More than the sum of their parts?

Clustering is becoming more prevalent in the biosciences, despite concerns over the sustainability and economic effectiveness of science parks and hubs

Throughout the world, the biosciences rank prominently in governments' economic development agendas. While the traditional leaders in the field—the USA and the UK—strive to defend their top positions, contenders such as France and Germany are investing heavily in biotechnology to bolster their economic development. Italy and other countries, in which a once-strong manufacturing industry faces fierce competition from emerging economies, also hope that turning their attention to biotechnology will help them to turn the tide. Even developing economies, notably China and India, have 'hopped on the bandwagon', convinced that biotechnology will contribute to their growth. This trend is apparent not just at national levels; local officials also hope that raising the biotech flag will attract businesses to their regions.

Despite different starting points, many of these efforts eventually converge on the creation of a science park: a group of interrelated companies, universities, institutions and service providers, supervised by an administration to promote real estate development, technology transfer and partnerships between tenants. Of course, science parks are not only for biotech companies—a considerable number focus on other technologies, such as computer science—but biomedical research is a common trait.

Not surprisingly, science parks are an expanding business. Politicians and local developers harbour dreams that their initiative will eventually grow and attract jobs and income. The International Association of Science Parks (Malaga, Spain), which represents science and technology parks and business incubators from 62 countries, had 277 members as of January 2005, home to 55,000 tenants. The Association of University Research Parks (Reston, VA, USA) has more than 350 members, most from the USA and Canada, and the United Nations estimates that about 400 research parks exist worldwide (Wallsten, 2004a)—the real number is probably higher. India now has six biotech parks, and several more are expected. China is also heading fast in the same direction, and there are science parks under construction or planned almost everywhere, including Kazakhstan and Dubai (Table 1).

Most of these research parks and biotechnology incubators are established through direct or indirect public subsidies. Florida Governor Jeb Bush, for instance, allocated US$310 million in state funding to convince the California-based Scripps Research Institute to build an offspring in the Sunshine State. Construction of the Scripps Florida Campus has now begun in Palm Beach County, which supports the project with a further US$200 million. "I am truly excited about what the future holds for Florida in the realm of life sciences, particularly as we surge forward in biomedical research, advanced technologies, and discovery," Bush said (The Scripps Research Institute, 2005). At the national level, US Senator Jeff Bingaman has introduced the Science Park Administration Act of 2005, which is under consideration by the US Senate. If passed, it will offer tax incentives to companies that plan to locate in science parks, and tax credits for businesses that invest in universities and laboratories. In addition, Bingaman's bill will authorize grants to encourage new parks, create a revolving loan programme to upgrade existing parks, and establish a US$1 billion loan guarantee programme for the construction of approximately 20 new science parks. Elsewhere, the UK Department of Trade and Industry supported the creation of eight biotech incubators around Britain with £5 million from the Biotechnology Mentoring and Incubator Challenge.

However, it remains controversial whether this injection of public money is justified, as both positive and negative effects have resulted. Without a doubt, some parks have had a profound effect on economic growth. North Carolina's Research Triangle Park—the first and largest science park, established in 1959—and Singapore's Biopolis bustle with activity. Taiwan's Hsinchu Science Park opened in 1980 and now hosts 384 companies—focusing

Table 1 | A sample of biotech/life science parks being developed or planned around the world*

Name	Location/Country	Investment
East River Science Park	New York City, NY, USA	$700 million
Beijing Bioengineering and Pharmaceutical Industrial Base	Beijing, China	$241.5 million
Medipark	Brno, Czech Republic	$200 million
Thailand Science Park	Klong Luang, Thailand	$175 million
International Biotech Park	Hinjewadi, India	$140 million
Life Science and Biotech Center of Excellence	Astana, Kazakhstan	$50 million
DuBiotech	Dubai, United Arab Emirates	Data not available

Sources: Research Park Forum, Fourth Quarter 2005, www.aurp.net; Jia *et al*, 2003; Sansom, 2004; wire.cordis.lu; Thailand Science Park, www.nstda.or.th/sciencepark; International Biotech Park, ibpl.net/home.htm; Stone, 2005; DuBiotech, www.dubiotech.com. *Some of the listed parks also host activities in fields unrelated to bioscience.

primarily on semiconductors—which employ more than 100,000 people. In Europe, Imperial College London (UK) has traditionally paid special attention to technology transfer and the support of spin-out companies, and has just started construction of its Imperial BioIncubator "to promote and develop a new generation of spin-out companies" (Imperial College, 2005). In Italy, Science Park Raf emerged from the San Raffaele Scientific Institute and University in Milan, and is now home to seven tenants in the life sciences, including two international pharmaceutical companies.

> …there are science parks under construction or planned almost everywhere, including Kazakhstan and Dubai

From the point of view of a small biotech company, a science park or incubator offers clear benefits, such as access to laboratory space and equipment. For instance, Senexis, a UK company developing a new class of amyloid aggregation inhibitors, was initially established at the University of Manchester but then moved to the Babraham Bioincubator in Cambridge. "The Babraham research campus provides the flexibility and necessary infrastructure to grow a start-up company from an initial concept through to full commercialization," said Mark Treherne, Senexis' Chief Executive. "A location in the Cambridge biotech cluster enables Senexis to recruit experienced personnel to drive the company's future growth." In essence, science parks offer a protected environment for small companies, which allows them to survive despite their often-limited capacity to raise venture capital, a key problem particularly for European biotech start-ups (Critical I, 2005).

Conversely, many observers are concerned with the effectiveness and sustainability of science parks. Scott Wallsten, a scholar at the American Enterprise Institute for Public Policy Research (Washington, DC, USA) investigated the impact of science parks on job growth and venture capital in the USA and found that, on average, setting up a research park made no difference to the region's economic growth (Wallsten, 2004a). "I don't believe there are particular 'ingredients' that guarantee the success of a biotech park. The problem is that not every place can become a biotech hub. Just as every region wanted to be the next Silicon Valley in the 1990s, now every region wants to be the next biotech centre," said Wallsten. "It's a fad, and chasing fads is bad policy. Instead, policy-makers would be better off focusing on more mundane issues: for example, eliminating barriers to competition and making it easy for entrepreneurs to start businesses of all kinds."

> …science parks offer a protected environment for small companies, which allows them to survive despite their often-limited capacity to raise venture capital…

Indeed, some parks have largely failed to fulfil their objectives, or have even collapsed. Wallsten quotes the cases of the underperforming Texas Research Park in San Antonio (TX, USA) and the closure of the Maryland Science and Technology Center in Prince George's County (MD, USA; Wallsten, 2004a). Malaysia's BioValley, a US$160 million project launched in 2003, is also suffering (Cyranoski, 2005). There are reports of parks hosting biotech companies that do not produce research and development-intensive products and do not have innovative technologies at their core. Others accuse local developers, especially in China and India, of taking advantage of incentives and cheap land prices and exploiting the government-backed real estate bonanza (Jia *et al*, 2003). To complicate the issue, there is a general lack of key performance indicators to evaluate the effects of science parks on regional development. For example, it is generally difficult to gather data on the survival rate for biotech and life-sciences companies once they leave an incubator, which would give a good indication of the validity of the park's selection criteria.

The idea of science parks or incubators is based largely on the concept of 'clusters': concentrations of competing and cooperating companies, suppliers, service providers and associated institutions; a definition built mainly on Michael Porter's book, *The Competitive Advantage of Nations* (Porter, 1990). Clusters may differ widely depending on the type of products and services that they produce, their development stage and their economic environment, but some unifying theoretical principles do exist (Ketels, 2003).

In essence, clusters are regarded as potential drivers of economic development, owing to their ability to foster high levels of productivity and innovation. "Clusters of existing and emerging science-based technologies are critical factors in shaping the economic winners and losers of the first half of the 21st century," wrote the authors of a study on America's biotech and life-science clusters, conducted by the Milken Institute (Santa Monica, CA, USA; DeVol *et al*, 2004). "To create international comparative advantage in a knowledge-based economy, clustering innovative activity is imperative." As research in biotech is moving away from a simple sequential process—in which universities transfer their basic research to companies—towards a more complex open system in which universities, biotech research start-ups and large companies all have individual roles but share knowledge, clusters are increasing in importance, remarked Christian Ketels, Principal Associate at the Institute for Strategy and Competitiveness at Harvard Business School (Cambridge, MA, USA). "They provide the environment in which knowledge can flow across institutional boundaries most effectively."

The existing examples of successful biotechnology hubs exert an irresistible appeal to decision makers who want to create high-paying jobs, attract new companies and stimulate the socio-economic growth of an entire region. This is not an unreasonable strategy; for instance, the life-science industry around San Diego, ranked first by the Milken Institute's reports among American biotech clusters, is directly and indirectly responsible for some 55,600 jobs and US$5.8 million in income. Boston, Raleigh–Durham–Chapel Hill, San Francisco and a few other areas in the USA have succeeded in establishing real growth, the study found, and other shining examples can be identified in Europe, such as in Paris and Munich.

But can a successful and thriving biotech cluster be planned from scratch, or do clusters develop spontaneously only in specific locations? Judging from the plethora of existing initiatives, many believe that bringing together some basic ingredients—well-trained scientists, top academic institutions, venture capital and a catalyst like tax breaks or economic incentives—is sufficient to initiate a vibrant biotech community. However, it may not be so simple. "It seems like every region in the

> …on average, setting up a research park made no difference to the region's economic growth

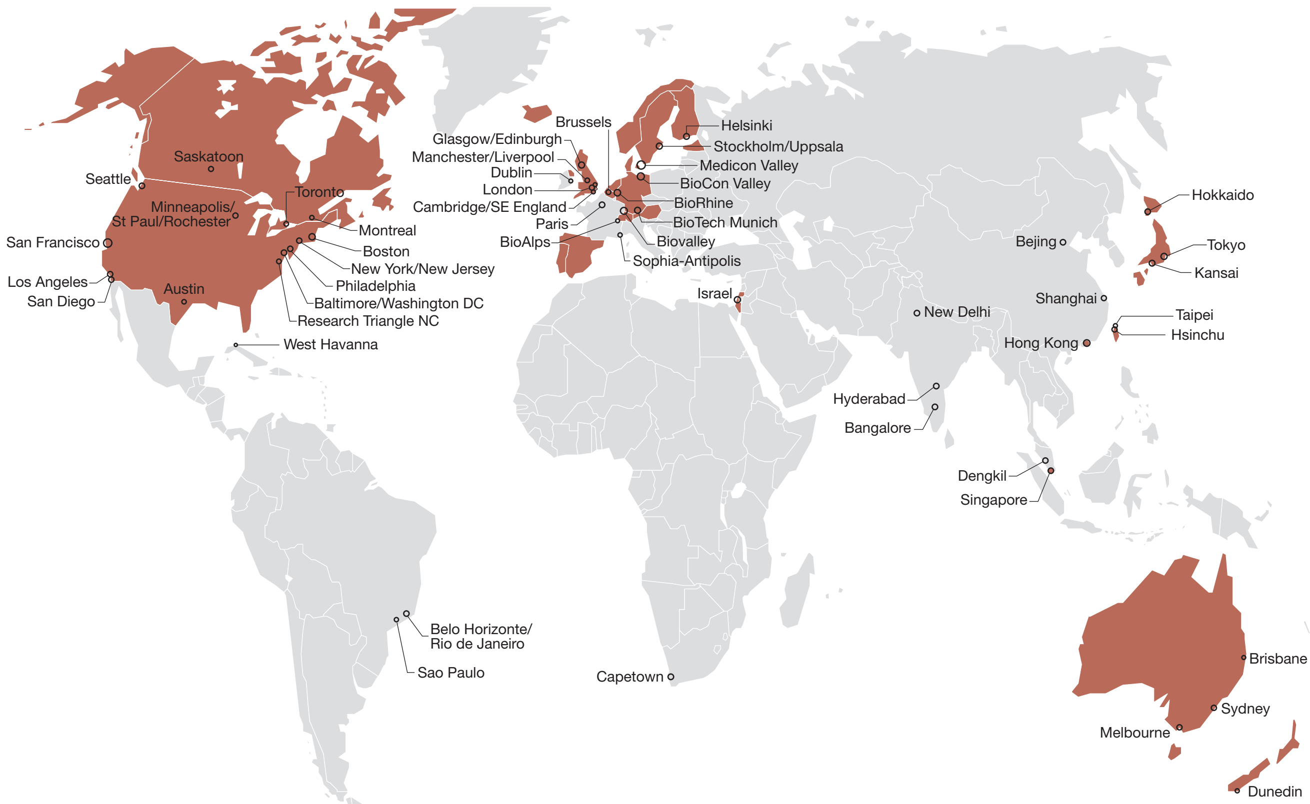

Fig 1 | The Global Biotechnology Clusters map. Countries coloured in brown rank highly in the Growth Competitiveness Index 2004–2005, World Economic Forum. Black circles represent selected biotechnology and life-sciences clusters. Fig adapted from image supplied by William Hoffman, MBBNet, University of Minnesota, Minneapolis, MN, USA.

[Organization for Economic Cooperation and Development] countries has by now a biotech park or biotech cluster initiative. Although this is an area with strong growth, everyone knows that only a minority of these will survive and prosper," warned Ketels. His view is shared with others. "Numerous regions in a number of countries seem to be trying to develop biotechnology clusters, but the most successful ones…have developed as a result of a coincidence of factors rather than as the result of deliberate design and public policy," found a report by the UK House of Commons Trade and Industry Committee (2003). "The cluster concept provides a good description of the factors involved in the success of biotechnology in certain regions. It does not, however, necessarily provide a blueprint for establishing biotechnology elsewhere." Although acknowledging that small, young companies can benefit from the concentration of biotechnology activity, the report observed that too many areas in the UK have targeted biotechnology as an industry to cultivate, and concluded that efforts should be aimed primarily at reinforcing the most competitive locations internationally. "Not only may considerable sums of public money be wasted in trying to force into existence local biotechnology companies, but also rivalry between regions may adversely affect those with existing strengths in the sector thus undermining the success of biotechnology in the UK as a whole," the report concluded.

Ketels believes that what really distinguishes the winners from the losers is not only a strong cluster-specific business environment and a critical mass of activity, but also the focus on a specific area or market for which the cluster provides unique value to companies and researchers. "We need to find better ways to evaluate the impact of biotech cluster initiatives. Counting start-up companies seems shallow, if they are financed by government funds and fail to grow into middle-sized companies, and this is what often happens," said Ketels. "We need to look at the impact of cluster efforts on different dimensions—their organizational success in winning and retaining members and organizing activities, their impact on improving the cluster-specific business environment, and their ultimate results on innovation and economic performance of the cluster." In its analysis, the Milken Institute used 44 different measurements to gauge the strength of the metropolitan areas in five categories: research and development inputs, risk capital, human capital, biotech workforce and current impact (DeVol *et al*, 2004).

> …many believe that bringing together some basic ingredients …is sufficient to initiate a vibrant biotech community

Notwithstanding these concerns, clustering is becoming increasingly prominent in biotechnology and bioscience, so mapping the distribution of clusters might help to understand why technology, economy and geography interact positively in some places but not in others. William Hoffman from the University of Minnesota (Minneapolis, MN, USA) has built a Global Biotechnology Clusters map, which charts the main hubs of biotech and life sciences worldwide as part of a larger project to map human technological development (Fig 1). "Maps can help answer or at least address a number of key questions," said Hoffman. "Where around the world is biotech really happening or beginning to happen? How important is economic geography now that the life sciences are spilling out of university, governmental and industrial laboratories into regional economies? Where is the search for 'biotech gold' breaking down national boundaries and political jurisdictions, with different regions and different countries banding together to compete in the global economy?"

Indeed, the biotech-clustering craze has already created another level of complexity: meta-clusters. These are transnational networks of clusters operating in geographically connected countries. Europe, in particular, is a fertile place for such initiatives. The latest is EuroBioCluster South, which was announced at the 2005 BioVision conference held in April 2005 in Lyon, France. The project will combine bioclusters from an area stretching from Heidelberg, Germany, to Barcelona, Spain, "to stimulate a supra-regional dynamic of scientific and technological growth and international outreach," according to an official press release (Grand Lyon, 2005). The EuroBioCluster's potential is expected to exceed that of Seattle, San Diego and San Francisco combined, and it will have "the largest concentration of life-science enterprises in the world, with the presence of both major groups and start-ups, research centres, universities and institutions."

ScanBalt is another main cross-border effort in biotech and life-sciences development, encompassing 11 countries and 85 million people in Northern Europe with 60 universities and 870 biotech-related companies. "We do not consider ScanBalt to be a meta-cluster but a meta-region, which is an important difference," clarified Peter Frank, General Secretary of ScanBalt. "Clusters have a certain dynamic connected to the fact that activities within a cluster are characterized by geographical proximity and a regional background, while a meta-region like ScanBalt BioRegion has a different and complementary dynamic." A basic role of ScanBalt is to coordinate between regional and national networks, promote the establishment of clusters and increase transparency and visibility of competencies in the region, explained Frank.

> … the biotech-clustering craze has already created another level of complexity: meta-clusters

Although the verdict is still out on the effectiveness of science parks, incubators and mega-clusters in boosting local development, they will be in fashion for some time. "Businesses—from high-tech companies to developers—that get money from these schemes are happy with their windfalls. Politicians are happy to hand out pork while looking like visionaries," wrote Wallsten (2004b). However, "the obsession with becoming the next biotech hub will fade in time, just as dotcom dreams did." But if a good-practice model prevails for the establishment of research parks and clusters, if it is based on a thorough evaluation of local dynamics, research potential and entrepreneurial environment, and if strict policies are enforced to select only technologically sound tenants and spin-offs, then there is space for reasonable optimism that these investments can spur high-tech and biotech progress, at least in some cases.

REFERENCES

Critical I (2005) *Biotechnology in Europe: 2005 Comparative Study*. Lyon, France: BioVision
Cyranoski D (2005) Malaysian biotechnology: the valley of ghosts. *Nature* **436:** 620–621
DeVol R, Wong P, Ki J, Bedroussian A, Koepp R (2004) *America's Biotech and Life Science Clusters: San Diego's Position and Economic Contributions*. Santa Monica, CA, USA: Milken Institute
Grand Lyon (2005) EuroBioCluster. Press release, 14 Apr. www.lyon-business.org
House of Commons Trade and Industry Committee (2003) *UK Biotechnology Industry*. Twelfth Report of Session 2002–2003. London, UK: House of Commons
Imperial College (2005) Spin-out News, 30 Nov. www.imperialinnovations.co.uk
Jia H, Jayaraman KS, Orellana C (2003) Biotech parks proliferate, despite concerns over sustainability. *Nat Biotechnol* **21:** 1259–1260
Ketels CHM (2003) *The Development of the Cluster Concept—Present Experiences and Further Developments*. Düsseldorf, Germany: Ministry of Economics, Northrine-Westphalia
Porter ME (1990) *The Competitive Advantage of Nations*. New York, NY, USA: Free Press
Sansom C (2004) EU expansion: enlarged horizons or false dawn? *Nat Biotechnol* **22:** 501–504
Stone R (2005) Central Asia. Visions of a biotech empire on the Kazakh Steppe. *Science* **308:** 1861
The Scripps Research Institute (2005) Scripps Research breaks ground for construction of Scripps Florida campus. *The Scripps Research Institute News & Views*, 26 Sep www.scripps.edu/newsandviews/
Wallsten S (2004a) Do science parks generate regional economic growth? An empirical analysis of their effects on job growth and venture capital. Working Paper 04–04. Washington, DC, USA: AEI-Brookings Joint Center for Regulatory Studies
Wallsten S (2004b) High-tech cluster bombs. *Nature* **428:** 121–122

Andrea Rinaldi
doi:10.1038/sj.embor.7400633

Ancient DNA research goes nuclear

A new technique to extract sequence data from nuclear DNA may reveal exciting new insights into evolution and phylogeny

It is one of the most fascinating questions we face: how did *Homo sapiens*—modern humans—evolve? When did they start using tools, how did they develop language and why did *Homo erectus* and then *Homo sapiens* thrived while other human species, such as the Neanderthals, became extinct? The availability of advanced genetic technologies, most notably the polymerase chain reaction (PCR), originally held great promise to answer these questions; in theory, sequencing the DNA from fossils could paint a picture of the molecular evolution not only of humans but of other species as well. In practice most of these expectations have not been realized, as the analysis of ancient DNA is anything but easy. The very small amount of DNA in fossil samples, the decay of the molecules over time and contamination with DNA from other organisms have proven to be considerable hurdles. As a