Singapore’s multibillion dollar gamble

How does a country one-fourth the size of Rhode Island with little history in biomedical science become one of the world’s biomedical research giants? The answer: with a pile of money and a large dose of chutzpah. Since 2000, Singapore has dumped more than US$2 billion into developing a biomedical research industry—from scratch. Is the gamble paying off?

A matter of life and death
Science is a notorious example of what economists call “increasing returns to scale”—groups of productive people feed off each other to create something that is more than the sum of its parts. The reverse is also true: isolated individuals will have a hard time generating momentum and are less productive. So how can you get a new hotbed of research started in a country with a limited history of biomedical research?

In the 40 years since gaining independence, Singapore has become one of the wealthiest nations in the Asia Pacific region. Per capita income, for example, has increased an average of 6.4% per year from 1965 to 2000. Yet that growth has been driven largely by manufacturing rather than knowledge-based industries. Singapore realized it had to make a change.

That change came in the late 1990s with the decision to emphasize knowledge industries, including biomedical science. The decision was spurred in part by the worldwide electronics slump, which drove jobs in the electronics industry—a mainstay of the country’s economy—to cheaper locations in Asia. And with no natural resources to bolster the country’s economy in times of hardship, Singapore needed other options. “The Singapore economy needed to diversify, to become like a table with many legs,” says Philip Yeo, Chairman of Singapore’s Agency for Science, Technology, and Research (A*STAR).

“The additional leg of biomedical science would stand us in good stead in riding the next big wave.”

This need to diversify spawned the Biomedical Sciences Initiative (BMSI), a plan masterminded by Yeo and hashed out in an all-night session with three of Singapore’s top doctors, Tan Chorh Chuan, then Dean of Medicine at the National University of Singapore (NUS), and oncologists John Wong and Kong Hwai Loong—a group Yeo refers to as the “biomedical sciences ‘Gang of 4.’”

Although the idea met with considerable skepticism, says Yeo, the government eventually (and reluctantly) gave him the green light. The plan was announced in 2000—one day before the unveiling of the human genome project—and devoted nearly US$2 billion over five years to the development of public and private sector biomedical research. For the government, failure of the BMSI is not an option. “When we say that Singapore is serious about science, we are dead serious,” said Second Minister for Trade and Industry Vivian Balakrishnau in his opening remarks at an October 2005 Keystone symposium on stem cells, senescence, and cancer—the first Keystone meeting to be held outside North America. “For Singapore, success is a matter of life and death.”

“The personnel payoff
Thanks to Yeo’s aggressive recruitment efforts, Singapore is now home to a bevy of acclaimed scientists. Among them are Sir David Lane, discoverer of the p53 tumor suppressor gene, who is serving a two-year stint as the Executive Director of the Institute for Molecular and Cell Biology (IMCB), and Edison Liu, former head of the Division of Clinical Sciences at the National Cancer Institute (NCI) in the US, who became the Executive Director of the Genome Institute of Singapore (GIS) in 2001.

Japanese cancer researcher Yoshiaki Ito, who identified RUNX3 as a tumor suppressor gene associated with stomach cancer, relocated to the IMCB in 2002—with his entire laboratory staff in tow—after reaching Japan’s mandatory university retirement age of 63. Also on board is molecular biologist Alan Colman, formerly with PPL Therapeutics—the Scotland-based pharmaceutical company that cloned Dolly the sheep. Colman, who received a S$6 million grant to relocate to Singapore, is now chief scientific officer of ES Cell International, a government-owned biotech company that is developing human embryonic stem cells for disease therapy.

Nobel laureate Sydney Brenner, a long-time advisor to the Singaporean government (he served as Chairman of...
Singapore’s Scientific Advisory Board (from 1987 to 1997), is now Chairman of the BMRC. Brenner splits his time between Singapore and the Salk Institute for Biological Studies in San Diego.

If you ask what attracted these scientific heavy hitters to Singapore—a country with a steamy climate, authoritarian government and a notoriously Draconian penal code—you’re likely to get a variety of answers. But the common denominator seems to be the “vision of Philip Yeo”—a phrase heard with an almost eerie regularity in Singapore. In fact, the universally glowing reports from Singapore’s expat scientists (along with A*STAR’s apparently strict requirement for scientists to obtain permission before speaking to the press) leave one wondering if the picture is a bit too rosy.

But the few complaints one can coax out of Singapore’s imported scientists tend to be cultural rather than scientific. The government’s fear of criticism, for example, has dampened artistic expression, meaning that Singapore’s cultural scene doesn’t measure up to that of most cosmopolitan cities. Others are put off by the lack of political opposition to the ruling People’s Action Party, who have been in power since Singapore gained independence.

But for those already in Singapore, the scientific bounty clearly outweighed the cultural drawbacks. And with researchers in the US and Europe complaining that funding is becoming increasingly difficult to secure, the stellar reports from Singapore’s expats—along with the no-strings-attached money given to new principal investigators (PIs)—might prove too tantalizing to pass up.

This was true for two of the most recent defectors to Singapore: cancer geneticists Neal Copeland and Nancy Jenkins, who recently relocated to Singapore’s IMCB from the US NCI. In addition to the funding crunch in the US, the duo cite restrictions on stem cell research and frustration with National Institutes of Health’s (NIH) new ethics policy—which forbids NIH employees from consulting for or holding financial interests in private companies—as part of the impetus to end their two-decade-long stint at the NCI.

“It also helps to have a lot of money,” says Copeland. “We didn’t even negotiate a budget [at IMCB], we just told them how many people and how many mice (thousands of cages)...then sent them a list of equipment we needed.”

The husband-and-wife team—who developed a technique to accelerate the identification of cancer-causing genes in mice—turned down offers from Stanford University and Memorial Sloan Kettering Cancer Center in New York, opting instead for what they saw as an opportunity to conduct science in a less restrictive environment than in the US.

Indeed, whereas the US NIH frowns upon scientists’ involvement in the private sector, Singapore’s A*STAR does just the opposite. Knowing that successful biotech companies generate both revenue and jobs, the government encourages researchers to apply for patents and, based on those patents, to launch biotech start-up companies—offering three-year leaves of absence and $150,000 in seed money as incentive.

The free-flowing money is also part of Singapore’s allure for younger scientists, along with the potential for upward mobility. “Because we are at ground zero,” says Lam, “there are many opportunities [for young scientists] and many positions available.”

A good example of this upward mobility is Thomas Dick, Head of the tuberculosis group at the Novartis Institute for Tropical Diseases, who moved to Singapore in 1990 when biomedical research was still in its infancy. Fresh out of graduate school at the University of Heidelberg, Dick heard that the newly founded IMCB was looking for postdoctoral fellows and thought “why not Asia, why not the tropics for a couple of years?”

Six years later, when the time came for Dick to venture out on his own, he questioned whether to stay in Singapore...
**IMMUNOLOGY PICKS UP SPEED**

Singapore may have lagged behind other countries in the immunology arena in recent years, but they’re now trying to make up for it. The immunology program at the NUS—still in its infancy at a mere two years old—is headed by Michael Kemeny, an allergy expert who was recruited in 2004 from King’s College Hospital in London. Although King’s College was then being made into a national center for allergy and immunology (along with Imperial College London), Kemeny was enticed by the idea of launching a new program in Singapore.

The fledgling program, which currently has 16 full and 14 associate members drawn from various departments and institutes at NUS and Biopolis, will be expanding its ranks in the next few years, with faculty positions available at the full, associate, and assistant levels.

On offer for those considering a move East are the program’s lavish new digs in the refurbished IMCB building (where it will relocate later this year), a collaboration-friendly research environment and an outstanding start-up package. “Within 1–2 years of coming to Singapore,” says Kemeny, “new PIs typically hold up to S$1 million of competitive funding.”

Kemeny also stresses the program’s proximity to a medical school and tertiary referral hospital, and its access to investigators across a multitude of disciplines—among them computational biology, epidemiology, neuroscience, microbiology, pharmacology, imaging, bioengineering, structural biology, and stem cell biology—which breeds a unique collaborative environment. “No other group in Singapore is able to work so closely with so many different specialities and experts,” says Kemeny.

This solid financial support helped convince Paul MacAry, an Assistant Professor in the Immunology program, to join Kemeny in Singapore. “The start-up package I was offered was significantly better than those from UK and US institutions,” says MacAry, whose offer included not only research funds and a competitive salary, but also subsidized living accommodations and an education allowance for his children.

But MacAry was initially skeptical. “As a postdoc in the UK,” he says, “there is a general consensus that the US and Europe are the only places where you can establish yourself as a good biomedical researcher.” On top of that was concern about feeling isolated as one of only a small number of immunologists in Singapore. He now thinks those fears were unfounded. MacAry, who moved to Singapore with his wife and young children, also praises Singapore as a safe and child-friendly place with a world-class education system.

With enthusiastic salesmen like Kemeny and MacAry and plenty of cash to import and train new talent, the immunology program seems poised for success.

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**Recipe for success**

Although biomedicine in Singapore seems to be off to a flying start, the country will need more than just manpower to ensure that their costly gamble pays off. To succeed, Singapore needs to turn basic research into revenue—a feat that will require other ingredients, including state-of-the-art facilities, support for manufacturing and research and development (R&D), and corporate partnerships.

For top-notch research facilities, one need look no further than Biopolis, a futuristic two-million-square-foot biomedical research complex that houses the sparkling new laboratories of A*STAR’s five research institutes plus dedicated space for biotech start-ups and pharmaceutical companies—not to mention restaurants, a day care center, fitness center, pub, and even a 7-Eleven convenience store. Biopolis—which went from concept to reality in an astonishing 20 months—was designed to foster cross-disciplinary collaboration and bridge the gap between academic and industrial research.

Construction of Biopolis Phase 2, which will add another 120,000 square feet of research space, is currently underway and is targeted for completion at the end of this year. Also under construction is phase 1 of a 390,000-square-foot center for physical sciences called Fusionopolis, slated for completion in mid-2007.

Pharmaceutical and medical technology companies are also setting up shop in Singapore. Pharma giant GlaxoSmithKline (GSK) first entered with bulk manufacturing facilities. It recently launched a preclinical research facility for neurodegenerative diseases, the first such facility in the Asia Pacific region, and its next investment in Singapore will be a US$70 million R&D pilot plant dedicated to converting experimental molecules into commercially viable drugs. Schering-Plough, Merck, Pfizer, and Eli Lilly also have active subsidiaries in Singapore.

or return to Europe. “As it turned out,” he says, “this step was quite easy here in Singapore, and the lab head position was attractive: it came with funding!” Since then, Dick has risen through the ranks from Laboratory Head to Assistant Professor to Associate Professor in regular three-year intervals.

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In 2004, Swiss pharmaceutical company Novartis teamed up with the Singaporean government to create the Novartis Institute for Tropical Diseases, which is focused on studying neglected tropical diseases such as Dengue fever and drug-resistant tuberculosis. Singapore’s biomedical initiative is also bolstered by partnerships with overseas universities including Stanford and Johns Hopkins universities in the US, Sweden’s Karolinska Institute, and Japan’s RIKEN Institutes.

Singapore’s collaborative approach to science is beginning to bear fruit. One example is the recent development of a diagnostic kit for avian influenza (HSN1). The kit, developed by local start-up company Veredus Laboratories Pte Ltd using nucleic acid primers designed at A*STAR’s GIS, allows for rapid, accurate diagnosis of human cases of avian flu and is currently being used in Indonesia.

But the real question is whether the biomedical science push is translating into jobs and revenue. The answer, so far, is yes. As of 2005, 10,200 people were employed in the country’s biomedical science industry, a figure the Economic Development Board hopes will increase to 15,000 by 2015. The biggest revenue source so far is the bulk drug manufacturing rather than the more recently established biotech sector. Biomedical manufacturing output is also on the rise, surpassing its 2005 target of S$12 billion a year ahead of schedule.

Keeping the ball rolling

Another part of keeping the biomedical ball rolling is keeping the money flowing—a nonissue for the Singaporean government, whose financial commitment to biomedical research has been unwavering.

On the heels of the initial BMS Initiative comes the Science and Technology 2010 Plan, announced in February of this year, which will commit another US$5 billion over five years toward bolstering public and private sector R&D. With its chunk of the change, the BMRC will focus on translational research with the hope of turning basic research discoveries into clinically useful and commercially viable products.

But money alone will not ensure success. According to Yeo, the most important elements for maintaining momentum in the biomedical sciences are “two-legged ones, people!” Indeed, Singapore needs to maintain a critical mass of scientists, preferably while lessening its reliance on imported talent—currently about one third of all scientists in Singapore are foreigners. To do this, Singapore has begun to nurture its own scientific workforce. Another brainchild of Yeo, this endeavor involves a complete revamping of the country’s education system—from overhauling the primary school curriculum to offering scholarship programs that fund undergraduate and Ph.D. science training either locally or abroad—to bright Singaporean students.

This training comes with strings attached: A*STAR scholars are committed to six years of research at an A*STAR research institute after graduating. More than 300 students are now in the Ph.D. pipeline, with the first eight scholars completing their Ph.D. training in 2005 and another 18 expected to follow this year. A*STAR is also fishing out younger students with its new Young Researchers Attachment Program, in which pre-university students from around the globe study at Singapore’s secondary schools and junior colleges, spending vacations on stints at A*STAR’s research institutes. Those that do well are then eligible for A*STAR scholarships.

Whereas the US NIH frowns upon scientists’ involvement in the private sector, Singapore’s A*STAR does just the opposite.

As with his recruitment efforts, Yeo sets the education bar high. Those who are funded are allowed only three years to complete their undergraduate degree and five for their Ph.D. training—all while maintaining a 3.8 GPA. “When you first start out at 18 years old,” says Pearlne Teo, an A*STAR scholar who earned her undergraduate degree in biology at Johns Hopkins University, “it seems like a pretty tall order.” Teo, who is now working toward a Ph.D. in immunology at Stanford University, says the GPA requirement is a source of grumbling among her fellow A*STAR scholars, particularly at Stanford, where only about 10% of the class receives an A grade.

Perhaps the biggest hurdle that Singapore faces in revamping its education system is cultural. In a country where education is notoriously rote and rigid, it remains to be seen whether A*STAR students will measure up in terms of scientific creativity. As the first crop of Ph.D. graduates are just now returning to Singapore, only time will tell.

Former Singapore Prime Minister Lee Kuan Yew famously stated that air conditioning was the most important invention for lifting tropical developing countries out of their heat-induced lethargy. Now, Singapore is taking the next step—attempting to make the inventing process itself an integral part of the economy. Yeo, for one, is betting on success. “We have the funds, single-minded focus, long-term planning, and industrial investment experience—and the daring to go for it.”