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Singapore - Aiming to create the Biopolis of Asia

Memo by

Anna Sandström - VINNOVA

Preface

In December 2006, VINNOVA was assigned by the Swedish government to conduct an international benchmarking of the Swedish sectorial innovation systems in pharmaceuticals, biotechnology and medical technology. Case studies and international comparisons of different countries are important in assessing and understanding the Swedish conditions for life science research and innovation. It was decided to carry out a case study on Singapore since during the last decade the country has invested heavily in research and development in the biomedical field and achieved striking results both scientifically and in attracting industrial investment.

This study is based on data and information concerning policy, industry and science and addresses the trends and performance of the Singaporean Life Science innovation system. Literature and bibliometric studies as well as interviews have been used for the analysis. Accordingly, representatives of governmental bodies, venture capital firms, universities, and large and small life science companies have been interviewed. We would like to express our gratitude to those who have freely shared their time, experience and views with us. Naturally they are not responsible for any misinterpretations or omissions in the text, which has been written in part from a Swedish perspective. The memo was written by Anna Sandström, VINNOVA, project manager for the international benchmarking project.

VINNOVA in April 2009

Göran Marklund
First Deputy Director General, Acting

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1 Background

Language and population

As of September 2007, Singapore has 4.68 million inhabitants, of which 3.7 million are Singaporean citizens and permanent residents (termed 'Singapore Residents'). In 2006, the total fertility rate was only 1.26 children, the 3rd lowest in the world. The government is encouraging foreigners to emigrate to Singapore and the large numbers of immigrants have kept Singapore's population from declining.

The official languages are English, Mandarin, Malay, Tamil and English has been promoted as the country's language of administration since independence. The use of English became widespread in Singapore after it was implemented as a first language medium in the education system, and English is the most common language in Singaporean literature. However, the majority of the population speaks a localised hybrid form of English known as Singlish ("Singapore English"), which has many creole-like characteristics, incorporating vocabulary and grammar from Standard English, various Chinese dialects, Malay and Indian languages. The government has consistently tried to discourage the use of Singlish in its "Speak Good English" campaigns.

Political system

Singapore is a parliamentary republic with a multi-party system, whereby the Prime Minister of Singapore is the head of government. Since the 1959 general election, Singaporean politics have been dominated by the People's Action Party (PAP) which has remained in government ever since. According to the Press Freedom Index developed by Reporters Without Borders, Singapore ranked 146th out of 168 countries in 2006. Some offences can lead to heavy fines or caning and Singapore has laws allowing capital punishment for first-degree murder and drug trafficking. Amnesty International has criticised Singapore for having "possibly the highest execution rate in the world" per capita¹.

¹ <http://web.amnesty.org/library/Index/ENGASA360012004?open&of=ENG-SGP>

Education

The literacy rate in Singapore is one of the highest in Asia, at 95 percent (2006). The standard for the school curriculum is set by the Ministry of Education with a mix of private schools and public schools. There is no strict public-private dichotomy. Furthermore, the degree of autonomy, regarding curriculum and student admission, government funding received, and tuition burden on the students is classified into "government-run", "government-aided", "autonomous", "independent", and "privately-funded". In addition, international schools catering for expatriate students sometimes admit local students.

National University of Singapore, Nanyang Technological University and Singapore Management University are the three current universities in Singapore. There are also five polytechnics in the country (Temasek Polytechnic, Singapore Polytechnic, Ngee Ann Polytechnic, Nanyang Polytechnic and Republic Polytechnic).

Other research organisations include the National Institute of Education (NIE), a teacher training college, various management institutes, and vocational education institutes such as the Institute of Technical Education (ITE). A French business school, INSEAD, has opened a second campus in Singapore in 2001 offering MBA and Executive-MBA courses.

Economy

Along with Hong Kong, South Korea and Taiwan, Singapore is one of the Four Asian Tigers. The economy depends heavily on exports refining imported goods, especially in manufacturing. In 2005, manufacturing constituted 26 percent of Singapore's GDP. The manufacturing industry is diversified into electronics, petroleum refining, chemicals, mechanical engineering and biomedical products manufacturing. Singapore is the busiest port in the world in terms of tonnage shipped². The transportation industry comprises over 10 percent of Singapore's GDP. Singapore is also the world's fourth largest foreign exchange trading centre after London, New York City and Tokyo. The per capita GDP in 2005 was USD 26,833 and the unemployment rate was 2.4 percent as of 31 July 2007³.

Singapore has been rated as the most business-friendly economy in the world⁴, with thousands of foreign expatriates working in multi-national corporations. It is also rated by Transparency International as the least

² Asian Economic News, Jan 17, 2006

³ Singapore Department of Statistics

⁴ World Bank-IFC report, 2005/2006 rankings

corrupt country in Asia and among the world's ten most free from corruption.

Under the Infocomm Development Authority of Singapore (IDA), Wireless@SG is a government-sponsored initiative to build Singapore's Infocomm infrastructure. Working through IDA's Call-for-Collaboration, SingTel, iCell and QMax deploy a wireless network throughout Singapore. Since late 2006, users have enjoyed free wireless access through Wi-Fi under the "basic-tier" package offered by all three operators. This will last for three years.

Rainfall supplies approximately 50% of Singapore's water; the remainder is mainly imported from Malaysia. Presently, more catchment areas, facilities for recycling water (producing NEWater) or desalination plants are being built.

Singapore is growing its medical tourism sector. In 2003, 230,000 foreigners sought medical care in the country, and Singapore Medical services are aiming to serve one million foreign patients annually by 2012. In doing so it is expected that USD 3 billion in revenue will be generated and at least 13,000 new jobs within the health industries created⁵. Singapore hospitals are actively engaged in international healthcare accreditation, at least partly as a by-product of the aim to increase the income from medical tourism.

⁵ Statistics Singapore

2 Industry

Manufacturing has remained important to the economy, with its share of GDP remaining above 25% for most years in the last two decades. Thus in 2006 27.7% of Singapore's GDP was contributed by the manufacturing sector, and another 26.5% by ICT and financial/business services. Within the manufacturing sector, electronics, chemicals, engineering and the biomedical sciences jointly accounted for USD 219 billion (93%) of total manufacturing output (Wong et. al. 2008). In 2000, the Singapore government announced a strategic shift towards the promotion of biomedical science and technology in order to diversify from high dependence on IT/electronics manufacturing. The government's intention is to turn Singapore into Asia's premier hub for biomedical sciences across the entire value chain, from basic research to clinical trials, product/process development, manufacturing and healthcare delivery. The pharmaceuticals industry has had a presence in Singapore for several decades.

Big Pharma, Biotech and Medtech

As early as 1972, SmithKline Beecham (today part of GlaxoSmithKline) established the first pharmaceutical production unit in Singapore, producing antibiotics, and GlaxoWellcome (today part of GlaxoSmithKline) invested in a chemical plant in 1979. The company has continued to invest in Singapore and today both have production and R&D units. Seven of the top ten pharmaceutical companies in the world, such as Pfizer, GlaxoSmithKline, Sanofi-Aventis, Novartis and Merck have units in Singapore. All of the largest pharmaceutical manufacturing firms in operation in Singapore in 2005 are foreign majority owned.

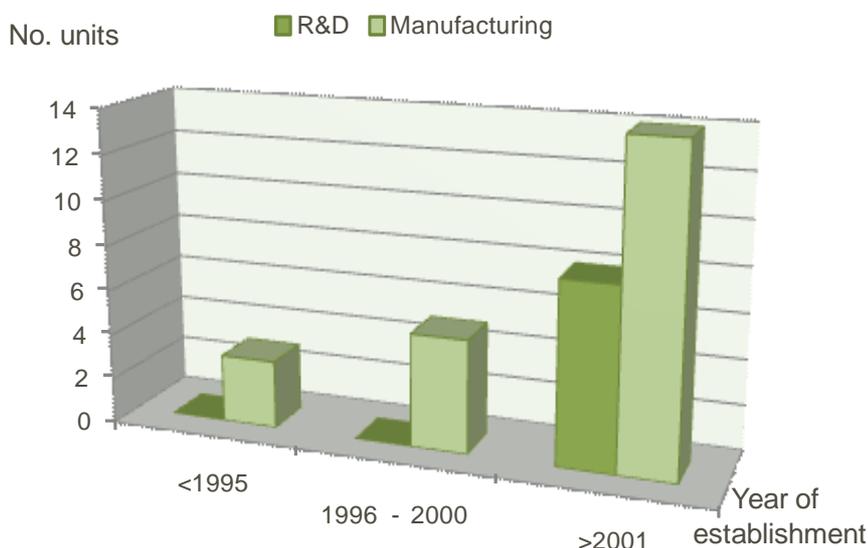
Top Life Science Companies in Singapore, 2005

Company	Mother company nationality
Glaxo Wellcome Manufacturing Pte Ltd	UK
Merck Sharp and Dohme Asia Pacific Services Pte Ltd	US
Beecham Pharmaceuticals (PTE) Ltd	UK
DSM Nutritional Products Asia Pacific Pte. Ltd	Netherlands
JMS Singapore Pte Ltd	Japan
Becton Dickinson Medical (S) Pte Ltd	US

The figure below illustrates the development concerning the number of R&D and manufacturing units in Singapore of the 50 largest Big Pharma companies in the world in terms of sales. The R&D units were all

established after the biomedical initiative was launched by the Singaporean government and the number of manufacturing units has also continued to grow steeply since year 2000.

Number of R&D and manufacturing (MFG) units in Singapore of the 50 largest Big Pharma companies in the world in terms of sales



Source: VINNOVA 2008

A study by Wong et al 2008, shows that the pharmaceutical industry in Singapore consists of more than 40 companies with a total of over 4000 employees and that the corresponding figures for medical technology is more than 60 companies and over 6,000 employees in 2006. The total life science sector thus includes about 10,000 employees distributed among more than 100 companies, which is an increase from 24 companies with 2,148 employees in 1980⁶. There has been an almost linear development of the number of employees since 1980. Pharmaceutical manufacturing output in Singapore has grown rapidly since 1980 (18% p.a.), reaching SGD 20.9 billion in 2006. Similarly, its value added has grown at 18.8% p.a. over the same period, reaching SGD 12.4 billion in 2006, according to the same study.

Several studies have shown that, compared to other countries with a tradition of attracting pharmaceutical production units, Singapore is also successful in attracting R&D units of multinational life science companies (e.g. ISA 2007; VINNOVA 2008; Wong et. al. 2008). At least 25 foreign life science companies have established R&D units in Singapore since 2000, predominately in medical technology, including companies such as Applied

⁶ In 2006, Sweden had almost 600 life science companies with 34,400 employees involved in manufacturing, consultancy, product development and/or R&D.

Biosystems, Becton Dickinson and Siemens Medical Instruments. An example in pharmaceuticals is Lilly Systems Biology (LSB), a wholly owned subsidiary of Lilly that was launched in Singapore in 2002 with generous, multi-year financial incentives from EDB. LSB's mission is to integrate various biological data and approach the problem of studying complex diseases from a more encompassing perspective of a cell and its system. Through intensive use of computational biology, LSB hopes to discover new drug-targets and biomarkers, and better understand mechanisms of action within the cell (Finegold et al 2004).

Singaporean start-up companies

At least two of the sizeable start-up companies have been started in partnership between the Singaporean Economic Development Board (EDB), via its investment arm dedicated to biomedical sciences Bio*One Capital, and foreign multinational companies. This is the case for S*Bio, established as a joint venture between Chiron and the EDB using Chiron's technology platform to develop products for cancer and infectious diseases, especially those in Asia. Another example is Merlion which originated as a joint venture between GlaxoSmithKline (GSK) and EDB. Today Merlion is privatised as a stand-alone business, which has obtained the GSK library of natural compounds along with its Asian samples containing close to half a million extracts. These are being screened in collaboration with international drug companies, including Merck, British Biotech and NovImmune. The contract bioprocess development company, A-Bio was started with funding from Bio*One Capital and took over a 40 L and a 200 L facility from a research institute in 2003. Its first clients were GSK, Novo Nordisk and Artisan Pharma and today the company is profitable. Few start-ups have originated in Singaporean academia.

The company ES Cell International is in the field of regenerative medicine and provides products and technologies derived from human embryonic stem (hES) cells. The company is conducting preclinical studies for its hES cell-derived products for the treatment of diabetes and cardiac diseases. ProTherapeutics develops peptide therapeutics suitable for oral (sub-lingual) delivery using a patented method to identify protein interaction sites. The company has commenced in vivo studies for one of its first products, an analgesic peptide to replace morphine. Both are Bio*One Capital portfolio companies.

Available start-up activity support includes business start-up advice, incubator services, business accelerators, R&D and test-bedding facilities and support for commercialisation. Venture capital can be found through Bio*One, for example, and there is also some private equity funding.

Part of EDB is the Business Angels Scheme (BAS) that provides capital for start-up companies or innovative firms that are less than five years old and developing new products. The BAS will invest up to USD 1 million in a company. This scheme is similar to the EDB's Start-up Enterprise Development Scheme (SEEDS) in encouraging business investment in innovative start-up firms. SEEDS give companies up to USD 300,000 in financing, but the investor must put in at least USD 75,000 and the start-up company must have been incorporated for less than three years in Singapore. The Micro Loan Programme provides loans of up to USD 50,000 at fixed or variable rates⁷ for small companies with less than 10 employees.

Current trends

During the latest two years, Singapore has attracted some manufacturing plants for biopharmaceuticals. Companies investing include Genentech, Lonza and GlaxoSmithKline. More investments in pharmaceutical R&D have also taken place. In 2007, Eli Lilly announced an expansion of its research centre in systems biology amounting to USD 150 million (SEK 1 billion). Also GlaxoSmithKline is expanding its R&D centre focused on cognitive and neurodegenerative diseases doubling the number of employees to about 60. Both the GlaxoSmithKline and the Eli Lilly units have thus attracted continued and expansion investments. In 2003, Novartis established an R&D unit in Singapore devoted to tropical diseases. This unit has about 140 employees in Singapore, ten in Switzerland and ten in Indonesia. The focus is to develop drug candidates for therapies against dengue fever, malaria and tuberculosis and the unit has facilities for medical chemistry and animal testing. The plan is for the first drug candidates to enter clinical trials in 2009. Novartis has had a long presence with manufacturing units in Singapore, and the network and track record helped in deciding where to locate this investment.

⁷ Singapore Government,
<http://www.spring.gov.sg/Content/WebPageLeft.aspx?id=b859b2c6-093a-4e75-9f0e-1c5bf2792a9c>.

Foreign investments (new and expansion) in Singapore 1st January 2006 to 31st July 2007

Investor	Location	Employees	Investment [USD millions]	Description	Type
Edwards Lifesciences (USA)	Changi	500	40.7	New heart valve manufacturing facility.	New
SGS (Switzerland)	Ayer Rajah	39	17.9	Lab for quality control tests of pharmaceuticals and medical devices.	New
Abbott Laboratories (USA)	Singapore	259	280.0	Plant for infant nutritional powder for the Asian market.	New
GlaxoSmithKline (Great Britain)	N/A	200	300.0	Vaccine manufacturing plant for bulk bacterial paediatric vaccines.	New
* Merck (USA)	Tuas	59	63.3	New plant, brings Merck's total investment in S-pore to USD 1 billion.	Exp
Codexis (USA)	Singapore	80	106.8	R&D facility to support its expanding generics business.	New
CombinatoRx (USA)	Singapore	10	6.8	R&D unit for infectious disease drug development.	New
Lonza (USA)	Singapore	94	48.5	Second large-scale biopharmaceutical manufacturing plant.	New
Fluidigm (USA)	Singapore	64	31.6	Product development centre for biomedical instruments.	New
Genentech (USA)	N/A	100	140.0	Plant for biopharmaceutical manufacturing.	New
Affymetrix (USA)	Singapore	94	48.5	New plant for biomedical tools manufacturing.	New
Bio-Rad Laboratories (USA)	Singapore	50	50.2	Manufacturing facility for diagnostic tools.	New
Eli Lilly (USA)	N/A	205	150.0	Expansion of drug discovery research activities.	New
Eurofins Medinet (France)	N/A	64	31.6	Laboratory supporting big pharma and biotechnology companies.	New
Rikevita (Japan)	N/A	33	2.3	Development centre.	New
West Pharmaceuticals (USA)	Jurong	100	30.0	Medical device manufacturing facility.	New

Source: OCO Consulting except for project marked * (ISA 2008)

A number of the manufacturing plants are located in the Tuas Biomedical Park, a large area intended to be devoted to bulk production of chemical and biological pharmaceuticals. In 2006, the manufacturing output grew to SGD 23 billion (SEK 106 billion), a 30.2% increase over 2005. Within a span of six years, manufacturing output has grown almost fourfold from the year 2000. Pharmaceuticals account for 91% of the total life science output while Medical Technology maintained its output levels at over SGD 2 billion, corresponding to 9%. Valued-Added grew by 47% over 2005 while employment expanded by 3.9% to reach 10,571. Of the total jobs in the life science manufacturing sector, 62% are in the Medical Technology sector.⁸

Attraction policies

EDB is responsible for bringing in investments and generating long-term economic value in the life science sector. This is primarily done through the Biomedical Sciences Group which develops industrial, intellectual and human capital in Singapore in support of the biomedical sciences, and Bio*One Capital which functions as an investment arm. Together, they work to attract companies to establish R&D operations in Singapore and develop the local manufacturing sector in the field (Finegold et al 2004). EDB has 500 employees and 19 foreign offices: USA (New York, Boston, Chicago, Dallas, Los Angeles, San Francisco and Washington), Europe (Frankfurt, London, Milano, Paris and Stockholm) and Asia (Tokyo, Osaka, Beijing, Shanghai, Guangzhou, Jakarta and Mumbai).

The features of the Singaporean offer to life science investors include:

- R&D and educational support⁹
- Tax incentives
 - Tax exemption for ten years for projects of strategic importance
 - Relatively low corporation tax

Thus companies can receive funding to expand biomedical sciences' R&D activities in Singapore or to train manpower. Financial support also comes in the form of tax incentives, business advice and incubator services. Before 2000, investments were focused solely on manufacturing but now foreign company R&D investments are also increasing.

Taxes

Corporation tax is being cut in many countries, especially in Europe. In order to keep Singapore attractive as a business location, the corporation tax

⁸ www.biomed-singapore.com

⁹ www.edb.gov.sg

rate will be reduced from 20% to 18% in 2008¹⁰. One competing location for Big Pharma manufacturing units is Ireland, with its corporation tax rate of 12.5%.

Today, there is a zero tax rate for new start-up companies for the first three years of incorporation. Thereafter there is partial tax exemption with a rate of 5% for the first USD 10,000 of income and 10% for the next USD 90,000. As of 2008, there will be a zero tax rate for the first three years or the first USD 100,000, and thereafter a 9% tax rate on annual profits for the next USD 290,000. For existing companies with a USD 10,000 income, there will be a 4.5% tax rate as of 2008 and thereafter a 9% tax rate for income of up to USD 300,000¹¹.

Venture capital

Over 150 venture capital companies are currently located in Singapore and jointly contribute USD 12 billion in funds with a large amount directed to the biomedical industry. More specifically, 25% of these firms are domestic, 40% are from North America and Europe, and the remaining 35% are from Asia. Although companies can go directly to venture capitalists for funding, many choose to use matchmaking channels to find a venture capitalist that can meet the specific demands of their company. One of these is the Singapore Venture Capital Association (SVCA) that started in 1992 with the support of EDB, aiming to promote, develop, and foster industrial growth. To do this, SVCA facilitates link up firms seeking finance with venture capital companies, as well as interacting with professionals in the venture capital and private equity industries¹².

¹⁰ International Enterprise Singapore,

http://www.iesingapore.gov.sg/wps/portal/!ut/p/kcxml/04_Sj9SPykssy0xPLMnMz0vM0Y_QjzKLN4g38nAHSYGYjvqRMJEgfW99X4_83FT9AP2C3lhyR0dFRQBOc5AF/delta/base64xml/L3dJdyEvd0ZNQUFzQUMvNEIVRS82XzlfMUZC.

¹¹ Singapore Government, 2006,

http://www.mof.gov.sg/budget_2006/budget_speech/subsection6.2.html.

¹² The Singapore Venture Capital and Private Equity Association,
<http://www.svca.org.sg/about1.htm>.

3 Biomedical sciences initiative

The growth in investments in biomedical sciences' R&D in Singapore has been rapid in the last decade. This has been especially the case since 2000. Between then and 2006, Singapore's total R&D expenditure on biomedical sciences grew at an average annual rate of 38.2%. The biomedical sciences' share of the total R&D expenditure has risen sharply, from less than 5% in the 1990s to over 20% by 2006¹³ but the share of around 22% is still lower than that of the UK and US (over 25%) (Wong et al, 2008). The share of biomedical-related patenting in total output of patenting by Singapore-based inventors still continues to lag behind its share of R&D spending (Wong et al, 2008).

Given the lack of an existing indigenous biomedical cluster, Singapore has made extensive use of international talent in developing its biomedical sciences. The Biomedical Sciences Executive Committee which leads Singapore's Biomedical Sciences Initiative is advised by the International Advisory Council (IAC), which comprises eminent scientists from around the world, including Prof Harriet Wallberg-Henriksson, (President, Karolinska Institutet, Sweden).

Attracting foreign big pharma companies

EDB has successfully attracted multinational companies' investments in manufacturing, R&D, clinical trials and other knowledge-intensive services to Singapore. The biomedical industry is largely dominated by foreign companies. All the largest pharmaceutical manufacturing firms operating in Singapore in 2005 were foreign-majority owned. In order to move these investments into higher value-added portions of the biomedical industry value chain, EDB encourages foreign companies to set up R&D or clinical research operations in Singapore.

Initiative focus in the second phase of the biomedical sciences is on infrastructure and industry to develop translational and clinical research. Thus EDB has moved to encourage investments in these areas. Examples of initiatives are the West Clinic Excellence Cancer Center (established in Singapore in 2006) and Eisai's Regional Clinical Research Centre (2007).

¹³ National Survey of R&D in Singapore, A*STAR (previously National Science & Technology Board)

Buildings

Singapore already has an efficient transportation system, high speed Internet network and a safe and clean city. Biopolis, a SGD 500 million physical hub was built to house the life sciences initiative. Biopolis is a nine-building complex with 185,000 m² of space. Five of the nine buildings accommodate A*STAR's research institutes. In two other buildings, about 20 companies have set up R&D facilities, including GlaxoSmithKline and Novartis. The Biopolis area is the largest infrastructural project initiated by the Singapore government. Biopolis allows start-up companies to reduce their R&D costs by taking advantage of shared facilities and shared scientific equipment such as X-ray crystallography and MRI equipment. Companies also have access to shared infrastructure such as conference and meeting facilities¹⁴.

Biopolis is focused on biomedical R&D activities and designed to foster a collaborative culture among the institutions present and with the nearby National University of Singapore (NUS), the National University Hospital (NUH) and Singapore's Science Parks. Biopolis also provides integrated housing and recreation facilities for the many foreign scientists to be attracted to work in the research facilities.

Singapore's seven biomedical public research institutes all have a presence in Biopolis, and are intended to attract biomedical multinational companies, start-ups, and support services such as lawyers and patent agents to locate there (Finegold et al 2004). The government hopes that creating such an agglomeration will generate informal networks for knowledge-sharing and accelerate the growth of a critical mass of biomedical expertise in Singapore. Current private-sector tenants in Biopolis include GSK, Novartis and Isis Pharmaceuticals.

Public R&D institutes

Apart from the increased funding of biomedical research at the established universities, Singapore has established a number of public R&D institutes in biomedical sciences. The distribution of biomedical R&D funding between universities and institutes has not been mapped.

Basic research right up to clinical trials are supported at the public R&D institutes using four types of grants: project grants, providing seed funding for new investigators; programme grants, supporting more extensive research programmes of established investigators; co-operative grants, sponsoring inter-disciplinary work, and lastly; core competence grants,

¹⁴ International Enterprise Singapore, http://www.biomed-singapore.com/etc/medialib/bms_downloads/newsroom.Par.0010.File.tmp/BIOTECH%200708.pdf.

intended to develop or strengthen capabilities in areas of strategic importance.

The following research institutes and units under BMRC are part of the biomedical sciences initiative:

- Bioinformatics Institute (BII)
- Bioprocessing Technology Institute (BTI)
- Genome Institute of Singapore (GIS)
- Institute of Bioengineering and Nanotechnology (IBN)
- Institute of Medical Biology (IMB)
- Institute of Molecular and Cell Biology (IMCB)
- Singapore Bioimaging Consortium (SBIC)
- Singapore Cancer Syndicate (SCS)
- Singapore Consortium for Cohort Studies (SCCS)
- Singapore Immunology Network (SIgN)
- Singapore Institute for Clinical Sciences (SICS)
- Singapore Stem Cell Consortium (SSCC)

The oldest of these units is the Institute of Molecular and Cellular Biology (IMCB), first established in 1987 at NUS. Four institutes in bioinformatics, genomics, bioprocessing and nanobiotechnology were established over the period 2000-02, while the existing IMCB was expanded. The BMRC Research Institutes focuses on building up core biomedical capabilities in the areas of bioprocessing; chemical synthesis; genomics and proteomics; molecular and cell biology; bioengineering and nanotechnology and computational biology. More recently, the Singapore Institute for Clinical Sciences (SICS) was established to expand Singapore's clinical R&D capabilities, while the Centre for Molecular Medicine was repositioned as the Institute of Medical Biology (IMB) to facilitate translational research.

The biomedical initiative also means increased investments at the established universities, the National University of Singapore (NUS) and Nanyang Technological University (NTU). A new bio-engineering division has been set up in the Engineering faculty at NUS in 2001 with the aim of crossing traditional departmental boundaries within the faculty and university by having policy decisions made by a Board comprising academic staff from the engineering, science and medicine faculties. Academic staff in the division hold joint appointments with other departments in the Engineering faculty and other faculties and research institutes. (Wong 2007). In 2001, the School of Biological Sciences was established in the College of Sciences at Singapore's second-largest university, NTU, while a School of Chemical and Biomedical Engineering has been established in its College of Engineering.

Biomedical sciences initiative research programmes in NUS are consolidated by the Office of Life Sciences (OLS). OLS brings together researchers from the five core faculties involved in life sciences to identify and agree on ten areas of research, grouped under the disease headings of: cancer, neurobiology/ageing, vascular biology/angiogenesis, hepatology, infectious diseases. Also the platform technologies of: bioinformatics /registries/molecular epidemiology, structural biology/proteomics/genomics, immunology, bioengineering, experimental therapeutics /medicinal chemistry/toxicology /clinical trials. (Wong 2007).

Attracting foreign star scientists

Because of the ambitious scale and speed of development of the biomedical sciences initiative in Singapore, the attraction of foreign talent has become an integral part of the government's strategy. This speeds the pace of development of the science base and aims to enhance the possibility of attracting top students to the field. A number of star scientists from countries such as the US, UK, Japan, Sweden and Germany have thus been recruited on short-term contracts which are easily renewed. Some of these have now left but in many cases continue to have part-time engagements in Singapore.

Training young local talents

In addition to these star scientists, the government is sending the top students from Singapore's education system to leading research universities around the world for graduate science and business education. The government pays for their education provided that they return to Singapore when they complete their studies. The scholarships, provided by A*STAR, target different segments of young talent, ranging from those seeking undergraduate and post-graduate studies to medical doctors seeking training to become clinician-scientists. As of 2007, over 100 students have been trained, with a target of 1,000 trained PhDs by 2015.

Promoting indigenous innovation

As already described, a number of initiatives have been launched to spur indigenous innovation through seed financing, business advice, incubator services and public venture capital funds. Singapore has no tradition of establishing start-up companies in the biomedical field and there is also a lack of similar ventures in other fields. There is thus a limited track record of indigenous innovation.

The main focus areas for Singapore's start-ups are drug discovery and development (e.g. S*BIO, established in 2000, Merlion Pharmaceuticals (2002), ProTherapeutics (2004)), medical devices (e.g. BioSensors (1990, listed in 2005), Merlin Medical (2002)), stem cells (ES Cell International

(2000), Cordlife (2002)), and bioinformatics (KOOPrime (2000), HeliXense (2000), ReceptorScience (2000)).

Until recently, only two drug-discovery companies had products; Lynk Biotechnology and AP Genomics. S*BIO has recently received an US\$25 Million upfront payment and equity investment and is eligible to receive Additional US\$525 Million in option & license fees and milestone payments for a collaboration with Onyx Pharmaceuticals, Inc. to develop and commercialise S*BIO's two novel JAK2 inhibitors. Also, Tragara Pharmaceuticals Inc. in 2009 announced that S*BIO has granted them a worldwide exclusive license to develop and commercialise the S*BIO novel multi-kinase inhibitor.

All the bioinformatics firms have some products on the market because product development in software is significantly shorter than for drugs. Nevertheless, a major commercial success has yet to emerge amongst Singapore's biomedical start ups (Wong et al, 2008).

Clinical research capabilities

The first phase of Singapore's biomedical sciences initiative (2000 - 2005) focused on establishing a foundation of basic biomedical research in Singapore. The second phase is focusing on the development of capabilities in clinical and translational research, while continuing to strengthen basic sciences (A*STAR 2007).

There are seven public hospitals, six national specialty centres on cancer, cardiac, eye, skin, neuroscience and dental care, and 16 private hospitals. There is also a primary healthcare network of 18 public polyclinics and over 2000 private medical practitioners. The country's healthcare system has a good reputation, attracting over 370,000 foreign patients in 2005 and having a target of 1 million by 2012. Other advantages include its compact size and a population with a mix of Asian ethnic groups, which makes it conducive to developing new treatments and technologies, as well as drug trials customised to Asian populations (Wong et al, 2008).

Thus far, Novo Nordisk and some of the large contract research organisations (CROs) have established clinical trial centres in Singapore but there are still relatively few clinical trials taking place in Singapore. This may be due to the strong and growing competition for the Asian clinical research market from Taiwan, Australia and Japan, which have the advantage of larger domestic markets and the fact that pharmaceutical companies may be reluctant to use these clinical trial centres due to an unproven track record (Finegold et al 2004).

As with other sectors within the biomedical sciences initiative, clinical research suffers from a lack of manpower. One scheme to improve the situation is the National Science Scholarship, offered by A*STAR and particularly targeting medical doctors who want to become clinician-scientists. Two other talent attraction and development schemes recently launched by A*STAR are the Singapore Translational Research Investigatorship, which aims to recruit world-class clinician-scientists and clinician-investigators to undertake clinical and translational research in Singapore, and the Clinician Scientist Award, which targets top local clinicians (A*STAR 2007).

In the development of clinical and translational research capabilities, consortia are initiated by BMRC to promote translational research links between the public research institutes under BMRC, universities and the healthcare sector. These include the Singapore Cancer Syndicate, Singapore Bio-imaging Consortium, Singapore Stem-Cell Consortium, Singapore Consortium of Cohort Studies and the Singapore Immunology Network. Activities in these consortia include funding of joint projects, engaging in joint training, and establishment of research infrastructure and links between local and overseas institutes.

As part of improving conditions for clinical and translational research, better medical education has also been in focus. Among the initiatives undertaken by NUS, the most ambitious has been the building of a second medical school. Unlike the existing one, which is in the British tradition of taking students directly from high schools, the new school was modelled after the US post-graduate, professional medical school, with students drawn from graduates of various disciplines and faculty-recruited to emphasise research excellence. The school was established in 2005 in collaboration with a leading US medical school (Duke University), and is located on the same campus as the largest public hospital (Singapore General Hospital (SGH)) to facilitate close interactions, particularly in research (Wong 2007). The NUS-Duke Graduate Medical School has a research-intensive curriculum based on the Duke University model of medical education. This focuses on developing clinician-scientists who will engage in translational research.

The infrastructure for translational research at NUS medical schools, and the hospitals with which they are co-located, is being further developed through a USD 140 million project announced in 2007. The plans include the development of new research buildings for laboratory research, investigational medicine units, and animal research facilities. Not only will research facilities be expanded, but the research infrastructure of the institutions involved will be integrated, resulting in two campuses for translational research: one comprising NUS and NUH; the other comprising GMS, SGH and the national disease specialty centres (A*STAR 2007).

Multidisciplinary research

An initiative for promoting international multidisciplinary research was put in place by the National Research Foundation's Campus for Research Excellence and Technological Enterprise (CREATE). The first research centre within CREATE builds on an existing relationship between MIT, NUS and NTU known as the Singapore-MIT Alliance, in which the three universities collaborate in graduate education and research. The universities have extended their partnership to form the Singapore-MIT Alliance for Research and Technology Centre, a research centre where faculty, researchers and graduate students from MIT collaborate with those from universities, polytechnics, research institutes and industry in Singapore and other countries in Asia. The first centre is the Centre on Infectious Diseases, with eight senior MIT faculty members and 17 Singapore collaborators from NUS, NTU, TLL and other public research institutes in the fields of biology, engineering, medicine and computing (NRF 2007).

Regulatory issues

The Bioethics Advisory Committee is an advisory body which was formed in 2000 to develop recommendations on the legal, ethical and social issues of human-biology research. Early on, they recommended that human cloning should not be permitted, but that stem cell research and the use of cloning as a therapeutic tool was to be allowed. Thus, the US National Institutes of Health allows the US federal government to fund research using Singapore-produced stem cells (Finegold et al 2004).

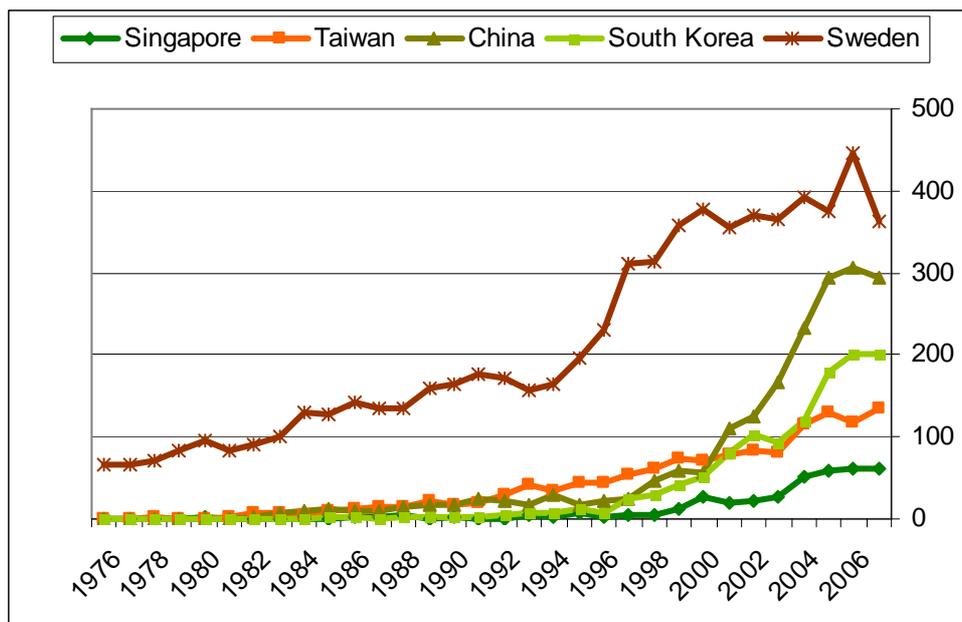
4 Scientific output

The focus of the Singaporean policy initiative regarding life science is on biomedicine. The biomedical focus, also including bio-engineering, is quite clear from the scientific publication pattern which shows a steep increase in publication volumes in relevant fields. Scientific publications were analysed in order to assess the scientific performance and collaboration pattern. To address the quality of the scientific publications, only life science and medical journals with an impact factor greater than six were included in the analysis. The impact factor is an average measure of how much articles in a particular journal are cited by researchers in other scientific publications. Two analyses were made, one on life science journals excluding clinical medicine journals and one of journals in clinical medicine.

Medical sciences

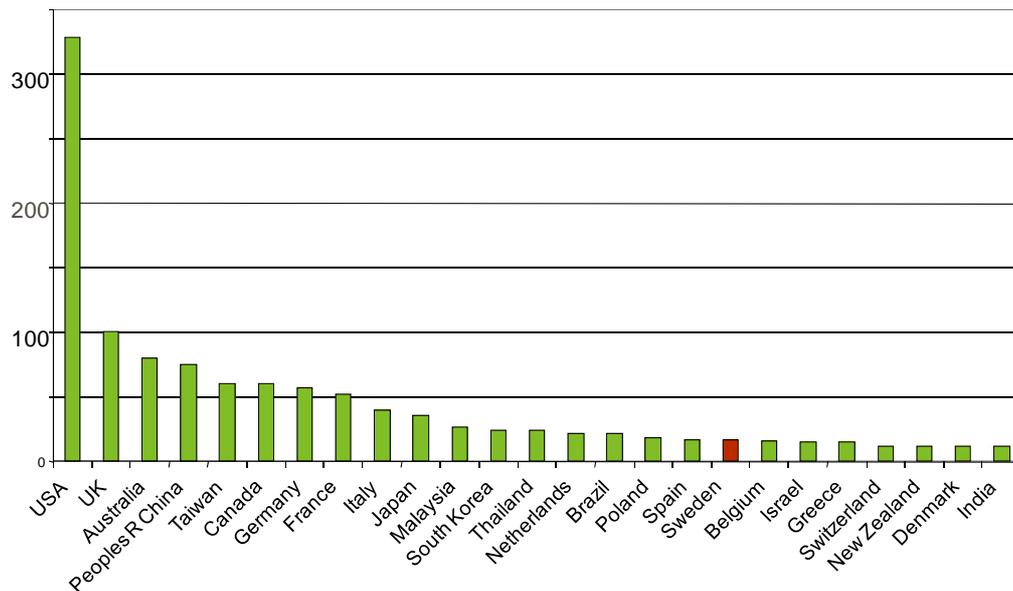
An analysis of the world scientific output in terms of publications in top medical journals indicates an impressive development for a number of Asian countries. Countries such as South Korea, Taiwan and Singapore, with populations of 48.3, 22.8 and 4.5 million inhabitants respectively, but also China, show a steep increase in the number of publications from very low starting levels in the early nineties. This is illustrated in the figure below comparing their output to that of Sweden.

Development of the number of articles by researchers in Singapore, Taiwan, China, South Korea and Sweden in non review top medical journals



The scientific country collaboration pattern can be studied in terms of the number of co-authored articles by researchers from different countries and organisations. US researchers topped the collaboration pattern with Singapore by a wide margin in top medical journals between 1991-2006. Compared to the collaboration pattern of countries with a long tradition of life science research, Singapore more often has researchers from Asian countries such as China, Taiwan, Malaysia, South Korea and Thailand among its collaborative partners in articles published in these journals.

Country collaboration with Singapore non-review medical journals with impact factor > 6 for 1991-2006

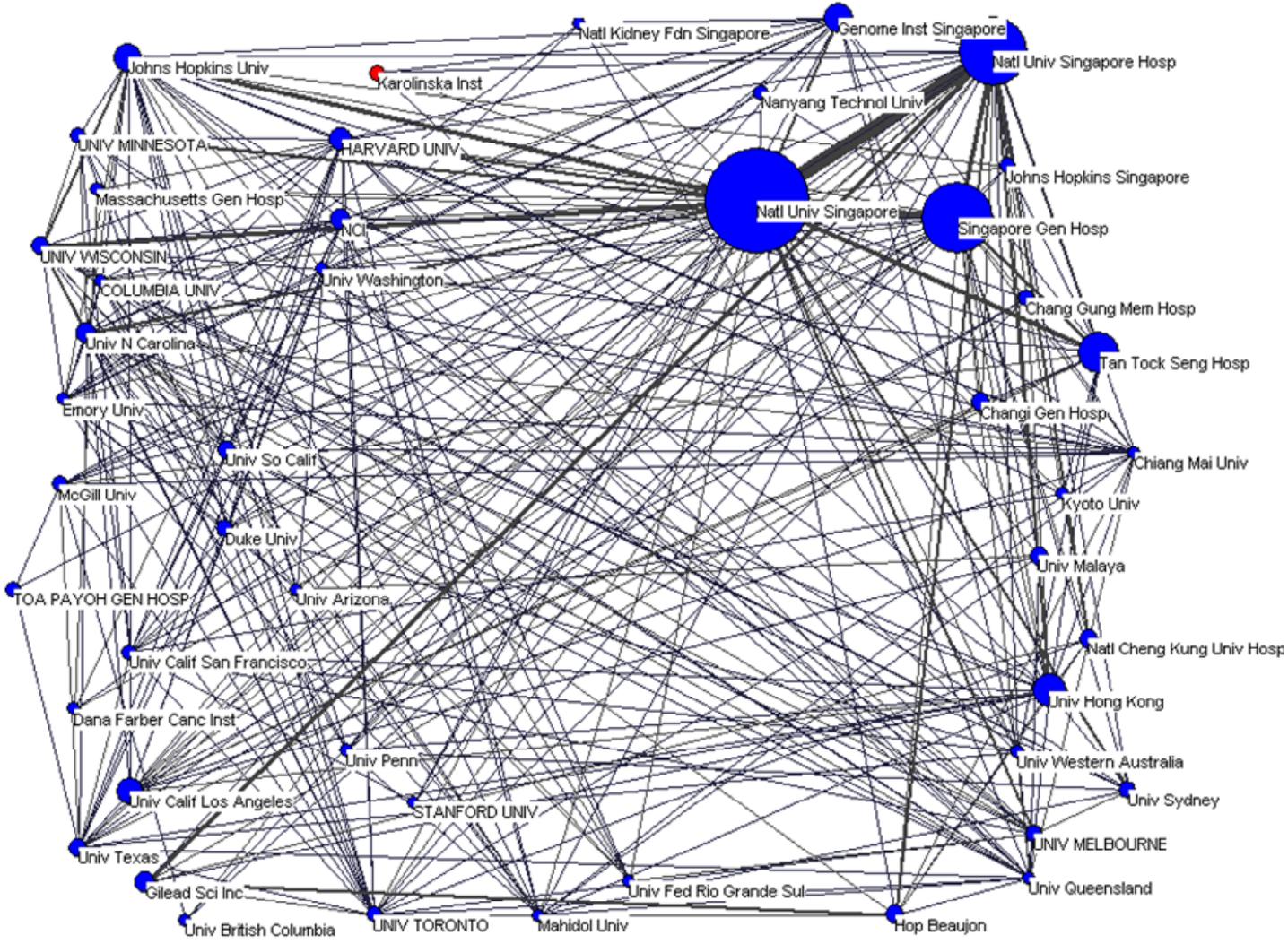


The leading research organisations in Singapore in top medical journals are the National University of Singapore (NUS), Singapore General Hospital, National University of Singapore Hospital and Tan Tock Seng Hospital. The collaboration pattern found in top medical journals with Singaporean co-authors is visualised in the figure below. Top non-Singaporean organisations identified include Johns Hopkins University, University of California Los Angeles, University of Hong Kong and Harvard University. Karolinska Institutet is the only Swedish organisation with a significant collaboration with Singaporean researchers.

A joint campus between US Duke University and National University of Singapore has been established in Singapore. The Duke-NUS graduate medical school is intended to complement the National University of Singapore's existing undergraduate medical school, based on the British model of medical education, in which students enter medical school after completing their Singapore-Cambridge General Certificate of Education (GCE) Advanced Level examinations (or equivalent) and then pursue a five-year curriculum towards a medical degree. According to the Singaporean

Ministry of Education, the establishment of a graduate medical school will increase the supply of doctors practicing in Singapore, give the country the flexibility to produce more physicians to meet future needs, and train doctors who are exposed to clinically-related research. Duke was likewise interested to form collaborations with NUS faculty and with academic and private research groups at Biopolis and elsewhere in Singapore to accelerate translational research and other research endeavours at Duke; and aid recruitment and retention of excellent faculty at both locations. Before this initiative Johns Hopkins University intended a similar endeavour in Singapore but those plans have been terminated.

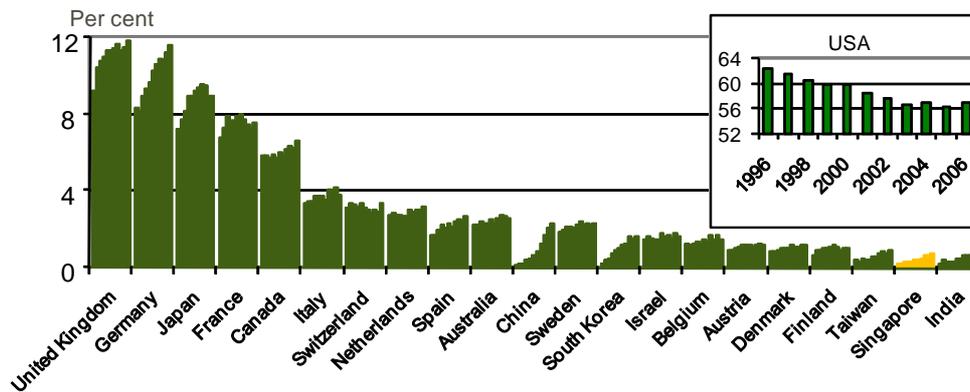
Singaporean collaboration pattern in top medical journals 1990-2007



Life Science

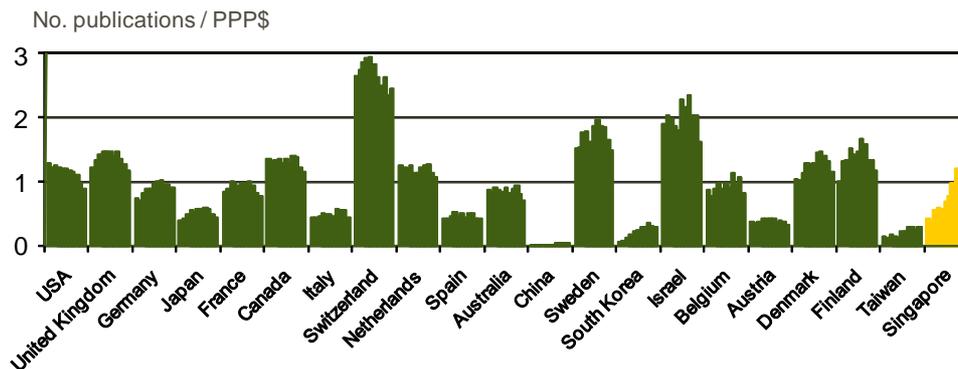
Between 2000 - 2006, the increased funding from the biomedical initiative was primarily aimed at preclinical biomedical research. In the second phase, increased efforts are being focused on clinical research. For such a small country, the development of scientific publications in life science journals in an international comparison is also impressive. The world share is higher than, say, India and has undergone a steep increase during the period studied.

Development of share of total world publication volume in non-review life science journals (impact factor>6) for top countries, 1996-2006



If the publication volume is put in relation to GDP the development is even more impressive. The results in recent years are then in the same order of magnitude as the top countries.

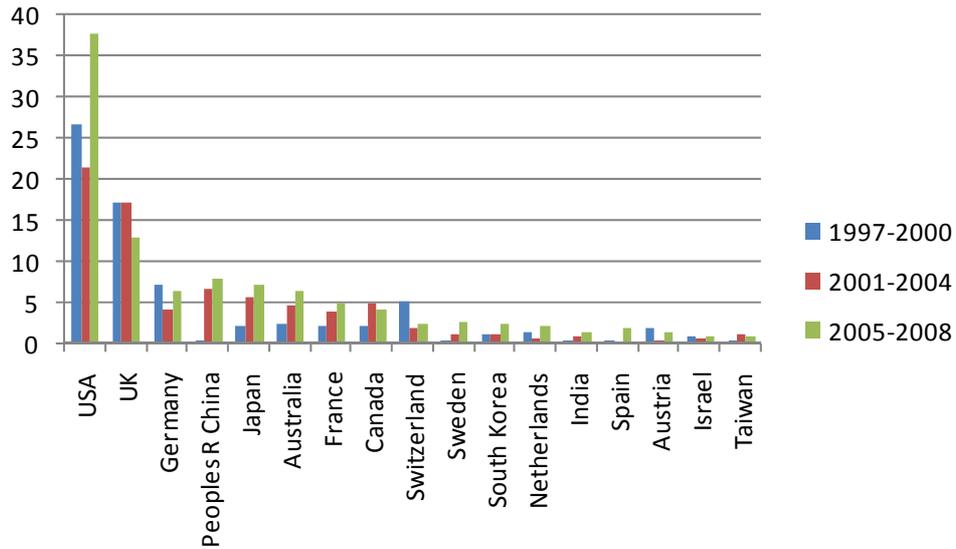
Development of publication volume in relation to GDP for countries with the largest publication volume in top life science journals, 1996-2006



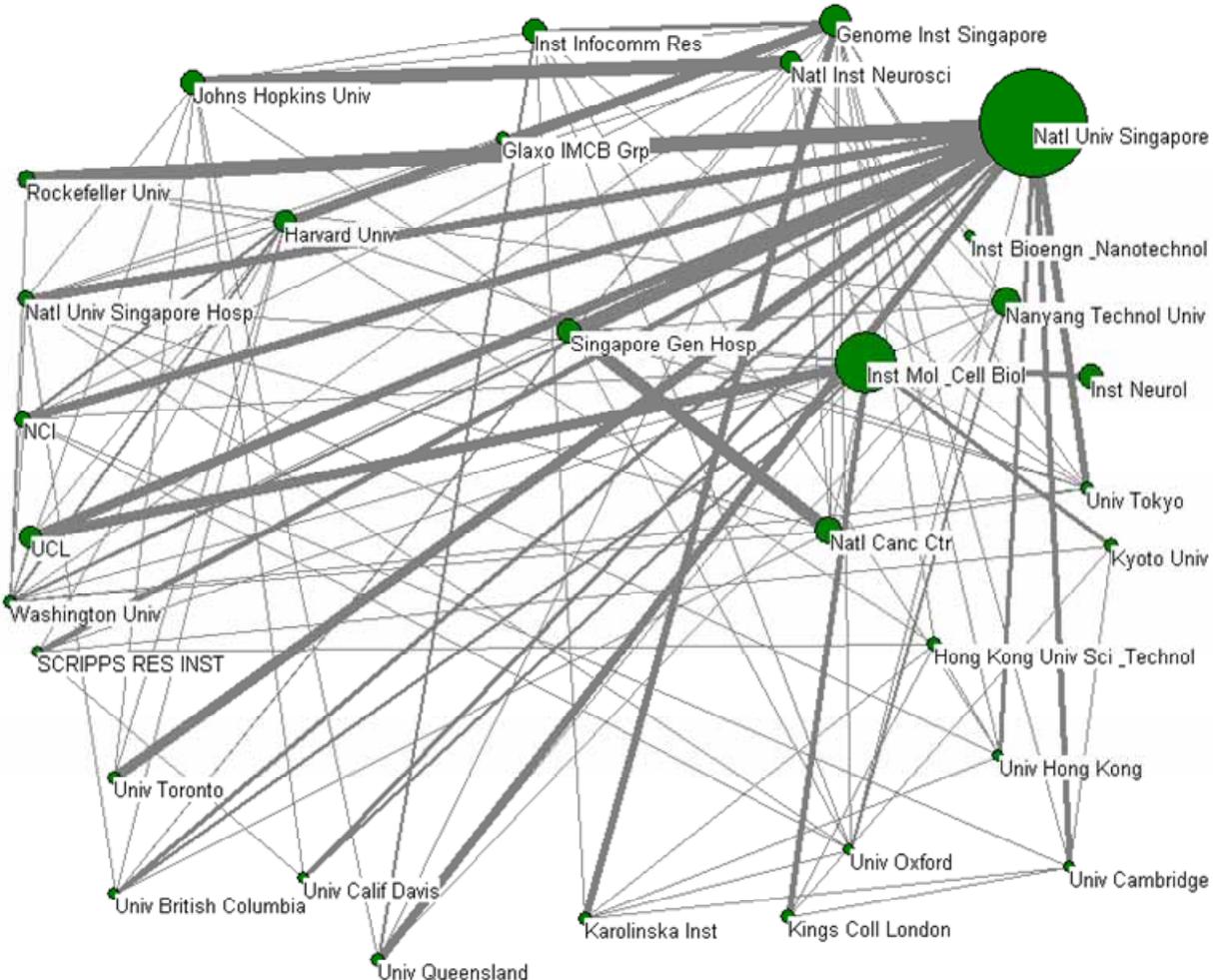
According to this analysis, the four most prominent research organisations in the field in Singapore are the National University of Singapore (NUS), the Institute of Molecular & Cell Biology, the Genome Institute of Singapore and Nanyang Technological University (NTU). The collaboration pattern found in Singaporean publications in top life science journals is visualised below. Top non-Singaporean organisations found in the

collaboration pattern include mostly US organisations such as Johns Hopkins University, Harvard University and Rockefeller University. The most frequently occurring organisations from other Asian countries include Hong Kong University of Science & Technology, Kyoto and Tokyo University. After these US and Asian Universities come the University of Toronto and then Sweden’s Karolinska Intitutet.

Average annual co-authorship share for countries with the largest co-authorship volume with Singaporean researchers in top life science non-review journals during three periods: 1997-2000; 2001-2004; 2005-2008



Collaboration pattern between the organisations with the largest publication volumes in the Singaporean dataset of top Life Science journals 1990-2007



5 Summary and conclusions

In Singapore, government involvement in the development of the life science sector focusing on biomedicine is clearly seen in the investments made in various types of initiatives. The government of Singapore has adopted a top-down, coordinated multi-agency approach, comprising measures for investment promotion, promoting R&D through developing public R&D institutes and providing incentives for private sector R&D as well as investments in infrastructure and education. One of the key components is the attraction of international firms and institutions as well as prominent researchers. Foreign big pharma companies are incentivised to establish operations and the promotion policies are pro-active, targeted and concentrated. Another strategy for building critical mass is the geographic agglomeration of players in the Biopolis facility. The long term goal is that the efforts will spur indigenous innovation. Funding and advisory bodies for promoting such endeavours are in place. Establishing a strong IP protection regime, and providing a strong public policy framework regarding bioethics and standards for clinical trials has also been important to attract foreign interest.

Thus the development of the biomedicine in Singapore is stimulated by a number of initiatives:

- International analysis before launch of initiatives identifying good practices and translating them to a Singaporean context
- International experts in advisory boards of initiatives
- Science and entrepreneurship in focus in education from an early age
- Sending the best students to top universities for PhD study and requiring them to come back to Singapore after finished studies
- Attracting foreign star scientists
- Advice and public venture capital for start-ups
- Investments in research infrastructure and buildings - attractive milieus
- Tax incentives and other incentives for investments by international companies
- Drastic increase in R&D funding

The initial vision of stimulating the development of a biomedical sciences cluster was driven primarily by perceived global market growth opportunities rather than local/regional market opportunities. In the second phase of the biomedical initiative a focus is also on leveraging on Asian health-care markets by engaging local/regional hospitals in translational

research as well as attracting Asian patients to Singapore for medical treatments.

It is difficult to already now address the success of the biomedical initiative since it has only been in place since year 2000. Also, it has in the present study not been attempted to relate the outcomes of the initiative to the investments made. The results so far however, shows that Singapore has been successful in attracting foreign direct investment by international life science companies, especially in manufacturing but increasingly also concerning investments in R&D units. There are about 100 companies in the life science industry with in total 10,000 employees and there has been an almost linear increase in the number of employees since 1980. There has thus not been an accelerated increase since the biomedical initiative was launched. The industry is dominated by multinational companies and the bulk of the employees are found in manufacturing. The continued and increased investments by multinational companies indicate good experiences both concerning manufacturing and R&D.

The building of scientific excellence seems to be on the way according to the bibliometric analysis. Scientific output in terms of scientific publications in high impact journals indicates an impressive development of the science base in relevant fields, although the drastic increase in publication volumes in high impact journals 2001-2003 has levelled off somewhat in the most recent years of the study, 2004-2006. The traces of indigenous innovation are still limited. This is probably to be expected given the short time the biomedical initiative has been in place and the notoriously slow nature of life science innovation processes.

Starting with attracting multinational companies and foreign talents seems effective in accelerating the development. It is unclear what effects this focus will have on the development of indigenous capabilities. A factor hampering the Singaporean biomedical development is the hierarchical society with roots in the culture, traditions and the political system. This has according to interviews, an impact on both the business and public sectors leading to risk-averse behaviour. Among middle management for example, this leads to individuals taking few initiatives of their own. After graduation, students often seek secure carriers in the military, public sector or foreign companies instead of those considered less secure and perhaps also less rewarding; carriers in academia or start-up ventures. According to interviews, there is also little tradition of entrepreneurship, especially in knowledge intensive fields.

Even though it is still early days, Singapore's experience suggests that the coordinated, strategic approach involving multiple government agencies and sustained investment over a long period is promoting the development of a

biomedical cluster with firms, excellent research environments, a skilled workforce and possibly also indigenous innovations for a country with few of these components in place to start with. The endurance of the policy makers to continue supporting the efforts with large investments seems to be long-term. The second phase of the biomedical initiative, focussing on translational and clinical medicine will be interesting to follow, as will the continued efforts to develop competences and capabilities to support the positive results thus far.

For Swedish research and innovation policy it is important to be aware of the focused Singaporean effort with its array of initiatives and to follow the development. It should be considered whether initiatives to encourage Swedish research and innovation environments to collaborate with the rising Singaporean counterparts should be provided.

6 Appendix

Interviews

Pär Ahlberger	Embassy of Sweden
Bertil Andersson	Nanyang Technological University
Amanda <u>Ang</u> Tian Wei	A*star, Biomedical Research Council
Jan Carlstedt-Duke	Karolinska Institutet
Patrick J. Casey	Duke University Medical Center
Mary Chan Bee Eng	Nanyang Technological University
Serena <u>Cho</u>	Bio*One Capital Pte Ltd
Brian W Dymock	S*BIO Pte Ltd
Yin Chin <u>Hew</u>	S*BIO Pte Ltd
Hazel <u>Khoo</u>	A*star, Biomedical Research Council
Ashish Lall	National University of Singapore
Kean Chong <u>Loh</u>	A-Bio Pharma Pte Ltd
Alex Matter	Novartis, Institute for tropical diseases
Darran Nathan	Progeniq Pte Ltd
Ying Yuan <u>Ng</u>	Economic Development Board, EDB
Lars Nordenskiöld	Nanyang Technological University
Sven Pettersson	Karolinska Institutet
Peter R. Preiser	Nanyang Technological University
Thommy Svensson	Swedish School of Advanced Pacific-Asia Studies
Martti Tammi	National University of Singapore
Jenny Tan	Pall Filtration Pte Ltd
Harriett Wallberg-Henriksson	Karolinska Institutet
George <u>Wang</u>	A-Bio Pharma Pte Ltd

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- 04 Swedish possibilities within Tissue Engineering and Regenerative Medicine
- 05 Sverige och FP7 - Rapportering av det svenska deltagandet i EUs sjunde ramprogram för forskning och teknisk utveckling. *Only available as PDF*
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- 07 Var ligger horisonten? - Stor potential men stora utmaningar för vågkraften
- 08 Vindkraften tar fart - En strukturell revolution?
- 09 Mer raffinerade produkter - Vedbaserade bioraffinaderier höjer kilovärdet på trädet
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- 12 Summary - Impact of Government Support to Automotive Research. *Brief version in English of VA 2009:02, for brief version in Swedish see VA 2009:11*
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- 04 The GSM Story - Effects of Research on Swedish Mobile Telephone Developments. *For brief version in Swedish or English see VA 2008:07 or VA 2008:06*

- 05 Effektanalys av "offentlig sädffinansiering" 1994 - 2004
- 06 Summary - The GSM Story - Effects of Research on Swedish Mobile Telephone Developments. *Brief version of VA 2008:04, for brief version in Swedish see VA 2008:07.*
- 07 Sammanfattning - Historien om GSM - Effekter av forskning i svensk mobiltelefonutveckling. *Brief version of VA 2008:04, for brief version in English see VA 2008:06*
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- 03 Sammanfattning - Användningsdriven utveckling av IT i arbetslivet - Effektivvärdering av tjugo års forskning och utveckling kring arbetslivets användning av IT. *Brief version of VA 2007:02, for brief version in English see VA 2007:13*
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Sverige 2006

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- 08 Sammanfattning - Effekter av den svenska trafiksäkerhetsforskningen 1971-2004. *Brief version of VA 2007:07, for brief version in English see VA 2007:09*
- 09 Summary - Effects of Swedish traffic safety research 1971-2004. *Brief version of VA 2007:10, for brief version in Swedish see VA 2007:07.*
- 10 Effects of Swedish traffic safety research 1971-2004. *For brief version in Swedish and English see VA 2007:08 and VA 2007:09*
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