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The role of research institutions in the formation of the biotech cluster in Massachusetts: The MIT experience

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Abstract
Based on the MIT experience and that of other US universities, the formation and sustained existence of biotechnology company clusters are discussed. A cluster's origin and continued health are dependent upon government funding of state-of-the-art science in universities and institutions. Effective technology transfer is also necessary with a formal legal infrastructure for university participation and sufficient funds to file patents. The formation of new companies requires a business infrastructure in the community and talented people: researchers; technology transfer professionals; entrepreneurial company founders; scientists and managers to staff the companies; and knowledgeable investors. Finding people gets easier as clusters grow. It takes a whole community to build a biotechnology cluster – but once built, the cluster can achieve a sustaining life that strengthens itself.

Keywords: *biotechnology clusters, technology transfer, start-up companies, university entrepreneurship*

Biotechnology 'clusters' are defined as geographical regions where a disproportionately large fraction of biotechnology companies are located. There are three major biotechnology clusters in the USA – the Boston/Cambridge area of Massachusetts; the San Francisco Bay area of northern California; and the San Diego/La Jolla area of southern California. This paper explores the factors behind the formation and growth of the Massachusetts cluster, but applies in large part to the other biotech clusters in the USA. The emphasis is on the critical role of research institutions in the formation of this cluster, highlighting in particular experiences at MIT.

The Massachusetts cluster accounts for almost 20 per cent of the total number of biotechnology companies in the USA – over 280 companies. Essentially all of these companies started as small, entrepreneurial companies within the past two decades, with the majority of them formed within the past 12–15 years. According to data from the Massachusetts Biotechnology Council, these companies now employ over 30,000 people. In addition, there are over 220 medical device companies in the region employing an additional 25,000 people.

Conventional literature on the formation of entrepreneurial clusters of companies in other high-tech fields has stressed the importance of supply chains, including large 'anchor' companies that provide the nucleus of highly trained personnel who spin off to form new companies, and which also purchase services and products from the new companies; and other vendors to the anchor companies and related suppliers, who form a symbiotic relationship with the entrepreneurial companies.[1] The formation of the biotech cluster in Massachusetts contradicts this model to some extent: there are no large pharmaceutical companies in Massachusetts – and the regions where

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the large pharmaceutical companies are located (primarily New Jersey and Chicago) have not spawned biotech clusters.

A DIFFERENT SUPPLY CHAIN

A different supply chain has led to the formation of biotechnology clusters in the USA. It starts early with fundamental support of basic research by the Federal Government, leading to the discoveries making biotech possible. Leading research institutions make the discoveries, develop the intellectual property and also train the scientists that form the biotech companies; where the research institutions cluster, the new companies eventually form. The supply chain continues with alliances between the biotech companies and the large pharmaceutical companies that will often be necessary to test, manufacture and distribute the drugs discovered by the biotech companies, but experience shows that the geographical location of the big pharma partners is unimportant. More important regionally are supplies of investment capital (and experienced investors), executive talent, trained scientists and a host of support functions: lawyers, accountants, real estate professionals and others who understand biotech entrepreneurship and can help fledgling companies establish themselves. Good airports are critical, and local communities attractive to highly talented personnel and their families are a competitive advantage.

The supply chain starts with basic research support from the Federal Government

Local infrastructure of venture capital, managers and service providers accelerate the cluster formation

BASIC RESEARCH: THE BEGINNING OF THE BIOTECH CLUSTER SUPPLY CHAIN

The chain starts with basic curiosity-driven research in biology and medicine supported by the US taxpayer, leading to the discoveries that underlie the biotech industry. In fiscal year 2003, the National Institutes of Health (NIH) funded US$21bn of research grants to universities, research hospitals and other research institutions. Decades of such funding, and the consistent belief of Congress, many presidential administrations and the American taxpayer in the value of such basic research, led to, among many other advances in biology and medicine, the genome revolution. This revolution transformed drug discovery from 'hit or miss' to discovery based on understanding of the mechanisms of the body and of disease pathology. New tools developed in basic research programmes become the 'platform technologies' for new biotech companies. Finally, these research grants serve as financial support for the training of new graduate students, postdoctoral researchers and medical residents interested in medical research.

World class educational institutions cause a 'brain drain' into a region

Locally, the Boston/Cambridge area of Massachusetts has an unusually large concentration of world-class research institutions – universities and research hospitals – funded in large part by the US Federal Government, and particularly the NIH, to perform basic discovery research in biology and biomedicine. These include, among others, the Massachusetts Institute of Technology, the Whitehead Institute, Harvard University, Massachusetts General Hospital, Brigham and Women's Hospital, Boston University and many others. Together, Massachusetts research institutions received over US$2.1bn in NIH research grants in fiscal year 2003, approximately 10 per cent of the national total.

From this research comes much of the 'feedstock' for new biotech companies: new discoveries, intellectual property (to be discussed in more detail below), knowledgeable scientific advisors for new companies and, importantly, well-trained scientists to staff the new companies.

HUMAN CAPITAL

A 1997 study by the BankBoston of the influence of MIT on the Massachusetts economy noted that 'Massachusetts is importing company founders as a result of MIT'.[2] The same holds for the other world-class educational institutions in Massachusetts: these highly selective

MIT chooses its students both on academic credentials and demonstrated leadership ability

Role models in entrepreneurship change student aspirations for their future careers

Patents to university technology are key in attracting investment capital

universities select the best and brightest students from around the country and around the world, creating an 'inward brain drain'. And, as shown by the BankBoston study, a large fraction of students who come to Massachusetts for university study or medical residences stay in the state after graduation. The BankBoston study further showed that 42 per cent of the high-technology companies formed by alumni of MIT were in Massachusetts, even though only 9 per cent of the undergraduates at the Institute were originally from Massachusetts.

MIT's admission criteria, particularly for undergraduates, contribute to the entrepreneurial spirit at the Institute and the ultimate impact of its graduates on the economy. In its highly selective process of evaluating candidates for admission as undergraduates, MIT looks not only for high academic achievement (grades, standardised test scores etc) but for a certain quality of 'leadership' – an intensity and focus that lead not only to achievement, but to an impact on others. Young people having these qualities often also possess the self-confidence that allows them to think unconventionally and to take risks – including the risk of joining (or forming) an entrepreneurial company.

The education of these students (and of their graduate student big brothers and sisters) stresses the fundamentals of science, rather than short-term applications, and students are involved in leading-edge research projects early in their undergraduate education. MIT's goal is to produce graduates who will have the capabilities of leading the future based on solid grounding and familiarity with the state of the art.

An important influence on these students during their education at MIT is role models in entrepreneurship who expose these students to entrepreneurial thinking throughout their time at the Institute. Many of the professors and the alumni who visit campus – and not a few of the students' friends – have started companies based on MIT technology. Role models are key elements in developing an entrepreneurial culture; the plethora of them at MIT and in the Boston/Cambridge area leads others to think that 'I can do it too' – and offers many resources for advice and strategy.

These resources are supplemented with a student business plan contest (the '50K contest', its name based on the US$50,000 prize) which encourages formation of teams including science and engineering students coupled with MBA students, with 80–100 business plan entries each year. Up to a dozen of these business plans achieve venture capital funding. And MIT has an increasing number of lectures and courses not only in the business school but also in the schools of science and engineering on the management of technology and on entrepreneurship.

Finally, the culture at MIT stresses that risk-taking is necessary for achievement, and, importantly, 'Failure is a learning opportunity – not a black mark'. The assumption is that these students are good enough that they can afford to take risks; they have sufficient talent, energy and self-confidence to recover rapidly from failure and learn from it to be more effective in their next endeavour. This attitude is critical for entrepreneurship.

INTELLECTUAL PROPERTY AND TECHNOLOGY TRANSFER FROM UNIVERSITIES

Although there is some debate as to the overall importance of the role of patents and other intellectual property in the transfer of technology from universities to industry and as to the need or utility of exclusive licences, the conclusions are confounded by the lumping together of data from many different technologies and business sectors. There is no doubt, however, that investors in biotechnology companies usually require a showing of exclusive rights to patents and other intellectual property by the company before they will invest – and that the great majority of new biotechnology companies' founding intellectual property is licensed from universities.

Technology licensing from universities was greatly accelerated by the passage of the Bayh–Dole Act in 1980, which allowed universities to own the patent arising from Federally funded research, and permitted them to grant exclusive licences and to charge royalties, which would be shared with inventors. Since close to 90 per cent of the basic research funds in American universities come from Federal funds, this law changed the face of university technology transfer.

The Bayh–Dole Act's primary purpose was economic development

Congress's primary purpose in passage of the Bayh–Dole Act was economic development: to translate America's lead in fundamental research into new cures for disease, new products, new jobs and new companies. The theory behind the law's application to university research was based on realisation of the embryonic nature of university discoveries and inventions. Since universities do not develop products, early investment by industry was needed to turn university findings into commercial reality – and such investment would invariably be at high risk, since neither the practicality of the inventions nor their market utility was proven. Patents, and particularly exclusive licences, could be used as an incentive for 'first mover' companies to make the investment: if the product succeeded, the patent would protect the initial investor from competition for a period of time, rewarding the initial risk-taking.

The Act provided a legal basis and economic incentive for universities to participate

Finally, the law provided an economic incentive for both universities and their researchers to patent their inventions and participate in the technology transfer process. Although the royalties gained from technology transfer are only a very small contribution to university budgets (averaging about 3 per cent of university research budgets for US universities), there is sufficient economic return to support the process, and considerable incentive for individual researchers. More importantly for the biotechnology industry, the technology transfer process allow for an organised and effective method for transferring university findings via protected intellectual property to form a protected technology dowry for new companies.

Since the passage of the Bayh–Dole Act, the number of patents issued to universities, hospitals and research institutions per year has increased almost 10-fold: from under 400 US patents in 1980 to over 3,500 in fiscal year 2002. In fiscal year 2002, American universities, hospitals and research institutions granted over 4,300 technology transfer licences, and over 400 new entrepreneurial companies were founded based on their intellectual property.

MIT's own statistics for technology transfer are shown in Table 1. With 80–100 licences granted per year by the Technology Licensing Office at MIT, over 25 per cent are to entrepreneurial new companies, formed to exploit the licensed technology. This means that MIT is starting 20–30 new companies each year, about a third of which are biotechnology companies. Table 2 gives a sampling of the biotech companies formed around licences to MIT patents.

Table 1: MIT Technology Licensing Office statistics: fiscal year 2004

- 510 inventions disclosed to MIT
- 159 US patents issued
- 94 licences and options granted
- 20 companies founded around MIT IP

Table 2: A sampling of over 40 biotech companies formed out of MIT since 1998 in a wide variety of fields

- Akceli: drug discovery arrays
- Alnylam : siRNA therapeutics
- Advanced inhalation research: aerosol delivery of drugs
- Matritech: bladder (and other) cancer detection
- MnemoSciences: shape memory polymers for medical devices
- Microbia: antifungal drug discovery
- Momenta: polysaccharide drugs/anticancer
- Ribocept: anti-RNA drugs
- Cardium: cholesterol transport therapeutics
- Sirena: anti-Alzheimer's drugs
- Microchips: chip-based drug delivery devices
- Galenea: anti-schizophrenic drugs

The variety of companies is interesting, ranging from drug discovery platforms to diagnostics to drug delivery systems.

THE 'VIRTUAL INCUBATOR' AT MIT

MIT does not formally 'incubate' companies. It does not invest MIT money in the companies, nor does it allow them to use MIT laboratory facilities. MIT also does not write their business plans nor participate in their management. Its formal role in starting up companies is confined to filing of patents and negotiating licence agreements with the companies. It will often take equity shares in the company as a partial payment of royalties, but it does not take board seats on the company. The objective is to keep a clear separation of the company from the university. MIT believes this separation to be necessary, so that the university itself concentrates on its mission of basic discovery research, dissemination of knowledge, and education, managing technology transfer as a 'by-product' of the academic process that should not distort the long-range mission. MIT has an unusually strict set of conflict-of-interest rules for the spin-outs, required because of the very large number of companies spun out (over 250 since 1987). Management by exception would not be possible given this large number. These rules are to be used as 'boundaries', but arrangements within the rules should be crafted efficiently and creatively. ('A firm wall between university and industry – but a wall with many doors.') The MIT conflict of interest rules for start-ups are shown in Table 3.

A virtual incubator keeps the academic and business roles separate

Although the formal role of the MIT Technology Licensing Office in start-up companies is limited, its informal role is much wider, defining the 'virtual incubation' function that encourages and accelerates the formation and growth of the start-up companies. The initial licence agreement itself contains terms that help. The financial terms are generally quite mild for the first few years of the company, reflecting the understanding that new companies are cash poor; and MIT's royalties on products are low, reflecting that the company will have to make substantial investments and contribute substantial intellectual property that it develops itself before the product reaches successful commercialisation. And an important part of each licence agreement – both for MIT and for the company – is the 'milestone' (or 'diligence') terms that require the company to raise minimum amounts of

Table 3: MIT conflict of interest rules for start-up companies

1. Faculty member may consult but not be a line officer in any company. Consulting activities should not use university resources and should not use students.
2. Faculty member must distinguish direction of research at university from responsibilities at company in which he/she owns equity.
3. The university will not accept sponsored research grants from the company if the faculty member owns equity.
4. No confidentiality of research results (any time). All research must be publishable.
5. Only patents, copyrights and tangible property can be licensed for compensation (no 'know-how' or 'trade secret' licensing can be done since this would preclude open publication).
6. Faculty members may not conduct the licence negotiations (nor attend the negotiations).
7. Consulting is 'third-party,' between the faculty member and the company. No tie-in with the licence.
8. Only very minimum commitment of future inventions (those dominated by previously licensed patents). No pipelining of 'improvements'.
9. Faculty member/founder who holds equity signs 'Conflict Avoidance Statement' promising:
   - Not to accept research support from company.
   - Not to suppress dissemination of research findings.
   - Not to use students on company-related work at MIT.
10. Arm's length relationship between the university and the company.
    - No MIT monetary investment in the company.
    - No board seat.
    - Equity managed by Treasurer of MIT – *not* the Technology Licensing Office (TLO).
11. TLO enforces diligence terms, payment of patent costs, other licence obligations 'just like any other company'. No special status for 'MIT start-ups'.
12. Yearly departmental overview of faculty outside interests.

Common sense: emphasis on the spirit (not just the letter) of the rules, administered by people with judgment and authority.

capital and to achieve progress in product development. The capital-raising milestones assure us that the outside market finds this company worthy of investment and that sufficient capital is raised to fund development.

MIT's virtual incubation incorporates many other functions. It meets with inventors to help them define the direction of the company and their own career aspirations. MIT can introduce them to consultants, potential executives and other advisors who can help them formulate their business strategy and write business plans. And, because of the long relationships with sources of investment capital, MIT can introduce them to venture capitalists and angel investors who may invest in the companies.

Maintaining contacts in the business community leverages resources to build companies

Thus, a key part of the technology transfer function at the university is to develop and maintain a wide range of contacts with the surrounding business community, leveraging these resources to help build our companies. Our model for starting up companies is dependent on a mature, entrepreneurial community surrounding the university.

THE ENTREPRENEURIAL COMMUNITY

Although MIT does not have an incubator for start-up companies, the surrounding Cambridge/Boston community provides an infrastructure of support in many ways for such companies. High-technology companies have been regularly spawned in the region for over 40 years, and therefore there is a large population of executives, lawyers, accountants, consultants, real estate managers etc who are experienced with new companies. The community is well connected. Networking organisations such as the MIT Enterprise Forum, the Massachusetts Biotechnology Council and many others keep people in contact with one another.

The region has an unusually strong network of experienced professionals and knowledgeable investors

Finally, the community has developed 'knowledgeable money': investors who contribute not only funds to start-up companies, but wisdom, guidance and the connections to management talent, business development opportunities and follow-on money. An important role is played by a new breed of high-technology angel investors: former entrepreneurs who founded and cashed out from successful companies and are now bringing wisdom, connections and experience along with their money. There are also venture capital funds that specialise in technology-based start-ups. Many even subspecialise in biotechnology, with partners and associates with MD and PhD degrees in biology and experience in the biotech industry.

THE SELF-FEEDING CLUSTER

Even with a base of world-class university research and resulting technology and intellectual property emerging from it, it is difficult to get a cluster started – and there is no simple formula for doing so. But once started, a cluster begins to feed itself in a virtuous cycle.

The biotech cluster 'feeds itself' through:

- Role models: people who have founded companies and can offer examples of success, and advice to new entrepreneurs.
- Management/founders: often new company management is recruited from other companies in the region. People who were just employees of early companies in the cluster acquire the skills and interests to become founders of new companies. New companies can also recruit other skilled personnel from the older cluster companies.
- Retention of new graduates: a cluster of biotech companies in a region encourages new graduates from the region's universities to seek employment in the region, consolidating the region's skills. As two-career families become more common, couples seek regions in which both spouses can find

Clusters feed themselves, each new company makes the next one easier to build

It takes a whole community to build a biotech cluster

employment and can move to other companies as their careers progress, without having to relocate.

- Infrastructure support: the region's patent attorneys, lawyers, accountants, recruiters, real estate managers, consultants and equipment suppliers develop special skills in biotechnology as they respond to the needs of the cluster.

- Technology transfer: as the universities and other research institutions develop more experience in dealing with biotechnology companies and biotechnology start-ups, they become more effective in starting new companies that add to the clusters. Success with technology licensing and spin-outs leads to revenue which funds the filing of more patents and more opportunities.

- Angel investors: local angel investors are the most effective, since they can offer their skills and experience in addition to their money. As clusters mature, founders of the early companies frequently become investors in the new companies.

- Venture capital moves in. At the start of the Massachusetts biotechnology cluster, there was very little indigenous venture capital. Most venture capital money came from funds located in New York, California and other regions. With the growth of high-tech clusters (both biotech and telecom) in Massachusetts, many of these funds opened new offices in Massachusetts, and many new venture funds were formed locally. Currently, the majority of new company financings in Massachusetts are led by venture funds with offices in Massachusetts.

FINAL OVERVIEW

Many elements contribute to the success of a biotech cluster. Its origin and continued health are dependent upon a continuing source of state-of-the-art science, usually from universities and research hospitals funded for basic research. The source of this funding probably needs to be from government; no private institutions can afford to fund sufficient speculative basic research to sustain the flow of discoveries necessary to support a cluster's growth.

Effective technology transfer is also necessary. The legal infrastructure for transferring inventions from the universities must be in place (and relatively non-bureaucratic) and sufficient funds must be available for the universities to file patents and protect their intellectual property.

Formation of new companies requires a business infrastructure in the community. A simple legal system for company formation, consulting, accounting and legal professionals to advise the company, and adequate space are all necessary. Good transportation into the region is critical as investors and business partners visit the company. And investment capital is of course critical.

Most of all, formation of companies and the subsequent development of clusters requires talented people: world-class researchers to lead the discovery; trained and talented technology transfer professionals; entrepreneurial company founders; scientists and managers to staff the companies; and knowledgeable investors who can both fund and guide the company, and the support professionals in the community.

It takes a whole community to build a biotechnology cluster – but once built, the cluster can achieve a sustaining life which strengthens itself and the community.

References

1. Segal, Quince, Wickstead (1985), 'The Cambridge Phenomenon', Segal, Quince, Wickstead Ltd, Cambridge.
2. MIT (1997), 'The Impact of Innovation', BankBoston Economics Department Special Report, March.