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From Ivory Tower to Industrial Promotion:
The Case of Yale University and the Biotechnology Cluster in New Haven, Connecticut

Shiri Breznitz

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Shiri Breznitz
Department of Geography
University of Cambridge

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Abstract

In 2001 Ernst & Young ranked the state of Connecticut seventh in the nation with respect to the number of biotech firms operating within its borders relative to its population (Ernst & Young, 2001). In 1993 there were only six such companies in the state. What led to this increase? This case study describes the development of the biotechnology cluster in the New Haven region of Connecticut, where most of the new biotech companies are located. Our research makes clear that the most important influence on the development of this cluster was that of Yale University. Other contributing factors include the roles played by the state of Connecticut, the city of New Haven, and the local pharmaceutical companies. However, there is little doubt that the dominant influence was the change in the attitude and policies of Yale towards biotechnology-based industrial growth that took place after the arrival of President Richard Levin in 1993. As such, the case confirms that universities can have an important impact on local industrial and economic development.

Key words: Biotechnology, university-industry relationships, technology transfer.

Shiri Breznitz
PhD Candidate
Dept.of Geography
University of Cambridge
Downing Place
Cambridge CB2 3EN
Sb443@cam.ac.uk

I - Introduction

In 2001 Ernst & Young ranked the state of Connecticut seventh in the nation with respect to the number of biotech firms operating within its borders relative to its population (Ernst & Young, 2001). In 1993 there were only six such companies in the state. What led to this increase? This case study describes the development of the biotechnology cluster in the New Haven region of Connecticut, where most of the new biotech companies are located. Our research makes clear that the most important influence on the development of this cluster was that of Yale University. Other contributing factors include the roles played by the state of Connecticut, the city of New Haven, and the local pharmaceutical companies. However, there is little doubt that the dominant influence was the change in the attitude and policies of Yale towards biotechnology-based industrial growth that took place after the arrival of President Richard Levin in 1993. As such, the case confirms that universities can have an important impact on local industrial and economic development.

In the first part of the paper we consider different theories bearing on the role of universities in economic development. The second part of the paper examines the region prior to 1993, by analyzing the representation of biotechnology and pharmaceutical companies, and the availability of resources from the state of Connecticut, local industry associations, and local universities, including Yale. The third part of the paper examines why and how the acceleration in the development of the biotechnology cluster occurred in the period after 1993. The last part of the paper describes the industry as it exists today.

II - Methodology

The development of the biotechnology industry in the New Haven Metropolitan Area (NHMA) was analyzed. The NHMA encompasses Fairfield and New Haven counties, which include the cities of New Haven, Bridgeport, Stamford, Waterbury and Danbury (U.S. Census website, 2003). The unit of analysis was the Pharmaceuticals and Life Science Research and Development Cluster within the NHMA.[1] To gain insight

[1] To confirm the existence of such a cluster, a location quotient [$LQ=(E_{ij}/E_j)/E_{in}/E_n)$] was calculated, where E_{ij} is the employment in industry i in region j, E_j is the total employment in region j, E_{in} is the national employment in industry i, and E_n is the total national employment. Employment in the pharmaceuticals and life sciences r&d cluster is based on NAICS 3254 Pharmaceuticals and NAICS 5417 Life Science

into the development of the biotechnology cluster we gathered information on the regional economy, including local universities, local and state-level policy units, industry associations, and relevant companies, including their date of foundation, source of technology, location, reason for choosing the location, source of employees, relationships with local suppliers and research laboratories (including university research labs), demand conditions, and inter-industry linkages. The data were gathered from two sources:

Interviews – Forty-five in-depth interviews were conducted in two phases: between December 2002 and May 2003, and between March – April 2005. Interviews were conducted with officials from both biotechnology and local pharmaceutical companies. [2] The sample included firms located both in and outside New Haven, and those licensing technology from Yale and those that do not. Interviews were also conducted at Yale University (with both administrators and faculty members), the Connecticut Bioscience Office, Connecticut United for Research Excellence (CURE) (the local industry association), and the city of New Haven.

Secondary Resources – including annual reports of CURE, the website of the state of Connecticut, and the websites of various companies. Other data were gathered from articles and books on biotechnology clusters, innovation policy, the role of the university in economic development, and industry reports. The information obtained from these sources allowed us to compare our findings on New Haven with those on clusters in other states, and to make several generalizations regarding the conditions that are important to the creation of a biotechnology cluster.

III – The economic role of the university

In this section of the paper we examine alternative theories of the economic role of the university. Following Beck et al, we define economic impact as:

R&D. The location quotient for this cluster is >1, which provides evidence of a cluster in the region (there is no significance to how much greater than 1 the number is).

[2] Five pharmaceutical companies have a presence in Connecticut: Pfizer, Bristol-Myers-Squibb, Prude, Bayer, and Boehringer Ingelheim. Most of these firms have research facilities in the state.

> " . . . . the difference between existing economic activity in a region given the presence of the institution and the level that would have been present if the institution did not exist" (Beck, Elliott, Meisel, and Wagner, 1995, p. 246).

What role can universities play in successful regions? The capacity for knowledge creation and diffusion in a university is large and has a potential impact on the economic development of the region in which the university is located. Jaffe, Trajtenberg, and Henderson found that the economic impact of universities is disproportionately felt locally. This research also found that university does not have more economic impact on the region than industry, and that patent citations were equally mentioned from both sources.

There are two ways to measure the impact of a university on a regional economy. The classical or "short-run" approach is to determine the institution's contribution to the annual flow of economic activity in the region. The "long-run" method focuses on the contribution of the institution to the continuous growth of human capital in the region (Beck, Elliott, Meisel, and Wagner, 1995).

The traditional way in which the regional impact of universities has been measured is by counting the dollars flowing into the region as a direct result of the presence of the university. Purchases of goods and services from regional suppliers – such as for office supplies, rent, food, cleaning services -- and payments by the university to employees who live in the region and spend their wages locally, are considered as impacts. In this method the effect of the university is measured only by direct inputs and/or outputs. Indirect impacts, such as firms started by graduates, or new products based on university research, are not taken into account.

The long-run method measures "the future income stream of graduates who stay to work in the area", as well as the economic impact of firms started by graduates, and commercial products based on university research and patents. This method has been used to calculate the return on public funds invested in higher education. Studies have shown that the result of higher education is higher levels of income. In urban areas the presence of universities seems to impact the growth rates, earnings, and composition of employment (Beck, Elliott, Meisel, and Wagner, 1995, p. 246). In sum, from a long-run

perspective universities can contribute to regional economic development by promoting better-paying jobs and encouraging the development of new industry due to the knowledge base influence in skilled labor and R&D. Both university and industry have reasons to collaborate. Public resources directed to university research, equipment and human capital can benefit both. From the university side, it is helpful to receive outside funding and a place for students to actually practice commercial work and research. On the other hand, industry can make sure that universities are working on current issues, making the studies reasonable and helpful to industry. This collaboration is important because it expands the sources of research on which industry can draw (Geisler, 1995).

In this study we evaluate the long-term impact of Yale University on the local and regional economy as a result of changes in university policies and practices that began to be implemented after 1993. We focus in particular on the increases in R&D investments, the number of companies, and the number of employees over time.

IV - Background – The region prior to the transition

This section of the paper provides a description of the region and its industrial capabilities prior to 1993. We first briefly review the historical background of Connecticut and the city of New Haven. We next introduce Yale University, its faculty, students, and finances. In the third part of this section we provide a detailed description of the local pharmaceutical industry, the location of constituent firms, and their relationships in the local economy. Next we examine the relations between the industry and the state government and the policy context for the biotechnology industry. Finally, we summarize the findings of this section and present a broad view of the state, the region, and the pharmaceutical industry prior to 1993.

4.1 The Region – Connecticut and the New Haven Metropolitan Area

Connecticut is situated on the Northeast coast of the United States, bordering Massachusetts, Rhode Island, and New York. Its population is roughly 3.4 million, according to the 2000 U.S. Official Census. Connecticut is often described as the "arsenal of the nation." It gained this reputation early in the 19th century when Eli Whitney and Simeon North began making firearms with interchangeable parts (generally recognized as the birth of mass production). Connecticut's manufacturing industry has since become highly diversified.

Connecticut is also a leader in such technologically sophisticated fields as metalworking, electronics and plastics. In the services sector, Connecticut is known for its strength in insurance. Connecticut began to earn its reputation as the Insurance State more than 180 years ago when marine insurance, the great grandfather of all modern forms of insurance, was first sold. Fire insurance was also first sold in CT, in 1794. Other forms of insurance, such as life, accident, casualty, and health, followed over the next century. Today, there are 133 insurance companies based in Connecticut. (www.CT.gov, 2005).

According to the 2000 census the total population of the New Haven Metropolitan Area (NHMA) is about 1.7 million, divided between New Haven County (population 824,000) and Fairfield County (882,567). Located in the heart of the Northeast Corridor, New Haven (population 119,491) is just 90 minutes from New York City, less than three hours from Boston, and only a day's drive from all the major cities in the Northeast. NHMA is home to seven institutions of higher learning, which provide access to cutting-edge research in critical areas such as medicine, information technology, biotechnology and architecture. The most notable of New Haven's schools is Yale University, the third oldest institution of higher learning in America.

4.2 Yale University

New Haven is the home of Yale University, one of the world's leading universities, known for its excellence in many fields, including the life sciences. In order to examine the university's capabilities in life sciences we analyzed the university's finances, faculty and student enrollment in the medical school and life sciences departments (such as biology) compared to the rest of the university. Although the university had many resources in these fields, its culture of non-involvement in the community in general and industry in particular created a situation in which it failed to reap the credit for several important discoveries, and the region lost an opportunity for economic development through university-industry collaboration.

In 1994, out of a total enrollment of 10,975 students, 704 were enrolled in the school of medicine and 219 in the departments of Biology and Molecular biology & Biochemistry. Out of a total of 729 tenured faculty members, 279 or 38% taught in the medical school and 36, another 5%, in the Biological sciences (The Office of Institutional Research, 2001). According to Yale's 1995-1996 financial report, income

from research grants and contracts represented 29% of total income, and totaled $262.2 million in fiscal year 1996. Of these funds, nearly 75% went to support programs within the medical school and the departments of biological and physical sciences and engineering. Of the $262.2 million, $203.6 million represented federal government funds, of which 80% were awarded by the National Institutes of Health (NIH).

One way to measure knowledge transfers from university to industry is by examining the rate of patenting by the university. In 1994, Yale spent $224,939,000 on research and development (R&D) and registered 16 patents. It is interesting to compare this with MIT, which spent $374,768,000 on R&D in that year and registered 99 patents (National Science Foundation, 2003).[3] Although patenting is only one measure of university involvement in the economy, these figures are broadly consistent with the reputation of Yale at that time as an institution that was only peripherally and episodically involved with the local economy and community. As President Richard Levin noted years later:

> "Outsiders have long regarded the presence of Yale as one of the city's major assets, but, except for episodic engagement, the University's contributions to the community did not derive from an active, conscious strategy of urban citizenship. It is true that our students, for more than a century, have played a highly constructive role as volunteers. Even a decade ago, two thousand students volunteered regularly in schools, community centers, churches, soup kitchens, and homeless shelters, but these volunteer efforts were neither coordinated nor well supported institutionally. When I became president in 1993, there was much to be done to transform Yale into an active, contributing institutional citizen…In prior years, however, the university had taken a relatively passive attitude toward the commercialization of its science and technology "(Yale Office of Public Affairs, 2003).

With the exception of a few departments such as pharmacology, Yale faculty were not encouraged to work on research with practical applications during this period. It was actually implied that the outcome of such involvement would have an unfavorable

[3] While MIT's R&D spending was 66.6% higher than Yale's, the patent ratio was 518.7%.

result on one's academic career. As one interviewee who served on the Yale faculty during the late 1960s observed:

> "One of the things that depressed me was that they did not want to do any application. You could consult but it was not a good status".

There were important discoveries during that period, but the Office of Cooperative Research had a somewhat passive view towards commercialization, and few discoveries were patented[4]. According to another interviewee:

> "[There was] Very little applied research in Biology, maybe in the medical school or Pharmacology, Chemistry department. In the Biology department it was looked down upon. For example we made the first experiments on the transgenic mouse and they [OCR] considered that not to be worthwhile in terms of invention."

> "Yale was very conservative for many years. Not a very active program. Yale actually lost a lot of intellectual property because of this culture. They did not patent on time."

4.3 Local Industry

Connecticut hosts five pharmaceutical companies: Pfizer, Bristol-Myers-Squibb, Purdue, Bayer, and Boehringer Ingelheim, most of which have a major presence in the state, including research facilities. Four of these companies are located in the NHMA. In 1995, a total of $1.2 billion was spent on pharmaceutical R&D in Connecticut itself (6% of the nation's total). Until 1993, most of the pharmaceutical companies did not have a formal institutional relationship with Yale but some had developed research relationships with specific labs or individual investigators. In this section we examine each of these companies by location and major activities. We will show that these companies were rich in knowledge and qualified people and from this perspective had the potential to spin out biotechnology companies.[5]

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[4] One invention that was patented during this period was the profitable drug Zerit®

[5] Since it was not possible to interview each of these companies, we do not have exact information on why these companies chose to situate themselves in Connecticut.

Pfizer --Pfizer came to Connecticut in 1946 in order to build a manufacturing facility. The company was working on fermentation at the time and for that it needed petroleum, molasses, and lime. Those arrived in containers by sea. The U.S. Navy's submarine shipyard in Groton was for sale and Pfizer bought it. Later, when the company needed more space, it moved its research operations from Brooklyn, N.Y. to Groton (50 miles from New Haven). Today, the 137-acre site at Groton conducts research on a broad range of diseases, including central nervous system disorders, inflammatory diseases, immunological disorders, cancer, diabetes, obesity, osteoporosis, and infectious diseases.

Bristol Myers Squibb - In 1986 the company opened a state-of-the-art research complex in Wallingford, CT (14 miles from New Haven) designed to house more than 800 scientists and support staff. The Wallingford Facility is a single, multi-wing building with 1 million square feet dedicated to drug discovery and drug development activities within the Pharmaceutical Research Institute. The following departments are represented in Wallingford:

- Infectious Diseases
- Applied Biotechnology
- Anti-cancer
- Neuroscience
- Combinatorial Chemistry
- Analytical Research & Development
- Metabolism & Pharmacokinetics
- Clinical Research

Purdue Pharma - The company (formerly Purdue Frederick) has its headquarters in Stamford, CT (42 miles from New Haven). Purdue Pharma concentrates its research and development on pain management and cancer. Prescription drugs include pain relievers MS Contin and OxyContin. It is also developing cardiac and respiratory therapies, as well as inhaled drug delivery systems. The firm markets products from other manufacturers in addition to its own. Purdue has research labs in Ardsley, NY and Cranbury, NJ and manufacturing facilities in Wilson, NC, Totowa, NJ, and Coventry, RI.

Bayer - This company arrived in West Haven. CT (4.3 miles from New Haven) after it purchased Myles Labs in 1978. Since the acquisition, Bayer's facilities in West Haven, CT have become the US pharmaceutical headquarters of Bayer. Bayer's activity in West Haven includes research and development, sales, marketing and the distribution of medications that aim to improve the health and quality of life of people worldwide. Bayer at one time had four research facilities around the world in Germany, Japan, the United Kingdom, and the West Haven facility in CT. Today the West Haven facility is Bayer's largest research facility. The UK facility has been closed, and both the Japanese and German facilities have significantly downsized. Major drugs produced at West Haven include the antibiotic *Cipro* and *Cipro IV*, *Adalat CC* for treatment of hypertension, *Precose* for treatment of Type II (non-insulin dependant) diabetes, and a worldwide, market-leading antibiotic.

Boehringer Ingelheim - This company's facility in Ridgefield, CT (43 miles from New Haven) is conducting research in the fields of cardiovascular, immunological and inflammatory diseases and is also conducting non-clinical development.

In sum, most of the pharmaceutical companies in the region have operated research-oriented facilities, staffed with scientists with a deep knowledge base. But interactions with researchers at Yale and other local universities have been limited. None of these companies had established institutional relationships with local research institutes, relying instead on opportunistic specific interactions between their investigators and individual researchers at these institutes.

4.4 State and Industry Relations

Between 1993 and 1996, the state of Connecticut provided no incentives for the development of the biotechnology industry.[6] Two biotechnology companies, including Genlogic, actually chose to leave the region during this period, complaining of a lack of support (space and finance).

At that time, too, there was no state-wide organization representing the biotechnology industry specifically, only the Connecticut Technology Council, an industry association that represents all of the high technology companies in Connecticut.

[6] Compare to Massachusetts that recruited a specialist to deal directly with the biotechnology industry in 1991 after the recommendation from Governor William weld's Commission on Growth and Competitiveness (Breznitz, 2000).

However, in 1990, responding to public concern over the safety and ethical implications of biotechnology in general and animal research in particular, the local pharmaceutical companies in Connecticut had established a 501c (3) non-profit organization called CURE (Connecticut United for Research Excellence). CURE's mission was to educate the public on biotechnology, specifically on the use of animals in research. Initially, CURE was not intended to be a lobbying or a representative body for the industry.

4.5 Summary

Examining the region in the period prior to 1993 and up to 1996, we find the availability of a knowledge base, skilled human resources, demand conditions and a supporting industry – conditions which might have been expected to have led to the creation and development and development of a biotechnology cluster. Yet by 1993 there were only six local biotechnology companies in Connecticut (compared to 129 in Massachusetts at the same point)[7]. These were: IBI (later bought by Eastman Kodak), Pharmacal Research, Protein Sciences, Alexion Pharmaceuticals, Neurogen Corporation, and Curagen Corporation. Only one of these companies, Alexion Pharmaceuticals, had licensed its technology from Yale University. Both Neurogen and Curagen had founders who came from Yale, but in neither case were relations with the university close. As a former executive at Neurogen stated in an interview:

> "Yale was inhospitable to technology spinouts. Blech brothers, a VC Company, started to ask how come Yale, that has such neuroscience expertise [does not spinout companies], and looked for the technology that built Neurogen. So John Tolman and Dorothy Gallagher left Yale for Neurogen,… The first chemistry was done at Wesleyan University since Yale was not hospitable. We could not get any collaboration with Yale."

V - Why and How Did the Transition Occur?

This section describes the ideas and actions implemented by Yale University after the arrival of Richard C. Levin as president in 1993. Although Levin also made many

[7] The six do not include the two companies that had left previously.

other changes at Yale, the discussion here deals in particular with those actions that concerned economic development, i.e. transfer of technology from university to industry.

5.1 Richard C. Levin becomes Yale's twenty-second president

The interviewees that participated in this study overwhelmingly agreed that the catalyst of the change in Yale's attitude toward research with potential practical applications was the arrival of Richard C. Levin as the twenty-second president of Yale in 1993. Levin, an economics professor, had a vision for Yale. He wanted Yale to be a "contributing institutional citizen" with a long-term commitment to the community (President's speech, 2003). By referring to Yale as a 'contributing citizen' Levin was referring to a broad range of activities at the university and not solely its role as an enhancer of economic development.

To pursue this vision the university conducted an in-depth study of the activities already performed by Yale in the community and decided to invest in four areas:

1. Economic Development - "The first area of focus was economic development. We had considerable faculty strength in the biomedical sciences, but no track record of encouragement or support for the transfer of technology to local businesses."
2. Strengthening Neighborhoods - "The second priority was strengthening neighborhoods. Here we believed that increasing the rate of home ownership could improve the stability of neighborhoods and the commitment of residents, and that the university, with 10,000 employees, had the leverage to help. We also believed that as an educational institution, we had human resources that could assist the work of the public schools."
3. Revitalize the Downtown Area - "The third area of focus was to increase the safety, appearance, and vitality of our downtown. We believed that this would greatly improve perceptions of the city and also directly benefit the university community, since we are located in the heart of downtown New Haven."
4. Improving the City's Image - "Finally, we focused on the image of the city, recognizing that improvement in its physical and material conditions was not in itself enough to change perceptions of the outside world. We needed to communicate as well" (Yale, Office of Public Affairs, 2003).

Coming into office in 1993, Levin in his first speech emphasized the importance of Yale's contribution to the local economy:

> "Our national capability in basic research was built by the far-sighted policy of public support for university-based science articulated during the Truman Administration and pursued consistently, though with varying intensity, ever since. Today, the scientific capability of American universities is the envy of the world. We neglect its support at our peril.
>
> As we seek to educate leaders and citizens for the world, as our discoveries spread enlightenment and material benefits far beyond our walls, we must remember that we have important responsibilities here at home. We contribute much to the cultural life of New Haven, to the health of its citizens and to the education of its children. But we must do more. Pragmatism alone compels this conclusion. If we are to continue to recruit students and faculty of the highest quality, New Haven must remain an attractive place in which to study, to live, and to work" (President's speech, 1993).

5.2 The Office of Cooperative Research

In order to support the focus on economic development, Yale rebuilt the office of Cooperative research (OCR). The OCR was established in 1982. At the time, the office was mainly dealing with licensing and tracking patents. There was no real attempt to create or promote technology transfer from the academic to the industrial arenas, although a notable success during this period was the licensing to Bristol-Myers-Squibb of the compound that became the highly successful drug Zerit®. Initially this license produced little or no income to Yale, but by 1998 it was generating royalty income of 30-40 million dollars annually.

In 1995, President Levin and Yale's provost at the time, Allison Richard, approached Gregory Gardiner, a former Pfizer executive, to take charge of the OCR with new roles and responsibilities. Gardiner, a former member of the Yale chemistry faculty, remembered the earlier lack of enthusiasm for research with practical applications, and was eager to help bring about change. Gardiner joined the OCR in 1996 and restructured the OCR into an office with new responsibilities.

> "The duties of the OCR include oversight for patenting and licensing activities, university inventions, and contractual relationships between faculty and industry. OCR staff work with Yale researchers to identify inventions that may ultimately become commercial products and services useful to the public. OCR staff engages in industrial partnerships to license Yale inventions. An important goal for the Yale OCR is to identify new ideas, cultivate venture funding for them, and facilitate their development into companies that become part of the New Haven economy" (OCR, 2003)

One possible interpretation of the decision to invest in the Office of Cooperative Research (OCR) and particularly in biotechnology was that it was a way for Yale to deal with a burgeoning operating deficit that by 1993 had reached $14.8 million. However, this deficit had started in 1991 under the presidency of Benno C. Schmidt Jr. and the university had moved to deal with it through budget cuts and by eliminating several departments. By 1998 the university had covered its deficit. None of the interviewees in our research either knew of or believed that there was any connection between the deficit and Yale's new policy of investing in applied research. Furthermore, expanding the role of the OCR and building closer industry-university relations would not produce immediate income in any case. Since the university accepted equity as part of the consideration for licensing intellectual property, the financial gains would not be realized until the company had been bought or had gone through an IPO (initial public offering).

There were many obstacles facing Gardiner and his team. One of the biggest challenges was to communicate the new priorities to the Yale faculty.

> "I was asked many times by junior faculty, "if I get involved with new ventures through the OCR, will I still get tenure?" I told the committee [Educational Policy Committee of the Yale Corporation (the Yale trustees)] that we have to get Yale faculty to understand it is O.K. At MIT, history says that this is OK but at Yale we need a change of culture" (Greg Gardiner, Former Director of the OCR).

In order to achieve this goal the OCR had discussions with departmental chairs and faculty to explain the institutional change and Yale's commitment to economic

development. They approached faculty who worked on applied research and had made important discoveries in the past. One of these faculty members recalls:

> "The OCR people came to professors who had records in licensing or industry interaction and asked for ideas to patent and establish companies. They came to my lab, they knew I worked in XXX and XXX. One of the compounds went to [NAME OF COMPANY]. They also recruited the management for the company. With the change, Yale has become more entrepreneurial but we are still responsible to our research and students."

An examination of the disclosure process found that there was a need to change the process so as to make sure that the efforts were placed with the inventions that were most likely to succeed. This resulted in a major shift in OCR policies towards seeking out new inventions early, examining them quickly, and investing time and effort only in the strongest candidates. In addition, the upgrading of OCR practices led to the identification and recovery of more than $220,000 of unpaid royalties from several licenses (OCR, 1996). Also, Recognizing that 80% of patents from Yale were in the biomedical field, the OCR opened another office in the School of Medicine with four staff members (OCR, 1998).

During 1996-1997, direct contacts with venture capital firms were established. The goal was not only to persuade venture capital firms of the relevance of university technology but also to convince them of the importance of creating new ventures in New Haven. The hard work of seeking appropriate investors eventually paid off and in 1998, after two years of effort, the first round of financing was concluded with $20 million for five companies.

An equally important problem was the lack of laboratory space for new business ventures. The OCR, with the office of New Haven and State Affairs at Yale,[8] set out to build laboratory space close to Yale's scientists. Accordingly, the university attracted two developers, Winstanley Associates and Lyme Properties, LLC, both of which had experience in building labs. Winstanley bought the vacant headquarters of the telephone company on George Street, and Lyme took over the development and management of

[8] Led by Bruce Alexander

Science Park on north campus (where the university and the city had been trying to build a science park for years without success.).

Today the OCR sees itself as a catalyst of economic development, but hopes that in the future its involvement will not be as important. The missions of the OCR today are to benefit the community by transferring academic inventions to the public, to impact the reputation of Yale University and its faculty, and to contribute to local economic development. It took six years (1993-1998) to implement the changes at Yale and at the OCR specifically. In August 1999 Greg Gardiner retired and Jonathan Soderstrom was appointed his successor as director of the OCR. As a result of the efforts by Yale in general and the OCR in particular fourteen biotechnology companies have been established in the New Haven Metropolitan Area, and many more are in development. See Table 1.

Table 1 – OCR Activities 1996-2000[9]

Activity	1996	1997	1998	1999	2000
New Licenses	28	25	45	20	47
Total Number of Active Licenses	233	190	235	244	270
License Revenue	$5,007,485	$13,091,174	$33,306,248	$40,720,584	$46,121,239
Invention Disclosures	89	80	65	39	36
Total U.S. patent applications filed	48	48	83	97	143
U.S. patents issued	13	24	24	33	32
Start-up Companies formed[10]	3	1	6	3	6

(Source: OCR, 2000)

It is important to note that building local companies is not the OCR's only target. From the 70 licensing agreements put in place by the OCR in 2003, only 10 were with local companies. The OCR promotes the transfer of Yale's technology to industry, local or not.

[9] The information provided in this table reflects all fields of technology and not just biotechnology.
[10] In general, not just in the New Haven Metropolitan Area, and not just biotechnology.

5.3 The Different Players

Yale and the OCR may have been the catalysts that created the biotechnology cluster in the NHMA. However there were other entities who followed Yale's lead and contributed to the success of its efforts. Most of these efforts were launched after 1998.

1. The State of Connecticut - In 1998, based on the work of 125 business leaders from Connecticut, six industry areas were identified as key sectors for Connecticut's economic development. These were: manufacturing, financial services, telecommunications, healthcare, high technology and tourism.[11] Basing its efforts on Michael Porter's cluster methodology, the state launched an industry cluster initiative under the Department of Economic and Community Development. The first attempt to launch a cluster was the Bioscience Cluster. There are two entities representing the state of Connecticut in this effort:

(a) *Connecticut Innovation (CI)* - created by the legislature in 1989, Connecticut Innovation was charged with investing in local companies in order to enhance economic development. The mission of the organization is: "Making equity investments in emerging Connecticut technology companies; providing essential, non-financial support to entrepreneurs; and conducting initiatives that address specific needs of Connecticut's technology sector" (CI, 2003). CI was originally funded by the state. But since 1995, CI has financed its equity investments solely through its own investment returns, and not taxpayer dollars. CI has several ways of investing. Although generally it is an active investor, participating in creating a company, writing the business plan and helping to select the management team, CI sometimes joins in the bridge round or series A of the financing process. Carolyn R. Kahn, PhD, a bio-scientist by training, has been appointed to lead CI's investments in Bio-Science.[12] Two major sources of funds are available to the local biotechnology industry:

- *The Connecticut BioSeed Fund* – This $5 million fund, administered by CI, provides seed capital to address the initial financial needs of young Connecticut companies, sustaining them until they are able to attract a lead institutional biotech investor for a Series A round of financing.

[11] The Bioscience cluster , including biotechnology and pharmaceutical companies, was identified as one of the high tech industries.
[12] CI invests in many fields and not just biotechnology.

- *The Bioscience Facilities Fund* - $60 million fund to underwrite the development of incubator and lab space. The state legislature created the fund in 1998, with $30 million of state monies, and charged CI with its management. CI contributed an additional $10 million, using proceeds from its equity investments. Since then the fund has committed more than $20 million to finance more than 225,000 square feet of laboratory and related space (Connecticut Innovations, 2003).

(b) *Office of Bioscience* – under the second cluster bill in 2001, the state of Connecticut allocated $100,000 to establish the Office of Bioscience under the Department of Economic and Community Development. The Office of Bioscience was built to support start-up and existing companies in the region, to provide all the necessary information on conducting business in CT, to bring new and existing out-of-state companies to the region, and to represent the life science cluster of Connecticut in national and international events (interview with one of the office's executives, 2003).

Other Connecticut incentives for the biotechnology industry include:

- *1996 Biotechnology Tax Incentive Package* - includes exemptions from sales, use and property taxes, and a 15-year carry forward R&D tax credit.
- *1999 Tax Credit Exchange* - Eligible companies which cannot use their research and development tax credits can exchange them with the state for 65% of their value.
- *Sales Tax Relief* - 50% and 100% exemptions are available on certain biotechnology industry materials, such as tools, fuels, equipment and safety apparel.

2. Connecticut United for Research Excellence (CURE) – CURE was originally an educational organization which somewhat unexpectedly in 1998 became the industry representative. In addition to its educational role, CURE had also been used prior to 1998 by many of the biotechnology companies as a venue to meet and discuss issues related to specifically to their (highly regulated) industry (this was necessary partly because the industry could not find a voice at the Connecticut Technology Council). In enacting the cluster bill, the state of Connecticut formalized CURE's unofficial role for the industry and made it the overseeing body for the bioscience cluster in CT. The state has also contributed some funds to allow CURE to broaden its educational activities.

Later most of the state funding was used to cover CURE's participation in the Office of Bioscience.

Today CURE (a) lobbies for the interests of the bio-pharmaceutical industry, seeking to preserve tax incentives for the industry at a time when the state is running a large budget deficit, and also works to develop a qualified labor force for the industry by creating certificate programs in local colleges, (b) educates the public in general, and children in particular, on the science of biotechnology through the BIOBUS program, hoping to stimulate interest in studying and working in life sciences, and (c) acts as a conduit for information needed by the industry (how to manage a laboratory, how to build an animal lab, etc.). Under CURE's auspices, CEO's, CFO's, Public Affairs, and Human Resource executives meet quarterly to share information on similar problems and solutions.

3. The City of New Haven – The city has provided help with infrastructure, such as streetlights and building sidewalks, especially in the area adjacent to 300 George St., a difficult part of town. As mentioned by one biotechnology executive:

> "The city administration is doing more than I expected. They support business. This area here was not a very good part of town, they renovated the area, put streetlights. We did not have a single incident of assault. The city government should take credit for that. The police force is very responsive."

VI - The Impact of Yale's Economic Development Initiative

6.1 The Cluster

Today the Connecticut cluster employs 17,985 people directly, and 35,857 through indirect and induced employment. It consists of fifty-eight biotechnology companies and five pharmaceutical companies, of which thirty-two biotech companies and four pharmaceuticals firms are located in the New Haven Metropolitan Area[13]. Five of the biotech companies are publicly traded: Alexion Pharmaceuticals, Neurogen, Curagen, Gennesiance, and Vion Pharmaceuticals. Of the biotech companies in NHMA, eighteen were created after 1996 with technology, ideas, or founders from Yale, and with

[13] This is not including several companies that are still developing but not fully operational.

the help of the Office of Cooperative Research (see appendix).[14] The Office is involved in developing product scenarios, financial projections and business strategies with the scientists. In many cases, the Office is actively involved in building the company, looking for the right management and investors that will succeed in taking Yale's technology to the market

R&D expenditures by the pharmaceutical industry in Connecticut have doubled since 1995 and today account for more than 12% of all R&D dollars spent by pharmaceutical companies nationwide (CURE, 2003)[15].

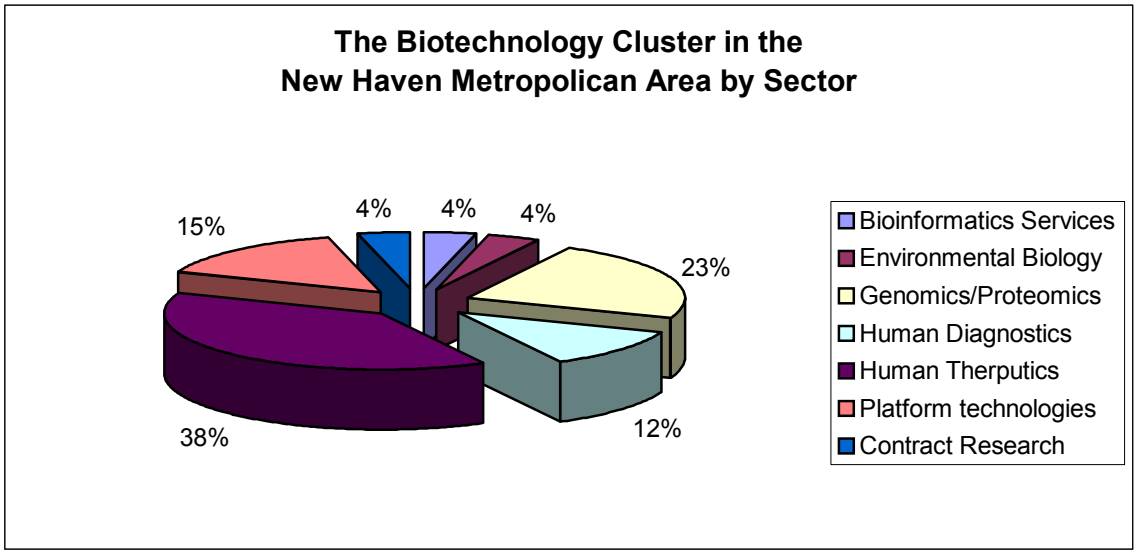
Table 2 - The Bioscience Cluster by R&D Expenses in Connecticut

R&D Expenses	**Year End 2000**	**Year End 2001**	**Total Growth**	**% Growth**
Biotechnology Companies	226,154,159	277,210,873	51,056,714	23%
Pharmaceutical Companies	2,434,900,000	2,904,933,799	470,033,799	19%
Academic Institutes	391,231,208	429,893,436	38,662,228	10%
Total R&D Expenses	**$3,052,285,367**	**$3,612,038,108**	**$559,752,741**	**18%**

(CURE, 2002).

The majority of the biotechnology companies in this area are working in the human therapeutic sector. This includes companies that are working in more than one sector. The results below are based on the self-definition of 15 companies in the cluster.[16]

[14] A total of fourteen companies were established after 1993. Vion Pharmaceutical was established in 1995, and thirteen more companies were established after 1996. See appendix.
[15] Compared to 6% of all R&D expenditures in 1995.
[16] Based on our survey.



6.2 The Local Pharmaceutical Companies

The local pharmaceutical companies have significantly changed their behavior. More weight is given to accessing the local intellectual base. There are constant connections between local Pharma and the local universities and research institutes, cultivated by Yale's OCR, CURE, and the Office of Bioscience. These connections include but are not limited to Yale and the University of Connecticut. Pfizer, for example, chose to utilize the local knowledge base through developing a direct relationship with Yale. Pfizer invested $35 million in a 60,000 square-foot clinical trial facility in downtown New Haven between Park and Howe Streets, which is owned by the State of Connecticut. Bayer initiated a scholar's program in 2003, under which a faculty member is appointed each year as a fellow and works closely with Bayer.

Today one can also find business relationships between local pharmaceuticals firms and the local biotechnology industry. Neurogen Corporation, a biotechnology company, and Pfizer began a two-year research partnership in 1998 to work on GABA neurotransmitter receptor based drug programs for the treatment of anxiety, sleep disorders, and cognition enhancement. Bayer and Curagen Corporation collaborate on obesity and diabetes co-development, pharmacogenomics, and toxicogenomics.

6.3 Yale University

Financing – According to Yale's 2001-2002 financial report, income from research grants and contracts represented 28% of total income (the same share as in 1994), and $417.6 million in fiscal 2002 (a growth of 59.2% from 1994). Of these funds, nearly 77% supported programs within the medical school and the programs of biological and physical sciences and engineering (compared to 75% in 1994). Of the $335 million in federal funds, 76.7% (compared to 80% in 1994) were awarded by the National Institutes of Health. A major difference in the contributions to Yale is that the state of Connecticut provided $83 million for research, training and other purposes.

With respect to outcomes, in 2002 there were fourteen biotech companies that were based on technology licensed from Yale, compared with only one in 1993.[17] Also, in 2000, Yale University registered a total of 29 patents compared with 16 in 1994.[18] Table 3 shows that Yale's patent 'productivity' (expressed as the number of patents granted per dollar of R&D expenditure) increased significantly during this period.

Table 3 – Sample of U.S Universities patents and R&D Expenses ratio[19]

	1994			2000		
	Patents	R&D Expenditures	Ratio	Patents	R&D Expenditures	Ratio
MIT	99	374768	0.00026 (1)[20]	113	426299	0.00027
Columbia	18	236417	0.00008 (4)	51	319693	0.00016
Cornell University	39	312683	0.00012 (3)	49	410393	0.00012
Yale	16	224939	0.00007 (5)	29	296706	0.00010
Duke University	29	220220	0.00013 (2)	32	356625	0.00009
Harvard	16	278459	0.00006 (6)	26	341810	0.00008
Ohio State	10	230515	0.00004 (7)	26	361399	0.00007

Faculty and students – Between 1994 and 2002 there was a 22.7% increase in the number of tenured faculty at the medical school, compared to an 11.2% increase at Yale as a whole. Student enrollments have grown by 11% in the medical school, compared to

[17] Only one Alexion licensed its technology from Yale. The other two companies, Curagen and Neurogen, were established by former Yale academics without a formal licensing.
[18] Compared to 113 in MIT. If we compare the number of patents in Yale and MIT on the same fields Yale had patents in 2000. Yale had 29 compared to 58 at MIT; a difference of 50%.
[19] Comparing universities with similar levels of R&D expenses, except MIT. Source: US patent office.
[20] Represent the rank in 1994.

an increase of only 3% in the general enrollment at Yale (Office of Institutional Research, 2001, 2003). According to Yale's officials, this increase in faculty at the medical school was not planned. It resulted rather from the growth in research grants and contract funding over the years. Another contributing factor was the hiring freeze in the arts and sciences schools during the early to mid-1990s. Furthermore, in 1995, with the appointed of Michael Merson, M.D as dean of the school of public health, there was an increase of student enrollment in the Epidemiology and Public Health departments at the medical school[21].

Faculty members at the Yale medical school whom we interviewed reported that there are benefits in having local biotechnology companies. The industry-university relationships allow scientific interactions, sponsorship of students, provide access to expensive equipment that is not available at Yale, and expose students to industrial practices.

> "Now, for example, we have a company that is occupying some space in the lab..... It is good to have them here, because you have interactions with them and transfer of expertise." (A faculty member at Yale).

VII – Conclusion

The main objective of this study was to gain insights into the role of innovation in local economic development. The central puzzle was to understand how a region which was host to only six biotechnology companies in 1993 had within a decade become a center of biotechnology, measured by the number of companies. The finding that a cultural change at a university was the main reason for this change gives this study particular significance.

This paper describes how in Connecticut, where until 1993 only six biotechnology companies existed, twenty-six biotechnology companies were established in a decade.[22] This surge of new business formation placed Connecticut seventh in the nation with respect to the number of biotechnology companies in 2001. We conclude that the development of the biotechnology cluster in New Haven can be directly linked to the

[21] The School of Medicine includes the M.D., Epidemiology & Public Health, and Physician Associate programs.
[22] See Appendix I.

initiatives of Yale University. The university investment as a whole, and the activities of the office of Cooperative research in particular, were the catalysts for the creation of many of the local biotechnology companies.

Universities have been at the center of many studies on economic development. Many researchers believe that universities have an important role in the development of local economies, although there are different views as to the role these institutions can and should play. This paper presents a case in which the power and capabilities residing in a university were the central factor in local economic development.

As much as this paper highlights the importance of Yale in the development of the biotechnology industry in the New Haven area thus far, it is also important to discuss the future of the industry. The future success of this cluster will not depend solely on Yale. In order for a high technology cluster to succeed there is a need for close and sustained knowledge transfer and cooperation among companies, universities, and local state and industry organizations. Although there are efforts underway to create a vibrant and communicative cluster, there is still a long way to go. Many of the local companies are not aware of all the available resources and do not see themselves as a unified cluster. The main channels of communication are between individual companies and university laboratories. There are still relatively few links between the companies in the region. Moreover, companies that did not originate from Yale have almost no relationships with the university. The fact that the cluster is divided between three major locations without a central place to meet and exchange ideas adds to the need for leadership that will connect all the players of this cluster: universities, biotechnology companies, pharmaceutical companies, state and industry representatives. More research is needed on these issues.

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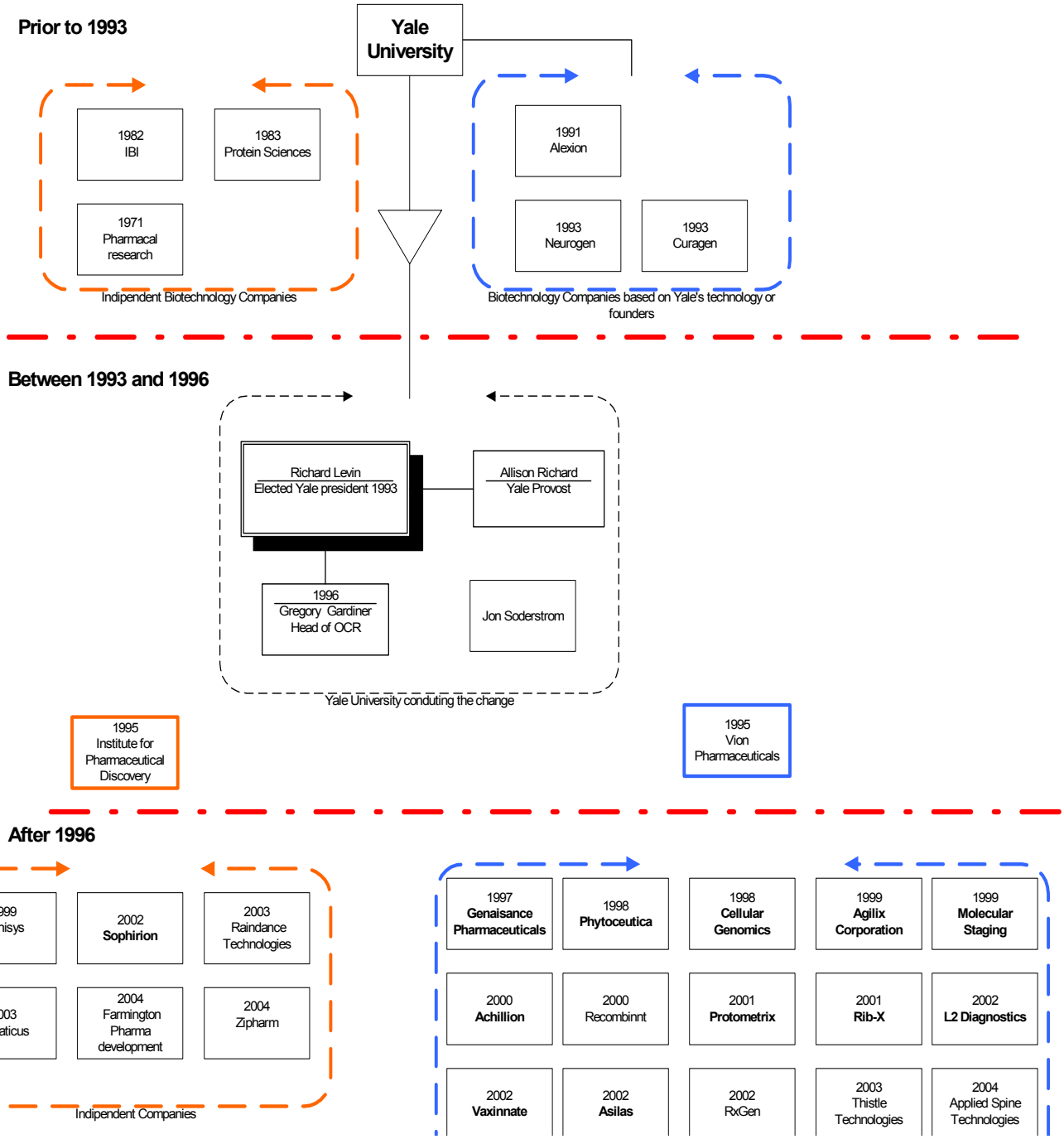
Appendix I

The biotechnology industry in New Haven, Connecticut 1993 - 2003



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Shiri Breznitz
PhD Candidate, Dept. of Geography, University of Cambridge
Email - sb443@cam.ac.uk

Research: My main focus is regional economic development. I am particularly interested in university-industry relationships and their influence on local economies.

Technion - Israel Institute of Technology
Technion City, Haifa 32000, Israel
www.neaman.org.il