# Chapter 5
# The University-Driven LISs

**Abstract** Theoretical conceptions of the role of universities in local innovation systems have evolved over the past 20 years, from an initial approach that stressed the importance of knowledge spillovers from university educational and research activities into their regional knowledge spaces, towards a new emphasis on the "third role" of universities, as animators of regional economic and social development. However the typical conception is that universities and research centres in developing countries take little part in stimulating the formation of LISs, with this mission instead being substituted by the state or large companies. This chapter analyses the role and the mechanisms through which universities can contribute to creation of LISs, first from a theoretical point of view. The theoretical arguments are then supported by an analysis of the role of the National University of Singapore, in driving the development of the "Biopolis" biotech LIS.

**Keywords** LIS · Universities · Third mission · Singapore · Biopolis cluster · NUS

## 5.1 The Role of Universities in Local Innovation Systems

Universities have long been recognised as providers of basic scientific knowledge for industrial innovation, through their actions in research and related activities. Such benefits were understood as particularly accruing to the agricultural and manufacturing sectors (Guston 2000; Smith 1990; Hart 1988).

Neoclassical economic theory explained the productive performance and competitive advantage of firms largely in terms of relative resource endowments (Hall 1994). The role of knowledge and of institutions involved in the creation of knowledge was seen as exogenous, though not unimportant, to the production system (Freeman 1995). The emergence of the national systems of innovation approach (Freeman 1991; Lundvall 1992) shifted the conceptualisation of the role of universities in economic production, bringing them "inside the tent", among the other actors with a direct role in shaping regional innovation systems (Cassia et al. 2008).



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There are two dominant approaches to perceiving this role: the triple helix model of university, industry and government relations, and the concept of the "engaged university", expressed in a second body of literature. The two concepts overlap, but also have important differences in emphasis. Both bodies of thought stress that universities are increasingly linked to place but they offer different analyses of the driving forces in the relationship. Further, there are significant differences in their assumptions regarding institutional norms and behaviours.

The triple helix model (Etzkowitz and Leydesdorff 1997) brought attention to the role of universities in regional economies, anticipating the multiplying incidence of hybrid university-industry-government relationships, as seen in recent resource and capital development projects. Particularly interesting among these projects are those involving property development for science parks and incubator facilities, to favour new firm formation (Etzkowitz 2002: 14).

The triple helix model offers a conceptualisation of innovation as occurring through non-linear, interactive processes, in a "recursive overlap of interactions and negotiations among universities, industry and government" (Etzkowitz and Leydesdorff 1997). One of the key insights of the model is that of the hybrid, repetitively growing, inter-institutional nature of relations among the "three helices". Instead of the traditional situation in which the institutional spheres of the state, university and industry were separate entities that interacted across strongly defended boundaries, the individuals and organisations within these helices are seen as taking different and mixed roles (Etzkowitz and Leydesdorff 1999: 113; Etzkowitz and Leydesdorff 1997; Sutz 1997).

Like the triple-helix model, the literature on the "engaged university" (OECD 1999; Holland 2001; Chatterton and Goddard 2000; OECD 2007; Uyarra 2010) also focuses on the third role of universities in regional development. However it differs in emphasising the "adaptive responses" open to universities as they embed a stronger regional focus in their teaching and research missions. The approach does not eschew the development of hybrid, boundary-spanning mechanisms for external engagement, but it inserts this into a broader, developmental approach that considers a range of mechanisms through which universities can engage with their regions (Power and Malmberg 2008). Universities, through their resource base of people, skills and knowledge, increasingly play a diversity of roles in regional networking and institutional capacity building. Staff, acting in both formal and informal capacities, act as "regional animators" (Chatterton and Goddard 2000: 481) through their insertion in outside bodies ranging from school boards and local authorities to cultural organisations and development agencies. Universities thereby make an important indirect contribution to the social and cultural basis of effective regional governance. In general, the developmental role of universities in regional economic and social development centres on the intersection of learning economies and the regionalisation of production and regulation.

However, the literature on the engaged university appears to downplay the empirical fact of differences in the missions of relevant institutions, and can be argued to oversimplify the capacity and willingness of universities to adapt their functions in response to external signals.

Both of these bodies of literature tend to distinguish the "generative" and "developmental" roles of universities in local innovation systems (Cooke 2002; Niosi and Bas 2001; Lundvall and Johnson 1994).

Universities and public research organisations have been given a much more prominent role in recent models of knowledge production (Charles 2006). Gunasekara (2006: 143) identifies two models of university involvement in regional development. First, the generative role serves regional needs directly, by providing boundary-spanning activities like incubators and science parks. Second, a broader developmental role is filled by adjusting research and teaching activities to regional needs.

In emerging nations, universities now play key roles in LISs. First, they can enhance the regional knowledge base through their international academic networks, serving as gateways for local businesses to reach external knowledge (Altbach 1998: 179; Fritsch and Schwirten 1998). Second, they can adapt knowledge from extra-regional sources to produce new forms that are more appropriate for the local innovation system. In doing so, they reduce entry costs for new technologies and open windows of opportunity for catch-up processes (Perez and Soete 1988: 476). Third, within the centralised character typical of innovation systems in developing countries, public universities usually enjoy greater autonomy than do other regional actors, maintaining substantial levels of control over their financial, personnel, and academic affairs. Universities that are fully or partially incorporated tend to establish even greater levels of independence, and are capable of responding still more efficiently to regional needs.

Bernardes and Albuquerque (2003: 868–870) conclude that linkages and feedback mechanisms among universities and industry have to be established in coevolution, during the catching-up processes. In the worst case, purely education-led growth will encounter a dead end if the university outputs have not been correlated to needs in the productive sector.

In the nascent innovation systems of developing countries, university-industry linkages differ markedly from those in the western experience. Emphasis is placed on human capital development with strong feedback from the private sector, the adaptation of innovations from more advanced countries, and the diffusion of appropriate technologies to local companies (Schiller 2006a, b). The bulk of new knowledge and technologies is traditionally acquired from extra-regional sources, for example via technology licensing and foreign-owned affiliates (Liefner et al. 2006). Universities are the only endogenous knowledge source in many developing-nation LISs and thus take wider responsibility in the whole process of economic development. Local SMEs are often almost completely lacking in technological capacities, and are in need of basic technical education and services, generally without advanced research.

Since the academic capabilities of universities in developing countries are expected to be low at the beginning of the catch-up process, knowledge transfers in projects with large or foreign-owned companies might in fact run from industry to university (Schiller and Liefner 2007).

In addition to the institutional barriers that limit university-industry linkages everywhere in the world, developing countries demonstrate several further restrictions that affect the efficiency of knowledge transfers (World Bank 2000). In such nations, faculty are still tied to the dominant duty of teaching, and may not be sufficiently qualified to provide students with up-to-date skills. Advanced research is hindered by a lack of equipment and funding, and academics' incomes are too low to attract top personnel. Sideline activities that generate additional income may in fact detract from academic duties. In addition, bureaucratic "red tape" at public universities can be burdensome.

### *5.1.1 Mechanisms for University Guidance of LIS Development*

A university that embraces its role and adopts the mission of contributing to regional or national development is referred to as an "entrepreneurial university". According to Etzkowitz et al. (2000), an entrepreneurial university is one that undertakes activities "with the objective of improving regional or national economic performance as well as the university's financial advantage and that of its faculty."

Prior to the triple helix model, the university was conceived as having the traditional two-fold mission of transferring knowledge through education, while also advancing knowledge through basic research. Adding to this dual role, the entrepreneurial university adopts the third mission of contributing to economic development.

The potential activities for achieving this third aim cover a broad and continuous spectrum, ranging from those originating in the traditional university roles to those that express the institution's new entrepreneurial nature, as suggested in Fig. 5.1.

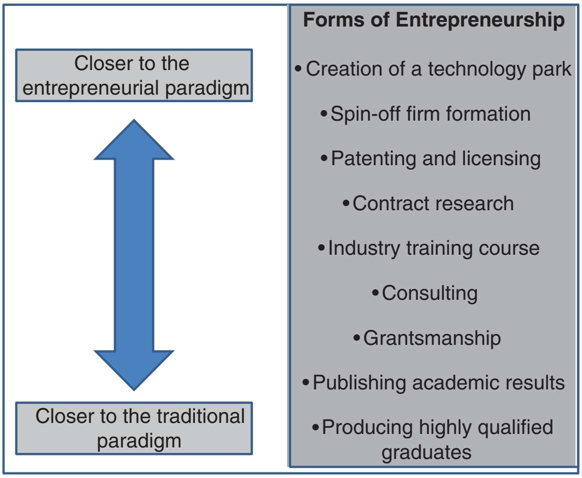


**Fig. 5.1** Spectrum of activities for the university "third role" from Philpott et al. (2011)

Considering the possible range of such activities, we distinguish three types of mechanisms that the university can apply to guide local development: (i) start-up development, (ii) university-industry collaborations, (iii) formation and research.

#### 5.1.1.1 Start-up Development

This category includes all initiatives where the university is an actor in creating the necessary conditions for support or guidance in the birth of new innovative firms in the local context. Such activities could take place through participation in science and technology parks, which create a formal site where firms (normally high-tech firms) can locate and interact with the university. These parks provide a seed bed for the development of multiple new ventures and can thus contribute to regional cluster development and employment. The infrastructure in turn contributes to the research capability of the university by attracting highly skilled individuals and technological resources to the region.

Another instrument for universities to promote entrepreneurialism is the creation of academic spin-offs, born for the commercial exploitation of research results. The creation of these new entrepreneurial ventures transfers technology from the lab to market, thus exploiting intellectual property and generating regional employment. Finally, the university can award licenses for use of its patented innovations. The original act of patenting the innovation documents the knowledge contribution of the university and allows the controlled transfer of the intellectual property to selected industrial partners, who can exploit the innovation for competitive advantage and wealth generation. Such licensing can both support existing firms and favour the creation of new entrepreneurial activities (Chang et al. 2009; O'Shea et al. 2008; Wright et al. 2006; Murray 2004; Shane 2004a, b; Di Gregorio and Shane 2003).

#### 5.1.1.2 University-Industry Collaboration

The university can collaborate with firms through a number of mechanisms, for development of various research activities.

Contract research facilitates company activities by solving practical problems that would otherwise deter business performance. Engaging in contract research also contributes to stronger social relations between university and industry that can lead to deeper research interactions in the future.

The university can institute training courses for skills improvement in the national or regional workforce in emerging areas of industrial technology and practice. This ensures that regional industry continually increases its internal skills base and maintains or advances its competitive position.

The university can also provide consultancy services, including the provision of personalised advice and mentoring for improvement in enterprise performance. All of these mechanisms develop linkages between university and industry that can be further exploited in the future. The university-firm relationship is in fact typically bidirectional, since the university will gain advantages on its own side of the cooperative activities. The potential benefits include company investment in university activities through mechanisms such as grants. Such investment enhances the reputation of the university, which attracts further industry to the region, and also tends to lead to development of "hard" academic entrepreneurship by individual faculty members (Powers 2004; Di Gregorio and Shane 2003; Van Looy et al. 2004).

#### 5.1.1.3 Education and Research

Obviously universities will continue to contribute to territorial development through their traditional activities of education and diffusion of research results. The development of specialised personnel capable of meeting current and future demand ensures that national industry can meet its staffing needs, and that it has the absorptive capacity to engage with university as part of the triple helix model.

As with the case of corporate funding for university research, the overall production and diffusion of research results enhances the reputation of the institution, attracting further industry and leading to harder forms of academic entrepreneurship (Powers 2004; Di Gregorio and Shane 2003; Van Looy et al. 2004).

## 5.2 The Biopolis LIS of Singapore

Singapore's continued competitiveness in the global knowledge economy is based on an ongoing series of government-driven upgrading and renewal programmes that steer institutions and the workforce towards swift adaptation in response to technical and economic trends (Yue and Lim 2002). In 2010, the Singapore Economic Strategies Committee issued a report presenting the key recommendation that over the coming decade, national growth should be productivity-driven, and that such growth should in turn be centred on the fostering of innovation.

Over the years, Singapore has indeed worked towards a comprehensive R&D ecosystem, comprising public sector research bodies, academic research institutes and corporate R&D laboratories. However R&D is not an end in itself. To serve as a driver of economic growth, enterprises must be able to create value from R&D investments and the resulting intellectual properties. Large domestic and foreign corporations, which benefit from strong state backing, have traditionally carried out the bulk of Singapore's innovation and commercialisation activities. For example for many years, the Economic Development Board has offered incentives to large foreign corporations to either relocate or build their regional R&D centres in Singapore. As a result, foreign corporations and large local enterprises accounted for 85.7 % of industry R&D expenditure from 2002 to 2010. Any innovation capabilities in the SME sector have largely developed through cooperation in testing for commercialisation, or from other spillover mechanisms.

Beginning with the 2010 decade, the national government has put increasing emphasis on broadening the base of innovative activities and bringing in local enterprises, especially SMEs (OECD 2013). In Singapore, such policies have the possibility of achieving relatively immediate effect in local development, given the nation's status as a city state. In this case, the national and regional innovation systems effectively coincide.

State promotion of the biomedical industry is just one aspect in the restructuring of the economy, from the former services and manufacturing basis towards a truly knowledge-based economy (Wong 2006a, b). The biomedical sector is part of the planned life sciences "pillar" of the national economy, flanked in turn by the further three pillars of the electronics, chemicals and engineering areas. The life sciences pillar as a whole consists of the core areas of pharmaceuticals, biotechnology, medical technology and healthcare services.

Singapore's State biomedical initiatives began in the 1980s, but it was only in 2000 that the biomedical industry was targeted as a core manufacturing area for major investment of national resources (Lee and Tee 2009). The State established three key agencies, charged with the long-term responsibility of creating a distinctive environment for the biomedical industry, from an international point of view.

The most important of these agencies is A*STAR, charged with the "creation and utilisation of intellectual capital, and the training of research manpower in the transition to a knowledge-based economy" (MTI 2006: 9). The agency was formed in 2001, based in part on the former National Science and Technology Board. It is described as "a luminous Constellation, charting the course of Singapore's Science and Technology progress, comprising the Biomedical Research Council (BMRC), the Science and Engineering Research Council (SERC), Exploit Technologies Pte. Ltd. and the A*STAR Graduate Academy" (Wong 2011).

The second agency is the Biomedical Science Group (BMSG), established under the Economic Development Board (EDB) of Singapore. BMSG is responsible for providing support to biomedical firms that set up R&D and manufacturing facilities, headquarters, or other high-value operations in Singapore. The third agency, under the EDB's investment arm, is Bio*One Capital, which manages investment funds for strategic biomedical technology and start-ups. These three government arms thus have different and complementary roles in the establishment of a biomedical science hub in Singapore (Lee and Tee 2009).

In the context of the industry-wide challenges in international pharmaceutical and biotech markets, Singapore has established itself as a highly conducive place to undertake research. The state has cultivated a network of government agencies, hospitals, manufacturing facilities, universities, R&D infrastructure, contract research agencies, and has provided for access to different workforce talents. The overall strategy has led to the development of a highly innovative culture. This, combined with significant government funding (S$16 billion to date, and S$3.7 billion over 2011–2016) and the promotion of public-private partnerships, has stimulated rapid expansion in Singapore's biotech industry. With this expansion has come the creation of many new jobs across the sector. The increase in employment opportunities provides prospects for local pharmaceutical and biotech professionals, as well as for foreign professionals who wish to enter further in the global market by taking up positions in Singapore.

The various policy aspects for the biotech sector came together in concrete form in 2003, with the creation of Biopolis Shared Facilities/Biomedical Sciences Institutes. "Biopolis" is a high-profile technology park, a physical space that brings together key Singapore biomedical research institutes, national governance bodies, and global and local biotech and pharmaceutical companies. The facility is intended both for internal economic development and as a platform to project Singapore's expertise into the region and the world. The concept of the technology park is to project Singapore as the "Biopolis of Asia", in fact to become the premier life sciences hub in a region where several larger States (China, India, Taiwan, South Korea) are also scaling up public investment in regenerative medicine and genomics (Wong 2006a, b; Salter 2007).

Biopolis has three principal objectives. The first is to serve as a focal point for scientific talent. This means attracting top personnel to carry out world-class research, and providing a fertile training ground for undergraduate and graduate students. Biopolis' role as a talent magnet is considered as the most important of all its contributions, and most crucial to growth of the biomedical industry. The second objective is to integrate and synergise the capabilities and resources of A*STAR's research institutes and to encourage cross-disciplinary research. The third is to bridge private and public sector research work by creating an environment that fosters exchange of ideas and close collaboration. The heightened interchanges between industry and research centre scientists will accelerate the translation of new discoveries to marketable products.

In joining with the National University Hospital and the National University of Singapore, Biopolis becomes a third connecting link in the biomedical knowledge channel, between academic biology and clinical applications.

Biopolis is the biomedical component of a larger technopole called "one-north", a 200 ha cluster of new-economy ventures, including local and large multinational ICT and media companies. The name *one-north* refers to Singapore's location slightly north of the equator. The urban design of the technopole features award-winning architectural structures set in a tropical ambience. *One-north* as a whole is a space devoted to creativity, flexibility and intellectual play (Wong and Bunnell 2006). The Biopolis laboratories are housed in buildings with names such as Proteos, Matrix, Centrius, Chromos, Nanos, Helios, Genome, Immunos, Neuros, Synapse and Amnios. The facilities have dedicated spaces for commercial researchers and house five of Singapore's seven biomedical institutes: the BioInformatics Institute, Bioprocessing Technology Institute, Genome Institute of Singapore, Institute of Bioengineering and Nanotechnology and the Institute of Molecular and Cell Biology.

The Singapore Tissue Network, a central tissue banking facility is also located here, along with the newly created Singapore stem cell bank. The global stem cell company ES Cell International and the multinational pharmaceutical company Novartis also have their laboratories and offices here.

Today Singapore has about 4,300 researchers and scientists engaged in in biomedical research. Companies such as Abbott, GSK, Pharmalogicals, Novartis, Merlion, Merck (MSD), S*Bio, Takeda, Inviragen and Cell Research Corp have all localised activities in Biopolis. However the technological park is not limited to pharmaceuticals and biotech. For example there are also a number of important medical device companies, including Medtronics, the world's fourth largest in the sector. The companies noted here, together with the many others active in Biopolis, produce annual outputs of over S$21 in medicines, nutritional products and medical devices for the global market. Among the smaller companies are Illumina, Scigen, Proligo Singapore, Chakra Biotech Pte, Invida Pharmaceuticals, Veredus Laboratories and Innogene Kalbiotech.

Companies like Cytos Biotechnology, bioMérieux, Humalys and Siena Biotech are all active in research collaborations in Biopolis. The combination of big pharmaceutical and biotechnology companies has led to creation of large numbers of life-science jobs, interesting both to the Singaporean and international employment markets. Current growth areas for investment in Singapore include biologics and rare and tropical disease medicine.

The initiatives by the Singapore government have clearly succeeded in attracting international firms to the scientific and technological park, but the National University of Singapore (NUS) has also played an essential role in transforming Biopolis into a true LIS, favouring the birth of local companies and stimulating cooperation between the research and entrepreneurial spheres.

## 5.3 The National University of Singapore in the Research Context

Established in 1905, the NUS is the oldest and largest public university in Singapore, with a total student enrolment of over 28,000, three-quarters of which are undergraduates. NUS is also the nation's most comprehensive university, followed by the other two public universities, Nanyang Technological University and Singapore Management University, both of which are younger than the NUS. Historically, government policies have emphasised public education. As a result there are no large private Singaporean universities, although there are many diploma-level private colleges and distance-learning programs. However since the late 1990s, the government had encouraged leading overseas universities to establish branch campuses and other operational presences in Singapore.

Until 1991 public R&D was concentrated in the higher education sector, particularly in the NUS, as well as in a small number of government agencies (Wong and Singh 2005). NUS has historically played a key role in Singapore's knowledge creation. It is consistently ranked as one of the top universities in Asia and is internationally respected for its high-quality research in science, technology and the humanities, and increasingly for research at the interfaces between these areas. The institution includes 16 schools and faculties, and 23 university-level research institutes and centres, focused on critical issues confronting Asia and the world. The university is also home to three of Singapore's five "Research Centres of Excellence" (RCEs), specialising in quantum technologies, cancer and mechanobiology, and is a partner in a fourth national RCE on environmental life sciences and engineering. According to the Nature Publishing Index (NPI) Asia-Pacific 2012, NUS is Singapore's leading research institution. It is ranked ninth in the Asia-Pacific region and is the first Singapore institution to enter the NPI Global Top 100, ranking in 76th position.

In 2013, the NUS placed 22nd in the Times Higher Education "World Reputation" Rankings. In the 2012/2013 QS world rankings by subject, the NUS emerged second among Asian universities for Engineering and technology, Life sciences and medicine, and Natural sciences, and first for Arts, Humanities and Social sciences. Again in the QS rankings, NUS also placed among the world's top 10 universities in 12 disciplines and in the top 20 for a further nine disciplines. The disciplines concerned range from those in the hard sciences (12 disciplines), to others in Geography, Sociology, Modern languages, Accounting & finance, Economics, and English language

Much of the research at NUS is integrated and multi-disciplinary in nature, with particular emphasis on themes such as integrated sustainability solutions for energy, water and the environment; ageing populations; biomedical sciences and translational medicine; global-Asian studies; finance and risk management; and materials science.

In 2012 the NUS had more than 2,270 research-active faculty. Overall, these researchers produced over 7,200 publications and filed roughly 470 patents and 270 invention disclosures. University departments and faculty obtained close to S$580 million in external research funding. The NUS's overall publication of primary research puts it in the top 1 % in 18 out of 22 categories surveyed under the Thomson Reuters Web of Science. NUS faculty serve as consultants and advisors to more than 50 industry and government bodies. Several leading companies have also chosen to establish research labs and partnerships at the NUS, including Siemens, GE, Zeiss and Agilent.

The NUS Kent Ridge campus, which includes the National University Hospital, is located within Singapore's main research district. The university facilities include the new University Town, a study and teaching centre, in turn co-located with the Campus for Research Excellence and Technological Enterprise (CREATE), which brings together top researchers from around the world. Nearby are Biopolis and Fusionopolis, with the A*STAR research institutes and a broad range of public and private labs. The proximity of all these institutions, enterprises and facilities promotes collaboration and synergy between NUS and the broad R&D community, and creates a fertile environment for education, innovation and enterprise.

The NUS is internationally respected for its high-quality research, and the outputs continue to grow rapidly. In 2012, some of the highlights were:

- close to 2,280 "research-active" faculty;
- over 7,200 papers published in internationally refereed journals;

- close to US $425 million in external research grants received;
- over 2,200 on-going projects;
- over 260 research cooperation agreements signed;
- 469 patents filed and 21 licenses granted;
- 276 invention disclosures.

The NUS is actively involved in international academic and research networks such as the Association of Pacific Rim Universities and International Alliance of Research Universities. One of its best-known cooperation ventures is with MIT. In 2007, the two universities created the Singapore-MIT Alliance for Research and Technology, or SMART Centre. SMART is a research and education centre specialising in five areas: Computational engineering; Calculus and systems biology; Manufacturing systems and technology; Advanced materials for micro and nanosystems; Chemical and pharmaceutical engineering.

As was traditional for public universities developed under the Commonwealth tradition, the NUS historically viewed teaching as its primary function, followed by its research role. The 1980s and 1990s saw an increasing emphasis on research, and in the mid-1990s the NUS added the further step of establishing a technology licensing office. The major impetus towards the third university mission came in the late 1990s, when a new vice-chancellor was appointed with strong support from several senior government ministers. Harvard-trained, with a background in American industry (General Electric) and ivy-league administration, the new vice chancellor significantly accelerated the pace of several existing initiatives, and initiated the explicit shift toward the "entrepreneurial university" model (Wong and Singh 2007, 2012). The new entrepreneurial focus of the National University of Singapore favoured local development in the broader sense and contributed directly to the birth of Biopolis.

### *5.3.1 The Role of the NUS in Development of Biopolis*

The opening of Biopolis in October 2003 effectively laid the cornerstone of Phase One of the Singapore Biomedical Sciences (BMS) initiative, following on several years of preliminary work guided by four people: Philip Yeo, Chairman of the Agency for Science, Technology, and Research (A*STAR), Tan Chorh Chuan, then Dean of Medicine at the National University of Singapore (NUS), and oncologists John Wong and Kong Hwai Loong.

However the BMS initiative also represented a refocusing of a decade of previous national and university efforts, in broader-based investment in technology. This previous experience demonstrated the need for greater focus, particularly in the biotechnology sector, and thus opened the road for the creation of Biopolis. The NUS participated directly in the preliminary phases of the BMS through the participation of Tan Chorh Chuan, dean of the medical faculty. NUS also anticipated and stimulated the formation of Biopolis through its long-standing educational role in the sector, producing the necessary experts. As early as 1983, the university had modified its teaching program to focus more closely on biology, and had introduced microbiology as a separate discipline instead of considering it as dependent on biology. As a result, the class hours in microbiology for second and third year students were more than doubled. However changes to the undergraduate curriculum only partly addressed the rising needs in biotechnology, as an emerging, research-intensive field. In fact one year later, a state administrator (Chua Sia Eng, Commissioner of the Parks and Recreation Department) provided a valedictory address for NUS science and pharmacy graduates in which he insisted that the graduates go on to join R&D programs in biotechnology so that Singapore could develop a strong base to tap the vast potential of this science. His call to science and pharmacy graduates to join postgraduate courses was intended to drive home the urgency for qualified biotechnology experts, but in truth seems to have preceded any substantial opening of genuine biotech-centred postgraduate opportunities. This was one of the motivations given for the setting up of the Institute of Molecular and Cell Biology in early 1985. According to NUS's vice-chancellor at the time, the new institute was intended not only to train a pool of competent manpower to service the biotechnology industry, but also offer true research careers to NUS graduates in chemistry and microbiology.

Thus in the early stages preceding Biopolis, the NUS reoriented its traditional activities in education and research specifically towards biology and biotechnology, creating the cultural substrate that would generally favour the birth of a science hub. The National University of Singapore also participated actively in the development of the sector as a whole, collaborating with business, and focusing its research and education in specific areas.

#### 5.3.1.1 Start-up Development

Relative to other universities in the global context, the NUS also moved early to develop its third mission. In 1988 it created the National Entrepreneurship Centre, which in 2001 became part of the NUS Enterprise Start-Up Runway (NUS Enterprise). Both organisations have had the mission of nurturing entrepreneurial learning and venture creation in the NUS community. The NUS also provides advisory services for students to assist them in identifying the paths that will develop the necessary knowledge, skills and contacts for their entrepreneurial initiatives. The NUS Overseas College offers potential entrepreneurs the possibility to broaden their contacts through continuous cooperation and learning in the field, working alongside actors who have created successful start-ups both in Singapore and in other nations. In this way, the NUS offers its student entrepreneurs the possibility of developing not only specialised scientific knowledge, but also the knowledge of business fundamentals necessary for development of their own activities. The NUS has also created Start-Up@Singapore (S@S), an instrument for stimulation and participation in development of territorial start-ups. Start-Up@

Singapore stimulates development of innovative ideas and encourages healthy competition between potential entrepreneurs by organising “global business plan” competitions that offer the winners financing to continue with their innovative activity. As of 2012, the S@S competition was in its 14th edition, representing a total of more than 3,500 teams and 10,000 individual participants, and had helped to spin off more than 90 start-ups. These have included award-winning businesses such as tenCube, FriarTuck, PerceptiveI, World Indigo, PurpleAce and Quantagen. S@S is in fact more than a business planning competition, having evolved into a program that leads students into experiential learning about entrepreneurship, engaging them in the early stages of the actual start-up process: writing a plan, building a team, learning networking skills, pitching to potential investors and getting mentor feedback.

The NUS has also developed more complex actions for development of entrepreneurialism, particularly in the form of NUS Enterprise Start-Up Runway, which is a true enterprise incubator. NUS Enterprise follows the growth process of the new firms, offering tailored services for the different stages of development: pre-incubation, incubation and growth.

In the pre-incubation stage, NUS Enterprise can help start-ups with market validation, user testing and consumer feedback, in order to achieve an optimal product-market fit. This ensures that the potential entrepreneur can build his or her product to cater to their target market, better positioning the new business for take-off. When the business idea is validated and the start-up moves toward the incubation stage, NUS Enterprise offers a wide range of specifically focused support services such as mentorship, talent recruitment and assistance with strategic reviews. It also offers start-ups their own operating spaces, situated in several dedicated infrastructure facilities: NEI@blk71; NEI@pgp and NEI@faculty-of-engineering. In this stage the NUS also provides guided access to its network of relationships, thus opening possibilities for the start-ups to enter markets such as the USA and China, through specific business hubs in territories such as Suzhou, Beijing and Silicon Valley. Start-ups can also leverage NUS incubation services such as mentoring, networking sessions, hot-desking facilities, and overseas grant support, to kick start new expansion stages.

The university also accompanies the start-up firm in the stage of gathering capital investment, supporting relationships with venture capitalists and “angel investors” who have interests in the start-up’s areas of activity. NUS also assists start-ups to access grants from the relevant Singapore statutory boards for encouragement of entrepreneurship. The university itself offers a series of grant programs: the Innovation and Entrepreneurship Practicum Grant, Action community for entrepreneurship, Spring Singapore Enabling Enterprise, the First Leap Overseas Grant and the Youth Social Entrepreneurship Programme For Start-Ups.

The NUS’s policies and programs for support of entrepreneurial activity have enabled the university to spin off rough 250 start-ups. Many of these have become successful firms in the biology and biotech fields, and thus contribute to the core structure of Biopolis.

**Examples of NUS biotech spin-offs**

***Lynk Biotechnologies***

Lynk Biotechnologies is an NUS spin-off incorporated in 2000, for the application of revolutionary technologies in design and development of innovative products, services and applications, for improved quality of life and well-being for all. One of the specificities of Lynk is its scientific planning approach, using SM@RT™ Drug Design, Receptomics™ and PharmaGlue™ technologies, as well as specific knowledge in proteomics. With this approach, Lynk has accelerated and improved efficiencies in the drug discovery process, shortening the lead stages from years to months. One of Lynk's first products was Biolyn™ shampoo, a hair care product based on natural materials, with active ingredients formulated using bio-transformed phyto-therapeutic agents, vitamins and minerals. The product maintains healthy hair and prevents hair loss and thinning. Lynk Biotechnologies is the brainchild of Lee Chee Wee, who developed the technological innovations for the founding of Lynk through his role as a research professor at NUS. Lynk has successfully commercialised these technologies and made them available to the public.

***AyoxxA Biosystems***

AyoxxA began life in 2008 as a research project to apply parallel biomolecular microarray systems for simultaneous detection of multiple protein biomarkers, in a single step. In the company's words, the innovation represents "Ferrari-level horsepower" in protein analysis, allowing hundreds of diseases, from infectious types to cancer, to be detected from a single blood sample. The new technology is a significant improvement over previous diagnostic technologies, which can detect only a handful of diseases in a single test run. The end results is faster diagnosis, meaning faster treatment for the patient.

The research team, led by Dieter Trau of the faculty of engineering, wanted to develop a product permitting cost-effective manufacturing. Their innovative work led to the incorporation of AyoxxA in 2010, with Professor Trau holding the position of Chief Scientific Officer and another team member, Dr. Andreas Schmidt, serving as CEO. The spin-off company is developing NUS's proprietary technology as a platform to allow simultaneous, precise and cost-effective protein analysis from minute samples.

***Clearbridge BioMedics, NanoMedics and VitalSigns***

Johnson Chen is a "serial entrepreneur", having launched three healthcare start-ups based on technologies licensed from the NUS. The series of company set-ups started when Mr. Chen met up with Lim Chwee Teck, a friend from past years at Cambridge, then a professor in the NUS departments of mechanical engineering and bioengineering, who was developing a technology that trapped tumour cells circulating in blood. Realising the commercial potential of the technology, the two friends spun it off as Clearbridge BioMedics in 2009. They translated the lab prototype into a commercial product and launched it as the ClearCell™ system, which detects, isolates and retrieves intact circulating tumour cells. As of 2011, ClearCell™ was involved in global marketing to the research community, while the company turned its focus to developing a new generation of the system for clinical applications.

Recognising that the NUS held further technologies with commercial interest, Mr. Chen then licensed another of Prof Lim's innovations: a bioresorbable and biocompatible nanofibre with good mechanical, physical and chemical properties. Clearbridge NanoMedics was set up to commercialise the technology for cosmetic and injury management applications. NUS then also introduced Johnson to an ultra-low powered electrocardiogram (ECG) chip, invented by Lian Yong, a professor of electrical and computer engineering. This let to establishment of Clearbridge VitalSigns, which is developing the NUS technology as CardioLeaf®, a fully-integrated 3-Lead ECG monitor, targeting both medical and fitness applications.

*Source* NUS Enterprise organisational website

#### 5.3.1.2 Patents and Licensing

As of 2013 the National University of Singapore had registered over 3,500 patents and issued 250 technology licenses. Searches in the World International Patent Office records show that the university holds 307 patents in the field of Medical and veterinary science and 207 in Biochemistry.

**Major NUS license agreements under Biotech**

***Factor C***

"Factor C" is a technology first developed in NUS labs that is now being applied globally in the development of safer injectable medications, such as vaccines and intravenous drugs. The same technology is also saving the lives of the horseshoe crab, an endangered species in many of its global habitats. The husband-wife team of professors Ho Bow and Ding Jeak Ling, respectively from the departments of microbiology and biological sciences, developed the original research, which has become one of the NUS's most successfully commercialised technologies.

Pharmaceutical and medical device companies routinely use horseshoe-crab blood to ensure medication and equipment are free from bacterial endotoxins. This is possible due to an enzyme in the crab's blood, Factor C, which triggers the clotting process when in contact with bacterial endotoxins.

However collecting horseshoe crab blood is a time-consuming and costly process. Professors Ding and Ho developed a method for laboratory production of Factor C, using a recombinant DNA-based system to clone the original enzyme. Not only does the clone succeed in reacting with endotoxins, and at very low concentrations, it also results as more stable and chemically-consistent than the natural form. With the support of the NUS Industry Liaison Office, this ground-breaking technology was licensed for production and introduced for global use. Lonza, the international life-sciences leader, has since incorporated the NUS technology into its endotoxin detection kits and online endotoxin monitoring systems. Another US-based company, BioDtech Inc., has applied related technologies in development of products for removal of bacterial endotoxins from pharmaceuticals and fluids.

***Rapid-assay diagnostic kits for detection of parasitic diseases***
Malaria and dengue fever are mosquito-borne tropical diseases that affect millions of people, while malaria kills about three million people per year. Rapid, accurate diagnosis is paramount for timely emergency response, treatment and containment. The standard test for the malarial *plasmodium* parasite is time-consuming, laborious, and can produce false negatives. Testing for dengue fever takes up to 8 days and can also deliver inaccurate results. However a medical-diagnostics company, using breakthrough molecular technology from the NUS, has developed rapid-assay test kits that detects the parasites in a matter of hours.

NUS researchers Ursula Kara, Robert Ting, Jill Tham, James Nelson and Theresa Tan discovered and patented the unique nucleic acid diagnostic primers for the parasitic vectors over a ten-year period, finally announcing the technology in 1998. A primer is a short strand of DNA/RNA that serves in the formation of longer strands. Using a single drop of blood, the highly sensitive polymerase chain-reaction technology can distinguish between different *plasmodium* species within 3 h. The dengue fever kit can detect the virus within three to 5 days after it first appears in the bloodstream, compared to the usual 8 days for standard immunodiagnostic methods. Detection enables earlier medical attention, which can be critical for preventing serious complications such as dengue haemorrhagic fever or shock syndrome. The NUS has licensed the technology to Veredus Laboratories, which is manufacturing and selling several different diagnostic kits. Singapore's National University Hospital has used the dengue fever kit for more than 3 years as a routine diagnostic tool. In addition, Veredus has produced the world's first validated commercial avian flu diagnostic kit, which cuts the time for accurate detection of the H5N1 virus from 7 days to as little as two. As of 2013, the company was also developing kits for encephalitis, Japanese encephalitis, yellow fever, chicken pox and SARS.

***Anti-restenosis drug***

Restenosis is a recurring occurrence of narrowing of the arteries. A new drug with a novel mechanism for preventing the condition was first discovered by Sim Meng Kwoon, an assistant professor in the NUS department of pharmacology. The drug des-aspartate-angiotensin I (DAA-I) acts on a receptor coupled to a specific prostaglandin pathway to suppress clot formation. The highly specific pathway limits any negative secondary effects. Currently, metal stents that are inserted into patients' blood vessels after angioplasty are coated with a bio-degradable polymer impregnated with drugs to prevent restenosis. However the existing stent drugs like Sirolimus and Paclitaxel are nonspecific immunosuppressant and anti-cancer drugs, which can also affect other cells.

In commercialising the technology, NUS has entered into a licensing agreement with Medlogics Device Corporation, a US start-up company founded by a group of professionals with experience in medical devices and stents. The agreement was the first ever case where a Singapore drug innovation will enter global commercialised through the United States. It is also the first ever case where a specific new anti-restenosis drug is being incorporated into an equally new Medlogics technology. Medlogics has a proprietary coating technology that enables the drugs to be applied directly to the stent metal, avoiding the use of biodegradable polymers. The technology reduces the cost of making the drug-coated stents, ensures consistent release of drugs, and reduces the inflammation caused by the polymers. Medlogics selected DAA-I as the first drug for application with the new technology, out of a short list of seven final candidates.

Similar to the other cases cited here, the NUS Industry Liaison Office played a key role in flanking Dr. Sim during the development and negotiation of the exclusive license agreement between the university and Medlogics.

*Source* NUS Industrial Liaison Office

#### 5.3.1.3 University-Industry Collaborations

The National University of Singapore is party to numerous agreements with major international biotech companies, such as Bayer Healthcare, Merck and GlaxoSmithKline. The trend towards these agreements is increasing, with 35 % growth between 2011 and 2013.

The collaborations between the NUS and private firms are of different kinds and cover a wide range of activities. In some cases they are true cooperative research projects drawing in widespread research teams of top professionals, such as in the case of current work towards a cure for diabetes using adult stem cells.

***Stem cell research project***
This research project, for the creation of insulin-secreting cells from the patient's own adult stem cells, unites a group of global leaders in basic research, clinical applications, industry collaboration and surgery. The main research focus is on the use of adipose tissue, but other sources of adult stem cells may also be investigated. The research team includes Bernat Soria, director and professor in physiology for the Alicante Institute of Bioengineering (Spain) presently an adjunct professor with the NUS department of surgery, and Sir Roy Calne, Professor of Surgery Emeritus at Cambridge. Dr. Calne was knighted in 1996 for his pioneering work in organ transplantation. The team also includes John Isaac, acting head and education director for the NUS department of surgery, head of the hepato-biliary pancreatic surgery division, and senior consultant to the NUS liver transplantation service. Finally, the team also includes Dr. Susan Lim, founder, chairman and CEO of Stemcell Technologies Pte. Ltd., an accomplished general surgeon in active surgical practice, known for her pioneering work in liver transplants and for performing the first transplants in the Asian region.

*Source* NUS website

In other cases the collaborations arise from funding agreements and grants by private firms, for research towards the solution of specific problems. For the NUS, there are numerous examples of this type of arrangement in the pharmaceutical and biotech sector.

**Major NUS-firm project collaborations**

*Bayer HealthCare Grants4Leads*
Bayer HealthCare's research and development focuses on identifying and developing new active substances for treating diseases with high unmet medical needs. The NUS collaboration initiative seeks to identify and develop novel small-molecule leads, particularly in the fields of oncology, cardiology, haematology and gynaecology therapies.

*Bayer HealthCare Grants4Targets*
Bayer HealthCare provides grants to the NUS for the exploration of attractive, novel drug targets in the fields of oncology, gynaecology, cardiology, and haematology, with the intent to accelerate the transition from basic research towards promising new treatment options.

*Eli Lily Open Innovation Drug Discovery*
Eli Lilly has established a program to provide NUS academic researchers access to proprietary, disease-relevant phenotypic assays (PD2) and sophisticated in vitro target-based assays (TargetD2) for the screening of small molecules targeting cancer, neurological disorders, and metabolic diseases.

*GlaxoSmithKline Academic Centre of Excellence Singapore*
The Academic Centre of Excellence is a virtual research network for projects of mutual interest to GlaxoSmithKline and Singapore academic scientists, as well as for development of partnerships to accelerate translational research and progress toward shared goal in providing accessibility to new medicines.

*LIMR Chemical Genomics Centre*
The LIMR Chemical Genomics Centre connects university and pharmaceutical scientists in a totally new public-private translational-research framework for testing the "druggability" of innovative cell-signalling targets, called Double-Blinded Drug Discovery® (DBD2).

*Merck Investigator Studies Programme*
This Merck-NUS joint program is designed to advance science and improve patient care by supporting the provision of drugs and vaccines, through total or partial funding of high-quality research that is initiated, designed, implemented and sponsored by external investigators.

*Source* NUS Annual Report

In other cases the university-firm relationships take the form of private financing for entire research centre programmes. In 2012–2013, the NUS received roughly 184 million US$ in this manner, 31 % of which was directed to the Yong Loo Lin School of Medicine, 12 % to the Duke-NUS Graduate Medical School and 8 % to the Faculty of Science.

#### 5.3.1.4 Education and Research

As noted previously, the NUS maintains a long tradition of education and research in the fields of biology, medicine and biotechnology, which has produced many of the qualified personnel involved in the birth and growth of Biopolis. Currently the NUS has 16 faculties and schools distributed over three campuses in the Singapore city-state: Kent Ridge, Bukit Timah and Outram. In terms of the growth of Biopolis, the most important of these are the undergraduate schools in medicine and science and the advanced-degree programs in medicine and science, including those offered by the Duke-NUS Graduate Medical School and the Institute of Systems Science, which are directly linked to Biopolis. In 2013 alone, the various faculties produced 1,637 graduates and 1,345 biological and medical sciences specialists.

In addition to carrying out its education function, the NUS has 23 research centres, including the Life Sciences Institute and the Singapore Institute for Neurotechnologies, both of which are specifically linked to Biopolis. The NUS also has four global-level "centres of excellence", two of which are at the core of the Biopolis cluster: the Cancer Institute of Singapore and the Mechanobiology Institute of Singapore.

**Biotech "centres of excellence"**

***Cancer Science Institute of Singapore***

The Cancer Science Institute was launched in October 2008, with the aim of positioning Singapore as a global leader in biomedical sciences. Its mission is to conduct a multifaceted and coordinated approach to cancer research, extending from basic cancer studies to experimental therapeutics. CSI Singapore is a state-of-the-art university research institute affiliated with and hosted by the National University of Singapore. The institute was founded on the basis of a $172 million "Research Centre of Excellence" grant, one of only five allocated by the Singapore National Research Foundation and the Ministry of Education.

The institute is an anchor for research expertise in two broad programs: Cancer biology and stem cells, and Experimental therapeutics. These are platforms for CSI Singapore's approaches to key research themes in leukaemia and cancer diseases of the liver and lungs, which are endemic in Asian populations. In addition, the institute has also recently started a working group on breast cancer, looking at Asian phenotypes. CSI Singapore is housed on three floors of the Centre for Translational Medicine, within the Yong Loo Lin School of Medicine. The location is opposite the thousand-bed National University Hospital and close to a main subway line providing a link to the A*Star research institutes at Biopolis, Duke-NUS Graduate Medical School and a second major hospital, the Singapore General. Core facilities and support technologies include the Centre for Translational Research and Diagnostics, a fluorescence-activated cell sorting facility, the Bioinformatics Core, a leukaemia cell bank, a transgenic and gene targeting facility and the Xenograft Cancer Models Facility. A number of the researchers working with CSI Singapore also hold positions at renowned international institutions such as the Beth Israel Deaconess Medical Center, Harvard Medical School, Brigham and Women's Hospital of Boston, Sweden's Karolinska Institute, the École Normale Supérieure and Johns Hopkins University.

***Mechanobiology Institute of Singapore***

The Mechanobiology Institute was founded in 2009, under joint funding from the National Research Foundation and the Ministry of Education. The aim of the institute is both to advance the discipline and benefit the Singapore population. MBI's primary research focus is the identification, measurement and description of the forces for motility and morphogenesis at the molecular, cellular and tissue level. Toward that goal, the institute is working to create a common international standard for defining these steps by developing powerful new computational models, experimental reagents, and tools for studying diseases of cells and tissues. These basic discoveries are then transferred to both the clinic and the classroom, as a basis and support for scientific progress in the field of Mechanobiology. Towards these goals, the MBI has developed memoranda of understanding with a range of organisations, promoting cross-talk and active collaboration between MBI and partner institutions such as France's Centre National de la Récherche Scientifique (CNRS), the Indian Institute of Science Education and Research, the National Centre for Biological Sciences in Bangalore (India), and the Waseda University in Japan. The focal areas for MBI research area: (i) stem cells and tissue engineering, (ii) development and cancer, (iii) microbes and pathogenesis.

*Source* NUS website

In terms of bibliographic indicators of research production, the NUS produces roughly 7,500 published papers per year and is ranked by Thomson Reuters Web of Science in the top 1 % of global institutions for 18 out of 22 categories surveyed. A search of Scopus Database shows that NUS researchers and affiliated research centres have produced 2,172 papers in the fields of medical sciences and biology.

In conclusion, we identify that the NUS serves as an important driver in the development of the Biopolis LIS, through:

- education and training of specialised personnel;
- high-profile research in the fields of biology and medicine;
- cooperation with local and foreign firms;
- creation of a system of innovative firms.

These NUS initiatives support the growth of the system by stimulating the direct and indirect creation of a network of local firms alongside the multinational firms present on the territory. The NUS initiatives favour the university-firm relations, and produce the binding effects that permit the system to transform into a true LIS.

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