Singapore has spent billions building a research heaven where top biomedical scientists have practically been handed blank cheques. But as this "city" welcomes more and more citizens, the time to deliver is approaching fast, says Emma Young

WITH its white walls, matching seats and floor-to-ceiling windows, the bar would not look out of place in London or Sydney. But there's something unusual about the clientele. At 2 pm on a Thursday, there are six people around a table. None of them is drinking alcohol, they all have notebooks and they are wearing lab coats.

This is the bar at Chromos, one of the seven buildings of Biopolis, the steel and glass symbol of the Singapore government's biomedical dream. Built at a cost of S$500 million (£160 million), Biopolis is spread over 18.5 hectares of land about 15 minutes' drive from downtown Singapore. It has room for about 2000 researchers in seven buildings, each connected by "skybridges". Five of these buildings house the publicly funded biomedical research institutes, while the others are set aside for industry. As well as offices, labs and bars, there are lecture theatres, a multimedia auditorium, a food court selling everything from noodles to German beer, and the Bistro Fabulous, where scientists can sit at tables in the sunshine and talk apoptosis or stem cells over scrambled eggs on toast.

It's not all rest and relaxation: construction work on Biopolis as a whole continues apace, while the finishing touches go on Phase One. By the end of this year a childcare centre, a biomedical library and a French restaurant will be in place. More buildings for biomedical companies will start to go up early next year followed by housing for researchers. All of this will bring Biopolis considerably closer to the dream of a self-contained science city.

Singapore's much-heralded big push into biomedical sciences started for real in 2000, with S$3 billion allocated over five years in addition to the cost of Biopolis. The aim was to make biomedicine the fourth pillar of the economy alongside electronics, chemicals and engineering. In the past 12 months alone, a slew of international joint ventures has been announced; some of the world's top biomedical researchers have been tempted with promises of unrivalled access to the funds, facilities and support they need – and Biopolis has opened its doors.

"The opening of Biopolis is very, very significant for us," says Kong Hwai Loong, an oncologist and executive director of the Biomedical Research Council (BMRC), part of the government's Agency for Science Technology and Research (A*STAR).

The initial focus of the biomedical plan was to create a solid base of research talent and capability. And that is still a priority, but compared with 2003, there is a discernible shift towards translating medical research into treatments and commercial applications. This is having an impact on the sort of researchers Singapore wants to attract and on the international deals it is seeking out. After a few years of breathtaking expansion, Singapore is becoming more selective about its development. "Biopolis represents a comfortable portfolio of basic research capabilities, so we are now asking ourselves, what do we really need to add? We no longer cast our net wide," says Kong.

This approach extends to the private companies that A*STAR wants to occupy those designer offices and labs. There has been more demand for space than is available, Kong says, and a new committee is busy deciding which companies best complement existing tenants.

Among those tenants is the Novartis Institute for Tropical Diseases, which opened up shop in Singapore in 2003 and moved into Biopolis in July. The NITD is plugging into the country's strengths in infectious disease research by concentrating on developing new treatments for dengue fever and tuberculosis. On another floor is Paradigm Therapeutics, which plans to extend the genomics-driven research on the central nervous system and metabolic diseases that it does at its UK home in Cambridge.
Apart from Ian Gray, Paradigm Singapore’s director of research, there are five researchers at Biopolis, with another three being trained in the UK. When Biopolis’s animal house is fully operational, the company intends to recruit more staff. The research animals are to be housed in a vast complex in the basement. When complete it will boast a wide range of shared facilities offering everything from glassware washing and lab supplies to DNA sequencing and X-ray crystallography. “There’s a whole host of shared facilities that we wouldn’t have been able to resource ourselves,” Gray says. But it wasn’t just the facilities at Biopolis that attracted Paradigm. In a science city, collaborating with academic researchers and other companies is a breeze, and potential research funding from Japanese pharmaceutical firms is a lure. It’s a two-way street, of course. From the Singapore government’s point of view, Paradigm was a desirable Biopolis tenant because of its expertise in an area in which the country would like to be a world player. “We want to make sure there are certain capabilities in Singapore,” says Beh Swan Gin, a medical doctor and head of the biomedical sciences section of the government’s Economic Development Board. “If, say, Paradigm comes here and does high-throughput animal model development, that area becomes a capability in Singapore.”

ES Cell International was another obvious choice for Biopolis. Along with cancer and infectious disease studies, embryonic (and adult) stem cell research is a must-have for the BMRC. Alan Colman, chief scientific officer at ES Cell International and a co-creator of Dolly the sheep, came to Singapore in 2002 in large part because the government was willing to invest in the company. “There was finance available here which was quite frankly impossible to get elsewhere,” he says.

Singapore also has a solid history of breakthrough stem cell work. In 1994, for instance, a group led by Ariff Bongso of the state’s National University Hospital was the first to successfully isolate embryonic stem cells, and Patrick Tan of the Singapore General Hospital has pioneered transplants of blood-forming stem cells from bone marrow to treat diseases such as aplastic anaemia.

And as well as actively encouraging stem cell research, Singapore is “permissive” compared with countries such as the US. Legislation very similar to that in the UK, which allows stem cells to be extracted from cloned embryos up to 14 days old, was passed by parliament on 2 September. Though until then, says Colman, “people assumed that these rules and regulations were already in existence”. He hopes that within a year his team will be able to cure diabetic animals using stem cells that develop into insulin-producing islet cells. And for basic research to support this work, Colman can call not only on his own team but on publicly funded researchers. A fifth of Colman’s salary is paid by the new Centre for Molecular Medicine, set up to translate research into treatments.

The first of the CMM’s research groups works on regenerative medicine, looking at how stem cells might treat spinal injury patients. Colman is a senior scientist at the centre, and the group has 10 posts to fill. He is hoping to help CMM fill those posts, and the quid pro quo for the company is that the areas he is nurturing, and which the Singaporean government is paying for, are of interest to ES Cell.

Over at the Institute for Molecular and Cell Biology, the oldest of the five public biomedical research institutes, stem cells are also central. Australians Victor Nutcombe and Simon Cool joined the IMCB last year after being poached from the University of Queensland to expand the institute’s work using stem cells to aid wound healing. The government’s desire to get a return on its biomedical investment is clear in the pair’s appointments. “The institute was looking at recruiting people who were explicitly trying to bridge the theoretical and practical gap,” says Nurcombe. “At Queensland we had a mature technology and some terrific preliminary data. The push into applications was a natural one. And the institute’s attitude is: make this happen, and as fast as you can. Australia also wants that, but has very little in the way of infrastructure to help researchers achieve it.”

A STAR has teams of people who are making sure that the all-important intellectual property rights are watertight, advising researchers about commercialisation and providing seed funding for new companies. Nutcombe and Cool say they have been assured of sufficiently high levels of funding and experienced staff to allow their lab to continue forging ahead while they think up and plan commercial applications. So far they haven’t even been given a budget limit. “I’m sure one day there will be a limit, but in this set-up phase it has been case of what we have needed we’ve got,” laughs Nurcombe. “We haven’t had a barrier to what we need yet. And that is as close to scientific heaven as you are ever going to get.”

And all this access to cutting-edge facilities, researchers with complementary expertise and apparently unlimited cash has attracted some of the world’s top biomedical names. Edison Liu, a former director of clinical sciences at the US National Cancer Institute, was appointed head of Singapore’s Genome Institute in 2001. In August this year David Lane, one of the scientists credited with discovering the cancer gene p53, and the second most highly cited medical scientist in the UK in the past decade, announced he would be taking a two-year sabbatical from the University of Dundee to head the IMCB.

This month Australian Ian McNiece is leaving his job as professor of oncology at the Johns Hopkins University in Baltimore, Maryland, to head the new Johns Hopkins Singapore biomedical division in Biopolis. And Axel Ullrich of the Max Planck Institute of Biochemistry in Martinsried, Germany, has moved out to lead the Singapore Onco Genome Laboratory.
at Biopolis, a joint venture between the Max Planck Society and A*STAR.

“What we want to do requires a lot of work, a lot of state-of-the-art instrumentation and a lot of money,” says Ullrich. “This would not have been available at Max Planck – at least not as quickly. It would have taken several years for me to set up something comparable and I’m not even sure if it would ever have been funded at the rate that we expect to be funded here.”

That rate is still being discussed, but Ullrich says he is confident that A*STAR will be as good as its word.

Ullrich, who has developed drugs to treat diabetes and breast cancer, is among the top 10 most-cited scientists in the world over the past 25 years. He has been on the BMRC’s International Advisory Council since its launch in 2000. This council of 13 world-class researchers provided Singapore with its masterplan for transforming the country into a biomedical hub. It is now co-chaired by Richard Sykes, rector of Imperial College London and former chairman of GlaxoSmithKline, and Sydney Brenner of the Salk Institute for Biological Studies in La Jolla, California.

In 2000, four months after the council’s first meeting, Ullrich remembers how members of the IAC were surprised to see architectural designs and finished plans for the city of Biopolis. “That is unique to Singapore, I think. The way from an initial idea to a finished product is extremely short and fast.”

That speed is possible because of the way Singapore’s government operates. Parliament only has one house, government ministers have strong executive powers and there is almost no room for public debate. If the government wants what you want – and they want biomedical scientists in spades – the benefits are clear.

This ruthless determination impressed Jackie Ying, who was the youngest-ever tenured professor at the Massachusetts Institute of Technology. In 2003 she was recruited to head the A*STAR Institute of Bioengineering and Nanotechnology. “I was a professor at MIT for 12 years, and they do have focused research centres and institutes, but this is on a much bigger scale and it’s being done in a very coordinated way,” she says.

Ying says she saw a way to make an impact that would have been impossible at MIT. The aim of the institute is to bring together a wide range of expertise, including mechanical, electrical, chemical and biological engineers, chemists, physicists, biologists, pharmacists, doctors, dentists and materials scientists. “If you go to parts of Europe or the US, you will see people working on bioengineering and a lot of people doing nanotechnology, but here we are focused at the interface, and I think that’s what makes us unique,” she says.

The institute has about 120 staff and PhD students from the world’s top universities, about half the planned number. Among other things, these researchers are working on using nano-composites to create tissue scaffolds to which proteins and cells will stick. The hope is that these will allow blood vessels to grow through them while providing mechanical robustness. “To do that, you really have to cut through all the different research landscapes,” Ying says.

Like heads of other publicly funded research institutes, Ying talks about the importance of commercialisation. None of the institutes has been set goals – whether it is for intellectual property or physical products. But the message is clear: Singapore will

**CAN YOU MAKE THE BIOTECHS BLOOM?**

With its highly trained workforce and stable government and economy, Singapore is an obvious choice for pharmaceutical companies wanting a manufacturing base in Asia. From AstraZeneca to Schering-Plough, most major companies have at least a presence in the state.

This helps explain why, in 2003, manufacturing output grew to S$11.3 billion, a 16 per cent increase on 2002. Some 84 per cent of the 2003 figure was down to pharmaceutical production.

But while Singapore’s Economic Development Board is hugely successful at attracting prestige plants, creating a successful biotech sector will be harder. The EDB’s strategy is to pick a small number of likely local winners and target the funding at them, encouraging quality over quantity.

“Hopefully the biomedical activity will start to generate new commercial entities, but it hasn’t immediately followed,” admits Guy Heathers, who is director of the Singapore branch of UK-based Biotech Research Venture, which spins off companies from academia, and acting director of BioSingapore, a biotech industry group.

Heathers has been in Singapore since 2001 after working in biotech across Europe and the US. Although access to investment has been difficult for biotechs worldwide over the past three or four years, Heathers says that it may have been more difficult in Singapore because it is a relatively new industry there.

There are about 30 biotech companies in the state, specialising in areas like drug discovery, stem cells and medical technology. None is making money from new drugs – it’s just too early – though some are beginning to get revenues from licensing deals. Merlion Pharmaceuticals, a homegrown biotech with a natural extract collection of more than 450,000 samples, recently signed deals with US-based firms Merck and Schering-Plough.

Access to R&D cash can be a problem. One hurdle is that, to be listed on the Singapore stock exchange, a company must be profitable. This is such a tall order that no native biotech firms are listed. Another hurdle is the lack of local investor experience in risky, high-tech markets. The EDB is leading the way with Bio*One Capital, part of the government’s biomedicine initiative. So far Bio*One has committed a third of the S$1 billion biotech fund to Singapore’s homegrown companies. Bio*One also invests in foreign biotechs to help kick-start industry via spin-offs.

Over time, the hope is that the need for a government fund will disappear when local venture capital groups see benefits from investing in biotech. Meanwhile, the state has a lot of control over how the biotech sector is developed. But, says Heathers, the question is: can you plan for success in biotech?
foster and develop basic biomedical research, but commercialisation is “strongly encouraged”.

For researchers like Nurcombe and Cool, this is good news. They want to develop new treatments, they are not averse to making money and they like Biopolis and Singapore – though Cool does miss the Queensland surf.

Ying, who spent some of her childhood in Singapore, is also enjoying life in the state. It’s an easy place to live, she says, and with cheap, high-quality childcare it’s a good place to be a working mother. With a broad programme for inviting visiting scientists and holding international conferences and seminars she doesn’t feel she has to go to the US to keep up to date with work in her field.

If there is anything that Singapore doesn’t have that some other biomedical hotspots do, she says, it’s a vibrant biotech sector. “We have a lot of multinationals, but we don’t have a lot of small and medium industries here. That’s what makes San Francisco and Boston exciting – they are biomedical hubs. But the government does have all this in mind,” says Ying.

And while it remains to be seen if a country really can create a successful biotech sector from scratch rather than watching one evolve, some are betting on success. Guy Heathers, a British expat and acting director of the biotech industry group BioSingapore, says: “The need to succeed is so great in biotech that I think it will happen. Singapore has put so much emphasis on the biomedical sector as the fourth pillar of the economy that failure is not an option.”

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