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very early-stage knowledge-based firms, whereas science parks and business centers appeal to businesses graduating from incubators and university spinouts.

Incubators can come with or without "walls". Most incubators provide property on a flexible basis, offering easy-entry and easy-exit tenancy terms, and will offer some common facilities and services. The level of provision depends on the individual incubator and the types of business it targets, but frequently incubators offer a central reception area, communal areas (e.g., meeting rooms, a café or restaurant, and kitchens), access to telecommunications, and sometimes shared secretarial services. These services alleviate the administrative burden the tenant companies must bear, reducing the need for equipment and personnel. However, a growing number of "virtual" incubators are delivering a similar package of business support and development services, but without a physical property. Case studies of the two very different types of incubators are outlined below (see "Innovation in Manchester" and "Incubation without walls").

Does incubation work?

Incubators have been created with the intention of achieving a wide range of objectives, primarily those at which small businesses are good: creating jobs, developing innovative ideas, diversifying the local economy, and broadly generating activity and wealth in a region by creating a vibrant small business sector. However, bioentrepreneurs may well ask whether they actually achieve such goals.

As a test case, in 2001, UK Business Incubation measured the impact of incubators (not specifically for biotechnology) on the local economy and work force in the United Kingdom. The survey[1] revealed that an incubator's client businesses provided an average of 167 jobs (full-time equivalents) per incubator and were home to an average of 30 client businesses. Most (60%) incubators also operate "outreach" services, helping and advising companies located outside the walls of the incubator. Incubators operating outreach activities supported an average of 106 additional businesses. Across the sample, an average of 75% of client companies turned over up to £500,000, but only 1.5% had a turnover of more than £5 million.

More importantly, companies housed within UK incubators had an average success rate of >80% compared with the national average of <50% (ref. 2) of all small- and medium-sized companies registered and trading in that year. Around 70% of incubators attempted to measure the impact of their client businesses, for example, on the basis of jobs created and financial performance. Such indicators have also influenced government policy and funding in this arena.

Such studies[3] do highlight the support for incubators, as well as their potential contribution. In particular, they highlight the usefulness of incubators in identifying and supporting potential growth businesses, helping technology transfer, developing innovation, and expanding the range of local businesses. However, because incubation has been operative in the United Kingdom for only a relatively short time, there is less evidence that they are generators of jobs and wealth. Perhaps this is to be expected given the nature of these facilities, which is to offer longer-term approaches to immediate start-up deficiencies. The true benefits to the economy are not likely to be evident for some years to come, but such is the nature of biotechnology.

1. UKBI Mapping Survey. http://www.ukbi.co.uk/other/pages_render. asp?page%5Fid=20
2. *Finance for Small Business in Deprived Communities*, 6th edn. Domestic Finance Division, Bank of England, London, UK, 2000
3. Chapman, P. & Hannon, P. *UK Incubators: Identifying Best Practice: Full Report.* UK Business Incubation, Birmingham United Kingdom, 2001

Innovation in Manchester

Maire Smith explains how tailored laboratory space and support from seasoned executives make Manchester Innovation an attractive home for startups in the northwest of England.

Manchester Innovation Ltd., a wholly owned subsidiary of the University of Manchester, was formed in September 1999 by the merger of Manchester Biotech, an incubator of young biotechnology companies, and Vuman, the technology commercialization arm of the University of Manchester.

Manchester Innovation has three goals: to manage all aspects of university-owned intellectual property, including licensing deals, spinoffs, and joint ventures; to manage the Manchester Incubator for young biotechnology companies; and to provide mentoring and incubation for university spinoffs.

The university first identified the need for an incubator in 1995, in the belief that early-stage biotechnology opportunities were more difficult to exploit in the United Kingdom than in the United States. An incubator was viewed as an important intermediary in commercialization, serving as a nurturing halfway house. The £15.2 million required was raised from a variety of sources, including the European Regional Development Fund (ERDF), Hulme Regeneration (a local charity), and the university itself. The building was officially opened in September 1999.

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What does the incubator offer?

The Manchester Incubator was designed to get early-stage companies up and running as quickly as possible. The campus-based building has 75,000 square feet of lab-ready, state-of-the-art space, a restaurant, and underground parking. The laboratories can be operated at Advisory Committee on Genetic Manipulation (ACGM) containment level 2 and are fitted with fume cupboards and exhaust thimbles for class II hoods for work with cell cultures and low-risk pathogens. All laboratories can be supplied with piped gases and de-ionized water. There are 16 laboratory suites with desk space and secondary support facilities, including darkrooms, coldrooms, and substantial additional office space. The building is set up for security-card access, and has communal meeting areas on each floor and a suite of meeting rooms. The restaurant also provides valuable opportunities for interaction, and contributes importantly to the "lived-in" ambience of the building.

Prerequisites for entry

It is important that companies entering the incubator be commercially sound. As a result, we expect prospective clients to have carried out the following steps:

- Defined the company's patent strategy and likely market potential for its products
- Written a robust business proposal
- Obtained at least seed finance
- Set up a board of directors and core team

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The preincubation process of evaluating the technology, defining a patent strategy, assessing market potential, and hiring good management personnel are prerequisites for successful startups. Most potential entrepreneurs need assistance to advance beyond the technology concept. The most common blind spot for bioentrepreneurs is a failure to evaluate realistically the market value of future products and to acknowledge competitors.

Indeed, there are many excellent products for which the market is simply too small to support a successful venture. The route to a market should be flexible, and in many cases the answer is to license technology to a bigger player for a fee, rather than launch a new company. Entry into an incubator should not be viewed as an easy means of commercializing ideas that have no real market potential. Only winning ideas get funding because venture capital understands the harsh realities of the market only too well.

An incubator helps a startup achieve proof of principle of its enabling technology faster than if it were to do it alone. Incubator management can also encourage the founders to limit dilution of their financial holding as much as possible. Early money is the most expensive money that the company will ever raise, because this is when the company is at its lowest valuation.

What have we achieved?

In its two and a half years, the incubator has become home to eight young biotechnology companies, and is currently full (see Table 1). These include both university spinouts and external startup companies, all of which have obtained external funding. Nearly 300 jobs have been created and, in total, companies in the incubator have so far brought more than £25 million in venture capital to Manchester. In addition, the incubator has acted as a major catalyst and hub for the creation of a biotechnology cluster in northwestern England.

Location, location, location

We can ask what variables have contributed to the success of Manchester Innovation. Key is its location: The Manchester Incubator is located within the Manchester Higher Education Precinct, which is one of the largest in Europe, encompassing the

University of Manchester, University of Manchester Institute of Science and Technology (UMIST), and Manchester Metropolitan University. The incubator itself has direct access to the School of Biological Sciences and the Medical School. St Mary's Hospital, the Manchester Royal Infirmary, UMIST, the Christie Hospital, and the associated Paterson Institute for Cancer Research are in close proximity.

The quality of local research is very important. In the recent Research Assessment Exercise, Manchester University was placed ninth among 136 UK universities and in a grading of research power, which takes into account overall performance as well as volume, the university was placed sixth. Indeed, 84% of active research staff in the university received the 5* or 5 rating, which is the top rating. This pool of scientific excellence can be expected to provide a continuing pipeline of good spinout opportunities.

Nevertheless, it should not be forgotten that very good science does not necessarily generate commercial opportunities. There are many examples of great "blue-sky" research that stays in the stratosphere and never results in a product. However, in general, there is a strong positive correlation between good basic research and commercial productivity. A number of studies[1] have shown that the large sums of public money expended on academic research produce a very substantial economic return.

Critical cluster factors

A variety of other variables, which have been identified as factors critical in the success of biotech clusters[2], have also been instrumental in the success of Manchester Innovation:

- There is a potential pipeline of deals from the strong local science base.
- Manchester is a hub for entrepreneurs and provides opportunities for many important interactions (e.g., with the Manchester Business School).
- Manchester is an excellent base for attracting new staff, because it has good communications and is a dynamic city to inhabit. The city has a large graduate population (e.g., 8,000 science/technology graduates per year from the University of Manchester alone).
- Seed investments come from the University Challenge Fund, a campus-based seed fund of £6 million set up by the Wellcome Trust, University, and the government; in addition, there is good access to the UK's venture capital and business-angel networks.

Incubator staff have extensive experience in the pharmaceutical industry, patents, legal agreements and marketing.

There is ample opportunity for companies to graduate into extended space in the nearby science parks in Manchester and Warrington in Cheshire and in Cumbria.

There is access to high-class legal and financial networks, and potential collaborators in the form of the pharmaceutical giants, AstraZeneca, Aventis, Bristol Myers-Squibb, and Eli Lilly.

Manchester Innovation participates in useful networks from various government Department of Trade and Industry (DTI) biotechnology initiatives, including the Biotech Mentoring Initiative and Biotech Exploitation Platforms, BioNow (a local network), and the UK's Bioindustry Association (a national network).

The environment is business-driven, and receives significant encouragement from national and local government.

The Manchester Incubator, through its excellent location, access to the pipeline of innovative research from the university, and a management team in Manchester Innovation experienced in commercialization, has helped to accelerate the formation of companies that are contributing to a vibrant, growing biotechnology cluster in northwestern England.

Table 1. Companies housed within the Manchester Incubator

Company	Website	Research focus
Renovo	www.renovo.com	Wound-healing therapies
Motac	www.motac.com	Discovery and development of therapeutics
Intercytex	www.intercytex.net	Tissue engineering
F2G	www.f2g.com	Functional fungal genomics
Epistem	www.epistem.co.uk	Stem cell biology
Yeast Research	www.yeastresearch.man.ac.uk	Yeast genome sequencing, and function
Fluid Technologies	www.fluidtechnologiesplc.com	Engineered bioproducts for natural flavor delivery
DxS	www.dxsgenotyping.com	Pharmacogenomics and DNA diagnostic–related services

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The advantages of an incubator

For bioentrepreneurs looking for a home for their startups, there are very obvious advantages of incubators: they permit company founders to conserve cash and accelerate the commercialization of their technology by providing, if necessary, interim management and access to professional advisers (e.g., legal and financial specialists and patent agents) and shared but secure laboratory facilities.

In addition, for a university spinout, incubators help to shift the startup's culture from an academic perspective to an entrepreneurial one. Incubator staff can help with branding the company, increasing the confidence of investors that they are dealing with a commercial entity separate from a university. A successful biotechnology incubator is unlikely to be just a supplier of cheap real estate with laboratory resources in isolation from a technology pipeline. The incubator should ensure that a company's first steps make the later ones easier.

In summary, a good incubator should help to turn ideas into a commercial reality.

The future for incubation

The initial success of Manchester Innovation has encouraged us to plan a second incubator, and the university has made land available adjacent to the present building. At this stage, definite funding has not been pledged, but we hope to be able to construct a building large enough to house future biotechnology startups and to offer some core technology facilities and a lecture theatre.

Is the pipeline of new biotechnology startups sufficiently robust to justify our optimism? Interesting results have come from asking industrialists to say which of their products could not have been developed (without substantial delay) in the absence of recent academic research[3]. Within the US health care and pharmaceuticals industry, 31% of all new drugs and medical products launched during 1986–1994 were said to fall into this category.

There is intriguing evidence to suggest that universities may be an even more important source of new drugs in the future. The decrease in the number of new chemical entities reaching the market in recent years is of concern to the pharmaceutical industry. While the number of mergers and acquisitions in the pharmaceutical industry has increased, so has the number of companies involved in pharmaceutical research and development. According to the *Scrip* review of 2001 (ref. 4), the number of small companies is increasing: Between 1997 and January 2002, the number of companies with only one or two projects increased by almost 200. The majority of these companies will have originated from universities.

Recently Sir Richard Sykes, formerly nonexecutive chairman of GlaxoSmithKline and now rector of Imperial College (London), reinforced the need to provide the "necessary environment" for growth of companies from academia. There is a compelling argument that part of the "necessary environment" mentioned by Sir Richard should include a properly managed incubator to promote entrepreneurial activity.

It is, of course, difficult to prove that incubators can assist university researchers to commercialize their ideas effectively, but certainly the Manchester experience is encouraging. The main beneficiaries of advances in biotechnology—the pharmaceutical industry—are increasingly struggling for innovative pipelines. Sustainable growth in many areas including health care is likely to rely increasingly on interdependent networks and alliances rather than scientific self-sufficiency.

Continuing success will be dependent on new mindsets and capabilities creating value from intellectual property. The contribution of emerging "can-do" locations such as the Manchester Incubator should help to sustain the competitive edge in the market applications of biotechnology.

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2. Biotechnology Clusters (August 1999) report by a team led by Lord Sainsbury, Minister for Science defined clusters as "geographic concentrations of interconnected companies, specialised suppliers, service providers, firms in related industries and associated institutions e.g., universities."
3. Mansfield, E. Academic Research and Industrial Innovation: An update of empirical findings. *Research Policy* **26** 773–776 (1998)
4. R&D revolution remains just around the corner. *Scrip* February, 72–73 (2002).

Incubation without walls

No bricks, no mortar … but lots of encouragement, introductions, good advice, and minimum conflicts of interest at the Massachusetts Institute of Technology, say Thomas Ittelson and Lita Nelsen.

Charles M. Vest, the president of the Massachusetts Institute of Technology (MIT), once said, "…the primary goal of university licensing and associated offices and policies should be to move technology rapidly to industry [for development]." And indeed, the MIT's Technology Licensing Office (the "TLO") has the responsibility of placing inventions generated at MIT into the commercial sector where they can be best exploited for the public good.

This article describes the TLO's "virtual incubator" approach to starting businesses from MIT technology—a "non–bricks-and-mortar" method of fostering entrepreneurial activities within the MIT community.

Spotting the startup

Most often, inventions at the Institute are incremental improvements (sometimes important) to existing technologies or potential product extensions. In general, most incremental inventions are suitable for licensing to existing businesses in the field. However, around one in ten inventions arriving at the TLO has the technical and market potential to support an entirely new enterprise.

Each year, MIT research (and subsequent patents) form the technological basis for 25 or so such entrepreneurial business startups. Over the past 15 years, the TLO has facilitated the formation of more than 250 such businesses, including such leaders within the biotechnology sector as Ariad Pharmaceuticals, Cubist Pharmaceuticals, ImmuLogic Pharmaceuticals, StressGen Biopharmaceuticals, and Praecis Pharmaceuticals.

So, what makes a good startup opportunity? Positive indicators include very early-stage research, a technology that has several potential applications, no existing companies dominating the field, and an inventor who wants to participate actively in his or her invention's commercialization. We find that embryonic technologies with multiple new markets are often best exploited by focused and dedicated entrepreneurs funded

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