SINGAPORE

Entering the Scientific Mainstream—Selectively

SINGAPORE—One wintry night in 1983, the shrill ring of the telephone abruptly woke Y.H. Tan from a nap in front of a roaring fire in his cavernous home near Calgary, Alberta. The call caught Tan unawares in more ways than one. He found himself on the line to Singapore, half a planet away, and the caller had a simple question: Would Tan come to Singapore to help found a molecular biology institute? Tan heard himself saying, "Sure."

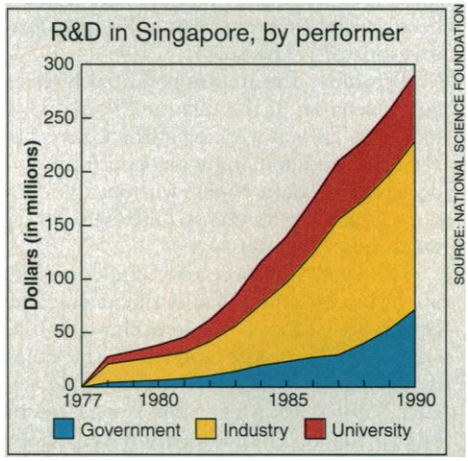
It wasn't until he hung up that Tan began to think about what he had just agreed to do. On the one hand, accepting the offer would give him a chance to return to his homeland. But Tan, then 43, had spent his entire professional career in the West, studying interferons at the U.S. National Institutes of Health, Johns Hopkins University, and the University of Calgary. And the pint-sized isle, which attracts outside notice mainly for its draconian drug laws, press censorship, and zealous campaigns to guard public morals, was a scientific Elba.

By saying yes, Tan was also agreeing to help Singapore enter the scientific mainstream. And by all accounts, his efforts have been a huge success. In just 6 years, Tan and the Institute of Molecular and Cell Biology (IMCB) have put Singapore on the international scientific map. Many of the institute's staff of 200 scientists were recruited from top labs in the West, and the almost 200 papers they have published have been racking up an impressive number of citations in the scientific literature. Richard Lerner, director of the Scripps Research Institute in La Jolla, California, came away from a review last year very impressed with what Tan has accomplished. "They have remarkable young talent," he marvels. "And they're very avant garde."

The institute is perhaps the most ambitious element in the government's strategy to use high technology to strengthen its economy. Underpinning this effort is a strong push in basic research at the National University of Singapore (NUS), which houses the IMCB. The university conducts one-third of Singapore's R&D, and NUS scientists have made their mark in several areas—especially in fields linked to such high-tech industries as materials technology, microelectronics, and information technology. A 1992 study for the U.S. Office of Naval Research concluded that the university's research in database systems and design compared favorably with work in the United States.

How did this remote island nation, with a population of only 3.1 million, manage to build such high-quality research centers? In contrast to conventional wisdom about the need for a "critical mass" of scientific talent and resources, Singapore has made an asset of its smallness. With a population and land area no larger than a medium-sized metropolis, the government has been able to invest heavily in education, housing, infrastructure and jobs while at the same time avoiding the sort of bloated, feuding bureaucracies common in larger countries. "The political system is streamlined," says Josef Friedman, the manager of Apple Computer's Far East Design Center, which opened early this year in Singapore. "You only need to talk to a few agencies" to get things done. Adds Tan, "There are very few places where the dialogue between scientists and policy makers goes on at such a personal level." And despite the government's heavy-handed approach in social affairs and politics, "I don't think that's interfered at all" in efforts to attract overseas talent, says geneticist Sydney Brenner, who chairs the IMCB's board of advisors. "Also, unlike its neighbors, there's absolutely no government corruption."

Talent scout. IMCB director Y.H. Tan.



Steady growth. Increases have been distributed relatively evenly among each sector.

The city itself is another selling point. Outsiders quickly fall in love with its remarkably clean and crime-free ambience and the azure sea only minutes away. Another attraction is its English-speaking, multicultural society—a postcolonial melange of Chinese, Malay, Indian, and British. "There's not a huge culture shock," says Catharine Pallen, a Canadian who heads IMCB's tyrosine phosphatase group. Asian scientists also find it a haven. Liu Jianwei, a Chinese postdoc at IMCB, recalls feeling like "a drop of oil in a bucket of water" during his studies in Germany. "IMCB is ideal for me," he says.

The government isn't bankrolling science because it is eager to unravel the pufferfish genome—one of IMCB's prime projects—however. "We'd rather focus on what we call economy-relevant research," explains the Economic Development Board's Philip Yeo, a slim technocrat who sports aviator glasses and speaks in rapid-fire clips. But "we have no hesitation in funding 'positioning R&D' that provides a place to jump off later, maybe 5 or 10 years down the line."

Singapore's decision to spend $13.8 million to build IMCB, as well as to provide the funds—now about $17.5 million a year—to operate it is a case in point. The decision was part of a broader strategy to develop biotechnology, a field that suits the country's needs: it requires few natural resources, has high value added, and can make strategic use of Singapore's global business networks. To nurture that industry, the EDB established Singapore Bio-Investments (SBI) Pte Ltd., which by 1991 had invested $41 million in 12 local biotech startups with 1428 employees making health care, food, and agricultural products. SBI also invests in overseas companies that might one day be strategic allies; San Diego-based Amylin Pharmaceuticals bought IMCB's first product, a transgenic rat model for Type II diabetes, to test a hormone called amylin as a potential treatment.

The investment in IMCB is already paying off, at least scientifically. An IMCB group has been at the forefront of research on tyrosine phosphatases, a hot topic in cancer research. Working with Brenner, another group has been sequencing the genomes of several fish species, which could serve as a reference vertebrate genome for the human genome project. The lab's novel assay systems have convinced Glaxo, the pharmaceutical giant, to establish a $31 million trust fund for a drug screening center within IMCB. Glaxo put up another $30 million for a neurobiology lab focusing on genes that are expressed only in the brain.

Encouraged by these successes, the government has expanded IMCB's research base by establishing the Bioscience Center, to provide core facilities for researchers at the national university, and the Food Biotech-

A Scientific Odyssey

PROFILE

Singapore is only a 4-hour flight from Hong Wanjin's native Fujian province, on the southeast coast of China. But it is light-years away from where the 33-year-old Hong, now one of the top young scientists at the Institute of Molecular and Cell Biology (IMCB), expected to find himself. As a youngster during the Cultural Revolution, "We had no exams," he recalls, a grin lighting up his face. During that 10-year period traditional academic subjects were banned from the classroom. "We enjoyed life."

The Cultural Revolution ended when Hong was in high school, and Hong and his classmates suddenly found themselves cramming for entrance exams to universities recently reopened. Hong won admission into Xiamen University, and his high scores meant he would study science. It wasn't a voluntary decision: "You just went, and the government assigned you a job" afterward, he says. In his final year, the government announced it would send students abroad for advanced training. Hong, like thousands of his contemporaries across China, began polishing his English for the qualifying exam, which he passed.

In 1983 Hong entered graduate school in biological sciences at the State University of New York, Buffalo. He earned his Ph.D. in 1988, and remained to do a postdoc on an 18-month visa. As the deadline approached for his return, however, China erupted over the prodemocracy movement, and soon after, Hong received a letter from the IMCB, inviting him to consider working there instead of returning to China. In 1989, Hong and his wife Zeng Qi, who had joined him in Buffalo, moved to Singapore. She enrolled as a graduate student at IMCB and quickly made her mark by breeding a transgenic rat model for Type II diabetes. Hong has found Singapore to be a second home, complete with his beloved kung fu movies.

In the lab, he and his colleagues are studying the mechanisms that direct proteins to migrate from the site of synthesis to the cell surface. Hong's group has identified parts of two proteins that anchor them in the Golgi apparatus, and has found that the compound brefeldin A blocks protein transport to the external surface of the plasma membrane.

For Hong, his shotgun marriage to science, brokered by the impersonal machinery of the Chinese education system, has blossomed into a passionate relationship. "You develop the interest along the way," he explains. "How does the cell organize itself?" He throws wide his arms and smiles gleefully. "It's very interesting! The further you get inside a system, the more fun it becomes. It's like in China: You get married first, and then you learn to love each other."

–J.K.

Partnership. Hong Wanjin and his wife, Zeng Qi, both work at IMCB.

nology Center. The Bioprocessing Technology Unit, opened in 1990, seeks to improve purification, synthesis, and fermentation methods for commercial production. The lab recently achieved large yields of TNF-ß, which other companies, including Genzyme in the United States and Boehringer Mannheim in Germany, are keen to put into clinical cancer trials. The National University Medical Institute, being built across the street from IMCB and the National University Hospital, is modeled on the U.S. National Institutes of Health.

If there is one critical bottleneck in the country's quest for scientific success, it is the shortage of qualified scientists and engineers. When he was hired, Tan recalls, "The government asked me, 'What are you going to make?' I said, 'I'll make you Ph.D.s.'" As part of his quest, Tan combs labs in Europe and North America to help fill some 20-30 new slots a year, and within days of the 1989 Tiananmen Square incident he sent inquiries to Chinese scientists who had just received their Ph.D.s in the West and were about to lose their student visas. His aggressiveness has worked: Over the past 5 years, 17 Western-trained Chinese scientists have ended up at IMCB.

To lure promising young scientists, Tan offers research freedom, ample funding and salaries of up to $50,000 for principal investigators. Those who accept also received 3-year contracts renewable only after a rigorous review. William Chia, a developmental neurobiologist who arrived at IMCB in 1990, says that the system is working: "There's been a visible improvement in PIs [principal investigators] ," he says.

Typically, Tan invites potential hires to give a seminar at the institute. For Chia, a native of Taiwan working at the University of Bristol, England, it was an opportunity "to do what you want to do" without the constant scrabbling for grants. "Life here is very much easier," he says.

However, Singapore's own students make up the biggest source of scientific talent. The British-style education system channels top-scoring students into science to the point that "there is a stigma if you don't do science," notes Delia Lai Siok Yew, a recent NUS graduate. The competition is especially keen for slots in molecular and cell biology. At the same time, Singapore's two polytechnic institutes are training technicians to fill the growing demand from biotech labs and industries.

Twenty percent of the national budget goes to education, including full scholarships right through graduate school. "We're very pampered," says Bernadette Murugasu, a fourth-year Ph.D. candidate at IMCB. In addition to tuition, graduate students at IMCB are paid $10,000 a year, which goes a long way for someone who, typically, lives with parents and works 12-hour days in the lab. But as Yeo Su Ling, an IMCB grad student, points out: "If you don't publish, you perish."

For all the advantages, students worry about being isolated by Singapore's relative obscurity. Participants at overseas meetings "kind of look you up and down," says one student. "They're surprised we speak English so well." Another student, Kanaga Sabapathy, believes Western journals would not consider articles from Singapore. "They'll look at people from anywhere in the United States before they'll look at us."

That attitude leads most students to go abroad for postdoctoral training. "I think it's healthy to be away from the system if you're going to compete on a global basis," says Devi Menon, who is about to finish her doctoral thesis. And global competition—intellectual and economic—is the force that drives Singaporean research. "I entered science with stars in my eyes," smiles her friend, Murugasu. "Marie Curie, Jacques Cousteau. Then you get shocked by the reality." Interjects Menon, "In Singapore, everything has to come down to economic assets."

While scientists elsewhere may preach about knowledge for its own sake, Singaporeans accept the fact that little basic research can exist in their country without an economic raison d'etre. Even recent immigrants agree that Singapore cannot afford to rest in the global race for talent and products. In fact, the sense of a shared destiny may be the country's most powerful asset.

–June Kinoshita