	1	0.1%

Source: Biotechnology Industry Organization 2001.

Conclusion

From an economic-development perspective, biotechnology is clearly a desirable industry. Although generally not among the largest employers in metropolitan economies, biotech firms have the potential to generate highly paid high-skill jobs. It is thus not surprising that as the industry's size and impact continue to expand, many regions across the United States are eagerly seeking to develop a biotechnology cluster. For some, this may mean building upon the early success of a few nascent firms. For others, it may mean working to expand a cluster that is already robust.

The present analysis set out to locate biotech activity by examining various indicators of research capacity and commercialization. The research revealed the relative strengths and limitations of the 51 metropolitan areas studied; from this examination a clear pattern of biotech activity emerged. Further analysis of these patterns helps illuminate the behavior of the industry, providing an indication of how it develops, how it is sustained, and where it might be heading. Several conclusions stand out.

The availability of venture capital and local entrepreneurship is critical.

What does it take to become a region in which biotechnology is routinely commercialized? The presence of at least some level of medical research activity definitely seems to be a prerequisite. All nine of the identified biotechnology centers have high levels of NIH funding and at least one medical research institution that is ranked among the nation's top twenty. None of the ten metropolitan areas with the lowest levels of NIH funding has even 10 percent of the U.S. average of biotechnology commercialization activity.

A strong research presence appears to be a necessary condition for biotechnology commercialization, but it does not seem to be sufficient. Four metropolitan areas—Chicago, Detroit, Houston, and St. Louis—have very high levels of research but below-average values of commercialization activity.

A critical factor in the development of biotechnology appears to be the flow of venture capital to new biotechnology businesses. The relative importance of capital availability is apparent upon considering the relative concentrations of research activity, capital flows, and the growth of new firms.

TABLE 18: RELATIVE CONCENTRATION OF BIOTECHNOLOGY ACTIVITY

Measure	Period	Herfindahl Index	Relative Concentration
Population	2000	0.05	1.00
Medical School Research	1985	0.06	1.28
	2000	0.05	1.10
Patents	1970s	0.17	3.67
	1980s	0.13	2.94
	1990s	0.08	1.81
Venture Capital	1995–2001	0.17	3.77
Research Alliances	1990–1995	0.17	3.82
	1996–2001	0.22	4.84
Firms Established	Before 1980	0.06	1.42
	1980s	0.08	1.72
	1990s	0.09	2.03

A low value represents low concentration, and a high value represents higher concentration. To simplify comparisons, we computed a measure of relative concentration by indexing the Herfindahl statistic to the concentration of population (1.00 means that in the 51 metropolitan areas a variable is exactly as concentrated as population.)

Comparison of the relative concentration of various biotechnology indicators in the 51 metropolitan areas studied (**table 18**) reveals several patterns. First, in recent years the levels of research activity (patenting and NIH funding for medical schools) have been much less concentrated than have been all measures of biotechnology commercialization. In short, research is relatively widespread, but commercialization is concentrated.

Second, during the course of time, research activity has become more dispersed, but biotechnology firm formation has become more concentrated. NIH research funding has become more widespread and is only about 10 percent more concentrated than population. Patent activity appears to be only half as concentrated as during the 1970s.

Third, flows of venture capital and research alliance funding have been especially concentrated, with recent relative concentration values triple those of research and double those of patenting.

Thus the nine leading biotechnology centers may account for a smaller share of NIH funding and patenting than they did two decades ago, but now they account for a larger share of new biotechnology businesses. These nine areas' share of NIH funding has declined from 63 percent to 59 percent of the national total, and their share of biotechnology patents has declined from 71 percent to 68 percent. At the same time, the share of new biotech firms in these regions has grown from 61 percent of all new firms prior to 1980 to 77 percent of all new firms in the 1990s. The critical factor in this process is the very high concentration of capital flows in biotech centers: the nine leading biotech regions account for 88 percent of all venture capital for biopharmaceuticals, 92 percent of the

most active biotechnology venture capital firms, and 96 percent of the dollar value of research alliances with pharmaceutical firms.

Why are these capital flows so concentrated into these nine biotechnology centers? The phenomenon would seem to reflect the agglomeration economies or critical mass of having a large number of biotechnology firms, workers, and investors all in a single location. These areas are more likely to have large numbers of professionals—both managers and research scientists—with previous experience in commercial biotechnology. The areas have concentrations of specialized financial expertise in the form of venture capitalists. Once established, these clusters of activity sustain themselves and even attract additional talent and additional money (especially in the case of alliances with pharmaceutical firms).

Developing a new biotechnology center is challenging.

Many U.S. metropolitan areas are hoping to develop stronger biotechnology industries in the years ahead. What does today's pattern of industrial activity suggest about the kinds of strategies that will be successful?

First, regions hoping to generate a biotechnology industry will need to look beyond strategies focused on significantly bolstering local medical research. The apparent scale of research funding required for becoming a biotechnology center may be beyond the reach of most metropolitan areas, as there is little chance that historically low-funded metro areas will substantially increase their share. In fact, none of the 51 metropolitan areas increased its share of NIH medical school research funding by even 1 percentage point during the last fifteen years. Furthermore, increased funding for research may have no effect on local commercialization. Even those areas with the largest funding increases (Pittsburgh and Cleveland, both up 0.9 percent in share since 1985) have lost ground in their share of biotech commercialization. Success in getting additional NIH research funding may in some cases be a substitute for increased entrepreneurial activity. Instead, the critical missing ingredient in most large U.S. metropolitan areas is likely to be the availability of venture capital for new biotechnology investments. Metropolitan areas looking to reap benefits from commercializing biotech-

nology may find policies to stimulate venture capital and to encourage local entrepreneurship to be the most important steps they can take to develop a local cluster.

Second, it seems clear that conventional industrial recruiting activities will be of limited utility. There is little evidence that biotechnology firms move from place to place. Biotechnology firms develop locally, drawing on the ready availability of talented workers, relevant research, and localized venture capital. Most firms are small, young, single-establishment firms that remain located in the metropolitan areas in which they are started. Consequently, metropolitan areas interested in biotechnology should focus on indigenous biotech development strategies.

Finally, at least at its current pace of development, even successful biotechnology strategies will take a decade or more to bear significant fruit.

Developing a biotechnology industry in metropolitan areas that do not already have a significant biotech concentration will require a considerable investment of time and money. The profile of the three metropolitan areas that have successfully developed a significant biotech presence in the past decade (Raleigh-Durham, San Diego, and Seattle) suggests the level of effort required. Each of these areas has had an average of \$500 million annually in NIH funding (in 2001 dollars) for more than a decade and \$750 million new venture capital investment during the past six years, and each area also has one or more of the nation's 20 top-ranked medical research universities and two or more of the nation's 50 principal biotechnology venture capital investment firms.

[T]he nine leading biotechnology centers may account for a smaller share of NIH funding and patenting than they did two decades ago, but now they account for a larger share of new biotechnology businesses.

The ultimate impact of biotechnology on metropolitan economies is unclear.

Biotechnology is a visible and rapidly growing industry, but it is not yet very large. Nationally, the best estimates suggest that fewer than 200,000 people work for biotechnology firms. Based on the average levels of pay for medical researchers and skilled technicians, these are good jobs. But will a successful biotechnology cluster generate enough jobs to be a major driver in a metropolitan economy?

Even in established biotechnology centers, the overall size of the biotechnology sector is small relative to the economy. For the nine leading biotechnology centers, the total level of employment in pharmaceutical manufacturing and life sciences research (a definition that includes many non-biotechnology firms) is equal to 3.5 percent of all manufacturing employment. In only two metropolitan areas—San Diego and Raleigh-Durham—is the combined level of pharmaceutical and life science research equal to 10 percent of regional manufacturing employment.

Most biotechnology companies seem to have little interest in growing to the size of incumbent pharmaceutical firms. Indeed, most biotech companies form alliances with pharmaceutical giants to obtain revenue; biotech firms that actually succeed in getting a product to market generally either license or sell their intellectual property to a large pharmaceutical firm or contract to such a firm for the product's manufacture, marketing, and distribution. At the metropolitan level, this means that the downstream economic benefits of production and marketing occur in the metropolitan areas that are pharmaceutical centers rather than in metropolitan areas that specialize in creating new products.

Metropolitan areas looking to reap benefits from commercializing biotechnology may find policies to stimulate venture capital and to encourage local entrepreneurship to be the most important steps they can take to develop a local cluster.

Much of the interest in biotechnology stems from the assumed parallels to the revolutionary impact of information and communication technology. Many assume that the new insights about the human genome will produce changes as sweeping as those induced by the personal computer and the Internet. It is of course impossible to predict, but there are some indications that the implications of biotechnology may be far less sweeping. The growth of computer technology was characterized by mass-produced technologies with constantly falling prices. Steady decreases in prices for computer processors, memory, and disk drives and for communication services stimulated their rapid adoption. No one has yet identified any biotechnology corollary to Moore's Law (transistor density doubles each 18 months and falls in price by one-half). Biotechnologies often tend to be quite expensive. Moreover, most biotech products are applicable to only a narrow fraction of the population. The widely heralded new anti-cancer biotech drug Gleevec, for example, may be useful in treating about 5,000 persons per year, at a monthly cost of \$2,000 to \$4,000 per patient (Stout 2001).

Nevertheless, predicting the future path of technological development, much less the economic impact of new technology, is extremely difficult. Even the experts have tended to err on the conservative side: the President of IBM once foresaw a market for no more than a handful of computers worldwide. Changes have tended to happen quite rapidly; a decade ago there were fewer than a dozen dot-com addresses in the world. But it does seem likely that when these as yet unimagined biotechnology breakthroughs come to pass, they will be the product of biotechnology companies located in metropolitan areas with a strong base of research and commercialization.

Appendix

Definitions of the Biotechnology Industry

Biotechnology is a new and rapidly changing industry that has yet to find a neat, separate categorization in either the old Standard Industrial Classification (SIC) code or the new North American Industry Classification System (NAICS). Even so, a general consensus about the contours of the biotechnology industry has emerged from industry participants, investors, and a range of comprehensive studies of the industry. Rather than rely on secondary statistics compiled by government agencies in broad industry classifications, industry analysts and researchers have relied heavily on primary microdata—firm level statistics on employment, investment, and activity. The present study follows this generally accepted biotechnology definition that has emerged, and it employs microdata from a variety of sources.

How the Industry Defines Itself

Those involved in the biotechnology industry—running companies, making investments, recommending stocks, and performing other tasks—seem to have a pretty clear idea of what their industry is and who is and is not part of it. The industry has come of age during the past two decades and has formed an industry association that defines and represents its interests. In addition,

major accounting firms have worked with the industry to compile widely recognized and commonly used data on industry sales, profitability, and investment levels. The definitions and databases used by these organizations may not coincide perfectly with each other, but they are broadly congruent, listing between about 1,000 and 2,000 firms nationwide that constitute the industry.

Two of the leading industry directories have been maintained for more than a decade by the Institute for Biotechnology Information and by the accounting firm Ernst and Young. These sources are well known and widely used by individuals in the biotechnology industry, and biotech firms have a strong interest in being listed in such directories to make themselves visible to potential investors and customers and to the pharmaceutical industry.

TABLE A1. INDUSTRY DEFINITIONS OF BIOTECHNOLOGY

Source of Definition	Description of Source	Definition of Biotechnology Industry
Biotechnology Industry Organization	Founded in 1993 by the merger of two predecessor associations from the 1980s. Now has more than 1,000 members, including about 800 in the United States.	“the application of biological knowledge and techniques to develop products and services”
Ernst and Young (Morrison and Giovanetti 1998)	Has produced surveys of the biotech industry since 1986. States that in 1999 there were 1,283 U.S. biotech companies, 327 of them publicly traded.	not defined (Some E&Y publications use BIO definition.)
IBI (Institute for Biotechnology Information 2001)	Has for 15 years produced the most widely used industry directory of the biotechnology industry. Latest database (2001) lists approximately 1,238 U.S. “biotechnology” firms. (IBI now known as Bioability.)	“firms founded to use new technologies as the basis of their R&D or manufacturing efforts” (Differentiates between pharmaceutical and biotechnology firms.)
PriceWaterhouse Coopers Moneytree (PriceWaterhouseCoopers 2001)	Produces Moneytree database and lists investments in “biopharmaceuticals.” Database lists more than 1,100 investments in 450 companies between 1995 and 2001.	“developers of technology promoting drug development, disease treatment, and a deeper understanding of living organisms, including biochemicals, cell therapy, genetic engineering systems, drug delivery, and pharmaceuticals” (Treats medical devices, health care services, and medical information systems as separate industries.)
Standard and Poor's 2000	Reviews industry for investors. Estimates that biotech industry has more than 1,300 public and private enterprises with 151,000 employees and that human therapeutics account for 75 percent of industry sales and human diagnostics 20 percent (1999).	no specific definition (Treats pharmaceutical firms separately.)

How the Industry Is Defined by Those Who Study It

Among the researchers in a variety of fields who have studied the biotechnology industry, fairly widespread

agreement exists concerning the definition of that industry. Most of the researchers who have undertaken comprehensive nationwide studies of the industry have embraced the industry definitions given in the first

table. A sampling of nationwide comparative studies published in a range of academic journals is presented in the second table.

TABLE A2. ACADEMIC DEFINITIONS OF BIOTECHNOLOGY INDUSTRY

Source of Definition	Description of Source	Definition of Biotechnology Industry
Goetz and Morgan 1995	Studied 734 firms in 1990 reported by Bureau of National Affairs (BNA) State-by-State biotechnology directory. Statistical analysis of locational factors including venture capital and fiscal policies affecting biotechnology firms.	“any technique that uses living organisms or parts of organisms to make/modify products, improve plants or animals, or develop microorganisms for specific use”
Hall and Bagchi-Sen 2001	Sampled 597 firms from combined base of 1,185 firms drawn from the 1997 IBI directory and the 1996 North American Biotechnology Directory. Analysis of factors influencing the location and performance of biotechnology firms.	“products and processes for the diagnosis, treatment, and cure of human disease, as well as the development of genetically customized animals, plants, and food”
Prevezier 1997	Studied 849 firms in 1991 as reported by Dibner. Examination of industry clustering of biotechnology firms and analysis of interrelationships and locational factors in different industry segments.	no definition
Paugh and LaFrance 1997	Relied on Ernst and Young data estimating 1,308 firms founded primarily to commercialize biotechnology. Overview of competitiveness policy issues facing the U.S. biotechnology industry.	a set of “techniques that use organisms or their cellular, subcellular, or molecular components to make products or modify plants, animals, and micro-organisms to carry desired traits”
Zucker, Darby, et al. 1998	Studied 751 distinct U.S. firms based on data on 1075 firms drawn from NCBC (IBI) for April 1990 and additional information drawn from Bioscan for 1989 through 1993. Analysis of role of localized presence of star scientists in determining geography of the biotechnology industry.	no definition
Gray and Parker 1998	Studied 1,308 firms identified by Lee & Burrill (E&Y) in 1994. Examination of location and organization of biotechnology firms based on product life cycle theory.	no definition (Distinguishes between biotechnology and pharmaceuticals.)

How the Industry Is Defined Locally

In addition to comprehensive nationwide studies of the industry, many states and regions have prepared analyses examining the local concentration of biotechnology-related economic activity. In almost all cases the definition of biotechnology is tailored to local perceptions. Every community, it seems, defines its local biotech industry in its own fashion, including and excluding sectors based on differing judgments. Almost all of these definitions include biotechnology as defined earlier, but they also reach out to draw in other activities under a wide array of terms including “biosciences,” “life sciences,” “biomedical sciences,” and “health care technology.” Many of these state and regional studies are used for marketing and promotional purposes; comparisons among local studies tend to be difficult or impossible. A study about Virginia reviewed a dozen studies in other states and concluded that there was “relatively wide divergence in the production sectors that are included in these classifications” and that the conservative approach would be to adopt the current BIO definition (Center for Public Policy 1999).

An expansive, customized local definition of a bioscience industry may be useful in promoting that industry locally or in highlighting unique local linkages between biotechnology firms and other sectors and institutions (like medical device manufacturers, agricultural chemical producers, or medical laboratories). But such definitions are not a reasonable basis for national comparisons, because most of the firms and activity in these other industries, nationally, are unrelated to the core of biotechnology. Moreover, focusing tightly on the biotechnology industry helps reveal the dynamics of industry growth and location in the fastest-growing, most technology-intensive part of the “life sciences.” Trends observed here are likely to be indicative

of the processes that will drive growth in other fields of life sciences if those fields also turn out to be significant future growth industries.

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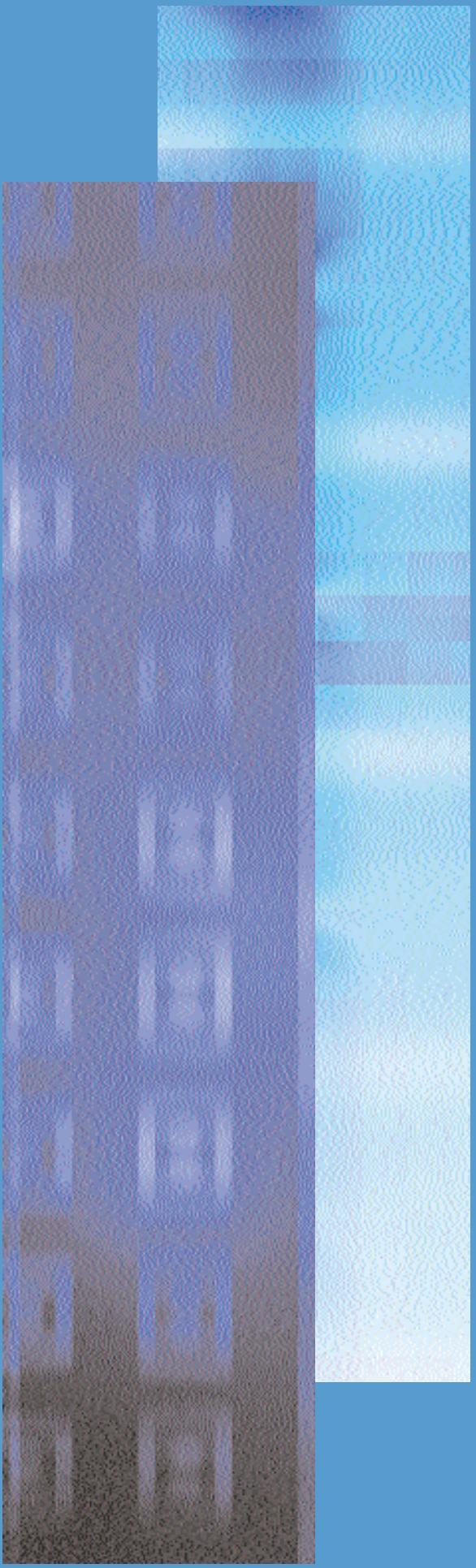
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FOR IN-DEPTH PROFILES

More in-depth profiles of the research and commercialization trends in each of the top nine biotech centers—New York, Philadelphia, Boston, San Francisco, San Diego, Raleigh-Durham, Seattle, Washington-Baltimore, and Los Angeles—can be found on the Brookings Institution Center on Urban and Metropolitan Policy website at www.brookings.edu/urban.





THE BROOKINGS INSTITUTION

1775 Massachusetts Avenue, NW

Washington, DC 20036-2188

Tel: 202-797-6000 • Fax: 202-797-6004

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