Hong Kong Innovation Project

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Biotechnology in Hong Kong:

Prospects and Challenges

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1. BIOTECHNOLOGY AND UNCERTAINTY

The global biotechnology revolution purportedly began during the late 1970s, when the biological "heuristic" in health care technology was expected to both rival and ultimately prove superior to existing chemistry-based approaches to health and health care. Rooted in new discoveries in genetics and the promise of genetic engineering, and fuelled by a flurry of government research support, venture capital and increasingly entrepreneurial universities, biotechnology was expected to revolutionize how human therapeutics were developed, screened, and delivered. Biotechnological tools were expected to rationalize drug development. They would lead to new diagnostic tools. Recombinant DNA techniques would allow scientists to re-engineer cells to produce new and "smarter" proteins, the basis for a new generation of therapeutics. The introduction of biotech would in effect re-structure global human health care industry, as pharmaceutical firms increasingly turned to smaller, specialized and more cutting-edge biotech firms for new screening techniques and drug candidates. Biotechnology was imagined as an enabling technology, a platform technology and a source of knowledge for advancing human health care. Simply put, the possibilities for applying biotechnology to health and health care seemed endless.

As with all revolutionary moments, however, the growth of biotechnology and the future development of a global biotech industry were inherently uncertain. As a science-based industry, it was unclear whether the science of biotechnology would actually result in more efficient and more effective health care interventions: will it work? Venture capital's enthusiasm notwithstanding, there was tremendous uncertainty surrounding

biotech's economic viability as well, especially seeing as new discoveries at the time were still considerably far-from-market: will it have value (Pisano, 2006)?

Between 1998 and 2003, $85 billion US was invested by the private sector in the US. Nearly $30 billion the US government is expended each year for upstream life sciences research (Casper, 2007). Yet, despite such large-scale investments, the global (and US) biotechnology sector, as an industry, has fallen far short of initial, albeit uncertain, expectations. Recent data from the 2000s, for instance, show that biotechnological techniques have not in fact resulted in more effective drug development processes. Biopharmaceuticals have not revolutionized the field of human therapeutics nor have they radically altered the business model of the conventional pharmaceutical industry. And economically, the global biotechnology industry has not fared particularly well (Hopkins et al. 2007). While there have been some – a small few – major success cases, the industry as a whole has lost billions of dollars ($40 billion according to a 2004 *Wall Street Journal* report). Two firms, US-based Amgen and Genentech, account for nearly 50% of all positive cash flow in the biotech sector. As of 2003, there were nearly 1500 biotechnology firms in the US alone, though less than 200 biotech products had actually made it to market (Pfeffer, 2004: 104).

It was against this uncertain backdrop that Hong Kong entered into the biotechnology sector during the early 1990s. Driven by the government's new industrial upgrading initiatives, and by leveraging Hong Kong's entrepreneurial spirit and transparent corporate regulatory environment, Hong Kong looked to make significant inroads into life sciences industry (Berger and Lester, 1997). Government commitment was high, by Hong Kong standards. Public funding for biotechnology R&D, allocated

through the government's industry support fund (ISF), increased from just 7% in 1994/1995 of the fund's total investment to over 40% in 1997/1998 (Tsang and Lo, 1998: 151). The Hong Kong Institute of Biotechnology (HKIB) was founded during the late 1980s, and an on-site incubation center for start-up firms was formed in 1996. The Biotechnology Research Institute (BRI) was established at the Hong Kong University of Science and Technology (HKUST) in 1990. In 2001, the Hong Kong Jockey Club Institute of Chinese Medicine was formed. The Chief Executive Tung Chee-Hwa announced during the late 1990s the government's ten-year blueprint for the modernization of Hong Kong's traditional Chinese medicine (TCM) industry. Simply put, a sector had been put into motion.

Though significant efforts were made to launch a domestic biotech industry, a sense of uncertainty regarding biotechnology's commercial prospects nonetheless quickly prevailed in Hong Kong. Reality set in. Technological and economic uncertainty in the global biotech sector is exacerbated by the fact that Hong Kong is a late entrant into the life sciences sector. Hong Kong is a laggard in technological innovation more generally. Research and development (R&D) spending amounted to just 0.38% of GDP in 1995 and had increased to only 0.79% in 2005. Meanwhile, other East Asian competitors such as Singapore and Taiwan spend 2.5% of GDP for R&D; Korea leads the way among late developing economies in the region, expending just under 3% in 2005. Moreover, in Hong Kong, government resources account for a relatively large portion of R&D expenditures. Industry makes up approximately 30% of the total R&D spending (Baark, 2005: 8), whereas in most other advanced economies firms account for between two-thirds and three-quarters of the national R&D bill. In the field of biotech specifically, the

number of firms in Hong Kong is quite small. The government suggests that there are between 250 to 300 "biotechnology-related companies," though this figure represents a rather expansive definition of biotechnology.[1] Industry insiders estimate that Hong Kong is actually home to less than 50 "true" biotech firms. Indeed, because of reasons related to scale, or lack thereof in Hong Kong, biotechnology's and bio-industry's uncertainties are intensely magnified. With a population of just 7 million people, Hong Kong's efforts to become a cutting-edge technology innovator are continually frustrated due to a relatively small talent pool, fewer resources in general, and the absence of a critical mass of firms in the life sciences sector. This paper illuminates ways in which Hong Kong may begin to overcome some of these challenges.

2. BIOTECHNOLOGY IN HONG KONG

Despite such uncertainty – after all, technological and economic uncertainty surrounding the biotechnology sector is a global concern – Hong Kong has made significant strides in building up its R&D capacity in the life sciences. In the biotechnology field specifically, almost all R&D funding comes from government coffers. As I indicated above, the ISF allocated over 40% of its funds to biotechnology projects during the mid to late 1990s. Prior to 1998, the applied research fund (ARF), the government's investment fund earmarked for industry, allocated $16.6 million HK of its total $97.3 million HK, or 17%, into biotechnology firms, of which one, Hong Kong Transgenic Ltd., was in fact an equity investment rather than a loan. By 2005, the

[1] The Innovation and Technology Commission (ITC) defines "biotechnology-related companies" to comprise "mainly healthcare-related companies with business in pharmaceuticals, medicinal or healthcare products of traditional Chinese medicine origin, and medical devices and diagnostics." The ITC definition of a biotechnology company does not stipulate that the firm be engaged in R&D.

government's Industrial Technology Fund (ITF), which had by then subsumed the ISF, had supported 57 biotechnology projects, accounting for 9.2% of the total number of ITF-sponsored R&D projects. These projects were funded about $161 million HK or nearly 10% of all ITF funds. Combined with R&D resources allocated for traditional Chinese medicine (TCM), life sciences-related industries accounted for over 13% total ITF disbursements through 2005.

The government's appetite for the uncertainties of biotechnology industry began to wane by the early to mid 2000s. After consultations with stakeholders in industry, government and the research community, the Innovation and Technology Commission (ITC), which was established by the government in 2000, unveiled in 2004 its report on a *New Strategy of Innovation and Technology Development*. The ITC identified 13 specific technology focus areas in the report. Biotechnology was not included. The ITC also introduced a new three-tiered funding system for R&D. Regular funds were to be provided for Tier 1 and 2 technologies. Biotech, however, was re-classified a Tier 3 technology, which meant that while it remained a government priority, funding for biotech was to be on an "exceptional basis" (Wan, 2005: 919). Five new R&D centers were established in 2006 to promote applied R&D. Again, biotechnology was excluded. The proportion of ITF-sponsored projects (counted as number of projects) in biotech continued to hover at around 9% through 2008. However, while the absolute amount of R&D funds for biotech remained at pre-2005 levels, the proportion of R&D funds (counted in dollars) granted to biotech projects decreased from almost 10% of all ITF funds in 2005 to just 6.8% in 2008. Moreover, the ARF, which had invested about 17% of its funds to biotech firms prior to 1998, ceased to make any new investments after

2004; during the intervening years 1998 to 2004, the ARF invested in only one additional biotechnology firm, Plasmagene Bioscience Ltd., an investment which amounted to $11.7 million HK or less than 3% of the ARF's investment portfolio between 1998 and 2004 (ITC website).

In addition to new injections of R&D funds designated for life sciences research during the 1990s and into the 2000s, significant efforts were made to create new dedicated research institutions in order to strengthen Hong Kong's R&D capacity in biotechnology. With an endowment of $300 million HK from the Hong Kong Jockey Club, the Hong Kong Institute of Biotechnology (HKIB) was established in 1988. Envisioned initially to be a center of applied biotech R&D, the HKIB was re-fashioned during the mid 1990s into an incubator for start-up biotechnology firms. The Biotechnology Research Institute (BRI) was established at the HKUST in 1990 with an endowment of $130 million HK, again from the Hong Kong Jockey Club. The Genome Center was created in 2002 as part of Hong Kong University's Li Ka Shing Medical School with an initial budget of $120 million HK. The Hong Kong Jockey Club Institute of Chinese Medicine (HKJCICM) was founded in 2001 as a subsidiary of the Applied Science and Technology Research Institute (ASTRI) with a $500 million HK donation from the Jockey Club. Functioning as both an R&D facility and a research funding agency, the HKJCICM endeavored to become Hong Kong's premier center for the "modernization" of the TCM sector. Parallel efforts were made at the Chinese University of Hong Kong (CUHK) where in 2000 its longstanding Chinese Medicinal Material Research Center was expanded to form the CUHK Institute of Chinese Medicine (ICM).

Eclipsing all these efforts to institutionally broaden Hong Kong's R&D base in the life sciences is the recent construction of the Hong Kong Science Park (HKSP), located adjacent to the CUHK, near the Sha Tin industrial park and under an hour's distance from Shenzen, Guangdong province. Phase 2 of the Park, completed in 2008, includes two buildings dedicated to biotech R&D. A total of fourteen floors of laboratory and office space have been made available to local and foreign life sciences firms. In order to attract start-up firms, the Science Park authorities have kitted an entire floor (with more in the plan as needed) in the biotech R&D buildings with basic laboratory benches and communal facilities. The Park also features an "enhanced" biotech incubation program for start-up enterprises, providing pre-venture firms with not only lab space and a biotech cluster, but also support for important services in IP management, investor relations and legal advice. The HKSP has recruited a new leadership team comprising Hong Kong returnees who bring with them bio-industry experience from abroad.

There is talent in Hong Kong. The consensus among local and foreign analysts of the life sciences sector is that Hong Kong's upstream research capacity is quite strong and internationally competitive. Unlike elsewhere (East Asia, Europe or North America), the majority of R&D funds in Hong Kong is allocated for research conducted within universities. Higher education R&D accounts for two-thirds of all R&D spending in Hong Kong. Post-secondary student enrollment in the sciences, specifically in the life and medical sciences, has been consistent and very high (HKSTP biotechnology initiative internal report, 2004). The major universities have also been transformed into high performing R&D centers. Not surprisingly, upstream research output among Hong

Kong's tertiary institutions is impressive. Erik Baark (2005: 10) shows that science and engineering faculty at Hong Kong universities account for the majority of all research publications (the remainder being in the humanities and social sciences). In 2001/2002, of the total 26,996 research publications from Hong Kong's eight leading universities, 15,602 or 58% were from science and engineering faculty. Of that, biology and medicine accounted for the largest share with 6,529 publications, more than the engineering field. In terms of quality of research, studies have shown that beginning in the late 1990s, the impact factor for Hong Kong's international academic publications in the life sciences field, while falling short of leaders such as the UK, nonetheless rank among several Northern European countries. The vast majority of these high impact publications have been concentrated in Hong Kong's two medical universities, the HKU and CUHK, as well as the HKUST (HKSTP biotechnology initiative internal report, 2004).

Recognizing that a solid basis in upstream research can be utilized further downstream, technology licensing and transfer offices were established inside research-oriented universities. Two of the largest and most active, in terms of disclosures and patents, are located at the HKU and CUHK. HKU's technology transfer office and its business development arm, Versitech, were formed in 1998 to capture commercial value from upstream research conducted at the university. Initially focused on the areas of information technology and engineering, Versitech turned to biotechnology during the early 2000s. According to Senior Manager Andrew Chan, over 80% of the patents managed at present by Versitech are in the life sciences field, even though most of its licensing and business activities continue to be in either IT or engineering.

he CUHK's Technology Licensing Office was also established in 1998, and similar to HKU's Versitech, the majority of disclosures and patenting activity in the CUHK TLO is in the area of biotechnology. The TLO has been very active in technology transfer. For instance, in the fiscal year 2006/2007, of the 37 disclosures (not necessarily in the life sciences) made to the TLO, 29 or 78% of them resulted in a filed US patent application. That same year, 19 licensing deals were finalized, equaling 66% of the number of patent applications filed. Licensing income earned in 2006/2007 by the TLO neared $1.2 million US, or roughly 2.6% of total research expenditures. To put that output into comparative perspective, MIT's income to research expenditure ratio in 2006 was 3.6% while Stanford's was 8.8%. Both MIT and Stanford are among the world's leaders in transferring technology. The average income to expenditure ratio, calculated from a survey of 155 universities, was just 0.9%, considerably lower than at the CUHK's TLO. In fact, between 1992 and 2008, the CUHK received a total of 288 disclosures, of which 203 or 70% resulted in patenting activity. Of those patented disclosures, 87 or 43% was transferred to industry in either a licensing deal or another mode of technology transfer (AUTM Licensing Activity Survey, FY2006).

Clearly, Hong Kong's efforts to enter into the biotechnology sector have been significant. Government funding in Hong Kong, while miniscule when compared to the levels of public investment in other advanced countries, has been disproportionately large in the life sciences. Institution building has been a priority. Nurturing upstream basic science research capacity, especially within universities, has also been a priority, reflected in Hong Kong's competitive output. At the same time, efforts have been made to translate upstream knowledge into commercially viable outputs. The "pieces" of a

biotech industry have begun to emerge in Hong Kong. Commercializing biotechnology, however, has lagged. The prospects of creating a commercially viable bio-industry in Hong Kong remain terribly uncertain.

3. THE CHINA PULL

Under conditions of technological and economic uncertainty, it is difficult to determine where best to allocate scarce resources, a conundrum that is all the more pressing in tiny Hong Kong where resources are very scarce. Resources, be they public or private, have to be allocated *somewhere*. Niches have to be discovered *somewhere*. But where? Though the Hong Kong government eschews vehemently the notion that the state ought to (or even can) "pick winners," Hong Kong's proximity and political-economic integration into China mean that allocative decisions have essentially been made for Hong Kong. China's pull is simply irresistible. And that strategy has been formulated, in part, by Hong Kong's economic policymakers. China offers "low hanging fruit" for would-be bio-entrepreneurs based in Hong Kong. Hong Kong can take advantage of its regional economy.

Hong Kong's economic integration with China and the pull of Chinese economic development more generally is inevitable given its close proximity to China and the official handover of Hong Kong back to the mainland in 1997. The Closer Economic Partnership Agreement (CEPA), signed by the central Chinese government and the HK SAR in 2003 and implemented the following year, is hastening the opening up of economic activity, especially trade, across the China-Hong Kong border. The Greater Pearl River Delta (PRD) region is the basis of Hong Kong's economic future and its

ambitions for industrial upgrading. With respect to the life sciences sector specifically, the HK SAR "is poised to play a significant role in the development of biotechnology industry in China" (Chang, 1999). During the early 2000s, about two-thirds of Hong Kong's pharmaceutical and health care related exports went to China (Nature, 2001: 5). Moreover, Hong Kong, given its global reputation as a services and logistics hub in Asia, is positioned to play a "supporting role" for biotech development in the mainland (Frost and Sullivan, 2002). Its advanced health care infrastructure and world-class universities make Hong Kong an ideal place to "bridge" global life sciences industries with China (Wong, 2006: 221-2). Indeed, due to Hong Kong's small local market and other scale-related bottlenecks (such as the small local pool of R&D talent), Hong Kong needs China as much as China needs Hong Kong if the former British colony is to eventually realize its ambitions in the knowledge economy.

Traditional Chinese Medicine

In the near term, Hong Kong's nascent life sciences industry looks to gain a significant foothold in the traditional Chinese medicine (TCM) market, especially the huge Chinese domestic market. To the extent that Hong Kong enjoys any comparative advantage in the human health care industry sector, it is in TCM manufacturing, a point emphasized in the 1997 *Made By Hong Kong* study (Berger and Lester, 1997). Ever since the TCM sector was highlighted by the HK SAR government during the late 1990s to be a key priority, R&D resources, both public and private, have been allocated for the "modernization" of the TCM industry. While there is no standard definition of TCM modernization, most understand the process to be rooted in the principles of evidence-

based research and the integration of TCMs into standard pharmacopeias. That is to say, most efforts in Hong Kong to modernize TCM involve the extraction and isolation (at the molecular level) of the active ingredient(s) out of traditional medicinal preparations, followed by the rigorous testing of such extractions. Extraction and lab testing are intended to demonstrate, through evidence-based research design, TCM's efficacy and safety. The Hong Kong Jockey Club Institute of Chinese Medicine is funding or participating in several R&D projects aimed at modernizing TCM in precisely these ways, most notably an ongoing collaborative effort with CUHK and Baptist University of Hong Kong to develop TCM product to treat irritable bowel syndrome. The ICM at CUHK is similarly running clinical trials for manufacturers of TCM products.

Institutes and universities in Hong Kong engaged in TCM R&D are increasingly working with industry, in large part because most TCM firms are without the R&D facilities or research talent to carry out their own research in-house. For instance, Vigconic, a TCM manufacturer and part of the Luk Industries Group, contracts clinical R&D projects to local universities to gather data on the efficacy and safety of its products. Eu Yan Sang Chinese Medicines invested $10 million HK in 2000 to seed a collaborative project with the CUHK, specifically a pharmacological study of the firm's "meno-ease" product. The initiative was co-funded by the government's ITF. For the CUHK, the research collaboration with Eu Yan Sang was about demonstrating "proof" of efficacy of traditional herbal formulas for mitigating the effects of menopause. From the perspective of the firm, the "modernizing" effort was intended to demonstrate for the market the product's efficacy and safety in inducing the body to naturally develop estrogen (rather than require the ingestion of the hormone). These sorts of R&D collaborations have

become increasingly common among the larger, more established TCM firms in Hong Kong.

Hong Kong's TCM industry is reasonably well developed. It is estimated that there are around 100 TCM firms in Hong Kong. For most companies, their core business rests in manufacturing, marketing and sales. To be sure, the local market in Hong Kong is rather significant. A growing percentage of people in Hong Kong opt to consult a Chinese medicine practitioner before going to a Western physician.[2] The majority of people in Hong Kong are estimated to have consulted a TCM doctor at least once, it not regularly, for the treatment of common ailments and illnesses (Lau, 2000). However, the limited size of the local market in Hong Kong and the large number of local firms mean that the *future growth* of Hong Kong's TCM sector requires expansion into the Chinese market. And the fact that until recently TCM regulations were relatively lax, excessive market crowding among local firms, especially small manufacturers without GMP certification, is very pronounced. Small firms may not survive in the long run while large firms are constrained in the ability to expand their operations into the Chinese market.

PuraPharm is one Hong Kong TCM firm which has gained sizable market share in China. Using proprietary technologies to derive novel molecular formulations from traditional herb mixtures, PuraPharm has built a core business around the production of TCM "granules," or the de facto isolation and manufacture of key medicinal ingredients. In order to gain closer access to raw materials (herbs), PuraPharm established early on manufacturing facilities in Guanxi province, China. As one of six firms to be granted a license from China's State Food and Drug Administration (SFDA) to produce TCM

[2] Interview with Abraham Chan, CEO, PuraPharm, Hong Kong, June 12, 2008.

granules in China, PuraPharm's primary market has been the Chinese mainland. China accounts for 65% of the firm's sales; Hong Kong, on the other hand, accounts for just 20%.

The case of PuraPharm is the exception, however. The reality is that for most TCM firms in Hong Kong, even the larger ones, the vast majority of sales (70% and higher) is in the local Hong Kong market. Though many firms are beginning to allocate resources to R&D and to modernizing TCM, most continue to largely focus on manufacturing, marketing and distribution within Hong Kong. There are several reasons for this. First, most firms in Hong Kong are not GMP certified and are thus restricted in their ability to export products, even to China.[3] According to local TCM manufacturers, attaining GMP certification is very costly and most firms are without the resources to upgrade facilities. Second, the investment community in Hong Kong has shown little interest in the TCM sector, despite the government's attempts to highlight this potential growth industry. Most TCM firms are small family-based operations. Only a handful has benefited from angel investors and even fewer have been acquired by a larger industry group or holding company. Firms are without the resources to expand. Third, despite efforts to more closely integrate and harmonize regulatory regimes in Hong Kong and China, registration of TCM products in China, especially if they are not registered as a health food, is extremely arduous for local firms. Not only is the registration process in China expensive (reportedly up to five times the investment required for registering a TCM product in Hong Kong), it is very time-consuming and sometimes arbitrary. Clinical trials can only be conducted at certain SFDA-sanctioned centers and inside

[3] One estimate indicates that fewer than 10 Hong Kong-based TCM firms are GMP certified.

"connections" are often required to gain permission. And as the SFDA attempts to re-builds its regulatory reputation after several scandals were revealed in 2005 and 2006, the registration pipeline has slowed considerably, reportedly taking three times longer than before.

Clinical R&D

Nature noted in 2006 that in "the life sciences, Hong Kong provides a strong clinical research infrastructure" that can be utilized to bridge Hong Kong to emerging biotech industries in China. Hong Kong's hospitals and universities are world-class in terms of research. Its intellectual property regime is considered to be very strong, both in legislation and enforcement. Legal transparency is a high priority in Hong Kong (Nature, 2006: 221-222). In other words, Hong Kong can, in the medium term, position itself to be a principal site for conducting clinical R&D for both multinational and Chinese firms and labs.

During the mid 2000s, after several years of negotiations, the Chinese SFDA and the HK SAR announced that data generated from clinical trials that had been conducted at Hong Kong's university-based hospitals would be recognized by Chinese regulatory authorities, making Hong Kong the only location outside of the mainland approved by the SFDA to permit clinical data transferability. Hong Kong could therefore capture a lucrative link on the biotech commercial value chain, especially as more and more multinational firms are looking to find a suitable gateway into China. Firms are assured by Hong Kong's enforcement of IP protection as well as its high quality clinical research and data collection capacities.

Despite commercial promise in this specific niche, clinical R&D capacity in Hong Kong needs to be strengthened. Most clinical trials conducted in Hong Kong tend to be phase 3 trials, which are the least risky and capture the smallest value-added. There has been little effort to solicit earlier phase 1 or 2 trials, which would require considerably greater expertise in clinical research but which would also capture more economic value. Improvements in this regard need to be implemented relatively quickly, however, as Hong Kong's window to gain market share vis-à-vis China in the clinical R&D business is quickly closing. Industry observers note that labs in Beijing and Shanghai are rapidly developing their capacities to handle clinical trials for both domestic and international firms. Most important, the Hong Kong government needs to hasten regulatory harmonization with the Chinese SFDA regarding clinical research and data transferability. The 2005 decision by the SFDA took years to negotiate, and it remains unclear how long it will be before the agreements are actually implemented. The scope of the agreement is also quite narrow, limiting the both the range of foods and drugs that qualify under the agreement and limiting also the specific research institutions in Hong Kong that can carry out a clinical trial. There remains work to be done over the medium term – in both Hong Kong and China – if Hong Kong is to leverage its relationship with China and its infrastructure for realizing commercial gains from clinical R&D.

R&D Collaboration

Over the longer term, there will be even more opportunities for Hong Kong-based biotech firms and research centers to collaborate with China's rapidly growing life sciences industry. There is considerable R&D talent in China willing to work in Hong

Kong. During the late 1990s, roughly half of the life sciences researchers based in Hong Kong originated from China (Nature, 2001: 5). Institutional collaborations are being forged by Hong Kong and mainland Chinese labs. The flow of talent and knowledge is not only one way, from China to Hong Kong, however. Hong Kong-based firms are looking to locate their R&D operations in China in the near term. For instance, Hai Kang Life Sciences (formerly Hong Kong DNA Chip), a Hong Kong-based start-up developing a novel lab-on-a-chip product, moved their principal R&D facilities and university collaborations to Beijing University early on in the company's development. In order to generate a short term revenue stream, Hai Kang Life Sciences performs GMO testing in its Hong Kong facilities. Meanwhile, the firm's core technology business, the development of DNA chips, takes place in China. SinoMab is another commercial example of Hong Kong-China collaboration. SinoMab, a Hong Kong-based firm currently based in the Science Park, was initially founded on novel anti-body research that had been conducted in China. The firm has since developed a re-engineering technology used on anti-bodies in order to identify and develop new drug candidates. While much of the firm's intensive R&D takes place in Hong Kong, SinoMab has established a GMP-certified pilot plant in Shenzen. The firm also contracts out pre-clinical R&D to various research institutes in China.

Sustained R&D collaboration between researchers in Hong Kong and China is the basis for realizing Hong Kong's longer term ambitions of becoming a biotechnology industry *innovator*. Hong Kong readily taps into China's significantly larger (and cheaper) talent pool. Hong Kong-based firms can gain easier access to the Chinese market, especially if clinical and pre-clinical research efforts involve collaboration among labs

and firms in both places. To be sure, China is producing good science in the field of biotechnology. The Beijing Genomics Institute, the world's third largest genome sequencing lab and the first to sequence the Chinese human genome, recently moved its operations to Shenzen. The local government there has supported the BGI initiative by providing resources, attracting returnees from abroad and building up Guangdong province's life sciences R&D capacities more generally. Hong Kong can leverage these sorts of developments over the long term.

The key point is that while during the mid 1990s, the future of Hong Kong's life sciences industry centered on its ability to move up the manufacturing value chain, and specifically in the TCM sector, more recent developments during the 2000s laid the foundation for considerably more lofty ambitions over the longer term, which is to turn Hong Kong into a biotech innovator.

4. DISCOVERED IN HONG KONG?

Efforts to increase R&D collaboration among Hong Kong researchers and others in China and elsewhere signal that biotechnology stakeholders are endeavoring to develop Hong Kong's nascent life sciences industry further up the technology chain to capture greater value-added returns. Hong Kong looks to become a biotechnology industry innovator. To date, there has been very little output in this regard. This is not to say, however, that there have been no success cases in Hong Kong. For instance, the Biotechnology Research Corporation (BRC), the commercialization arm of HKUST's Biotechnology Research Institute (BRI), was formed in 2003 with a $175 million HK investment from the Hong Kong Jockey Club. The BRC formed a joint venture, TA

Therapeutics (TAT) Ltd. in 2005 with US-based biotech, Geron. R&D collaboration between Geron and the BRI was initiated in 2000. BRI and Geron are developing new telomerase activator drugs aimed at restoring cells in damaged organ systems, which are now in pre-clinical development (Business Wire, 2005). The plan is for TAT to bring new drugs to phase 1 clinical trial, after which time identified compounds may be licensed-out for further clinical development.

TAT is a rare success case in Hong Kong. And the reality is that product development in TAT still remains far from market. Biotechnology innovation at the cutting-edge is a very long and uncertain process. Even though Hong Kong has demonstrated considerable capacity in upstream research, especially given its size, translating discoveries from the university lab bench into a commercially viable product or service is an extremely high risk endeavor. In this respect, it is still too early to determine whether Hong Kong will be able to become a biotech innovator. Still, it is clear that there exists several "gaps" which need to be addressed at the outset (Branscomb and Auerswald, 2001). These will be addressed in turn below.

Midstream Capacity

Technological innovation requires the translation of upstream research into a commercial product or service. In the field of biotechnology, there are literally thousands of potential "leads," though the reality is that most will either languish or fail to make it to the market. Identifying viable leads is central to the innovation process; it is also the basis of uncertainty. The Hong Kong Science and Technology Park enlisted the prominent Danish –Swedish Medicon Valley cluster to prepare a report on the state of

biotechnology innovation in Hong Kong during 2003 and 2004. The HKSTP has since re-enlisted the Medicon Valley group to conduct further research in Hong Kong and the Pearl River Delta. Its task is to inventorize Hong Kong's stock of knowledge in the life sciences and to identify promising projects with commercialization potential. Identifying leads is only one challenge, however; applying IP and translating knowledge into a commercial product is another. This process is prone to market failure. Midstream institutions are needed to correct this.

Taiwan's Industrial Technology Research Institute (ITRI), considered to be the birthplace of Taiwan's globalized semiconductor industry, performs this midstream function in Taiwan's efforts at technology innovation and development. During the postwar period and into the current era of biotechnology innovation, engineers and scientists at ITRI "bring" technologies closer to industry. The ITRI bridges the public and the private sector by anchoring or participating in pre-market R&D consortia among firms. It further develops new technologies in-house and licenses them out to industry, or in many instances spins-out a new firm. In addition to revenues earned from licensing deals and from contract R&D services, the ITRI is publicly funded by the government's Ministry of Economic Affairs. Because the processes of technological innovation are prone to market failure, industry is unwilling or unable to perform this expensive and high-risk midstream function. This is especially the case with small firms and in economies where there is no critical mass of biotechnology enterprises. Industry thus tends to be risk-averse. ITRI, and other similarly publicly funded midstream R&D institutions in Taiwan such as the Development Center for Biotechnology and the National Health Research Institute, bear some of the risk and much of the costs of market

failure. Such midstream institutions compel otherwise risk-averse firms to enter into the biotechnology sector. They cannot overcome biotechnology's uncertainties, but they can help offload some of the risk from industry.

Hong Kong lacks these sorts of midstream mechanisms to help commercialize otherwise strong upstream research in the life sciences. The Hong Kong Institute of Biotechnology (HKIB) was created to fulfill such a midstream role, though due to the lack of resources, talent and promising projects, the HKIB was re-organized into an incubation center further downstream. It had failed to fill the midstream gap. Though the major universities institutionalized technology transfer offices (TTOs) or licensing offices (TLOs), most have not been effective in bringing university research to industry, especially to local firms. These offices lack resources, where often the biotech division is a one-person operation. Thus, TTOs and TLOs tend to be passive with respect to prospecting IP from within the university. They also have little experience in strategically managing life sciences IP (i.e. coupling IP), which reflects an overall lack of bio-industry experience among university IP managers. And university technology offices tend to focus on out-licensing IP rather than leveraging the university's IP to create new spin-off firms (HKSTP biotechnology initiative internal report, 2004). In the fiscal year 2006, for instance, the CUHK TLO, one of Hong Kong's most successful and active university-based technology offices, though it filed 29 US patents and negotiated 19 licensing deals not a single start-up firm was created. TLOs and TTOs simply lack the resources to jumpstart new firm creation (AUTM Licensing Activity Survey, FY2006).

There is no institutional equivalent of the ITRI in Hong Kong's biotech sector. Publicly funded research institutions dedicated to fill the midstream "gap" in the life sciences do not exist. When asked, most repeat the mantra that the Hong Kong government, unlike the state in much of the rest of northeast Asia, does not "pick winners." Reducing risk and uncertainty to incentivize otherwise risk averse firms to enter into the biotechnology sector is considered *excessive* government intervention. Things have begun to change, albeit slowly. The establishment of the Science Park and the creation of the Hong Kong Applied Science and Technology Research Institute (ASTRI), created in 2000 to facilitate the transfer of technology to local industry, are steps toward back-filling the midstream R&D gap in Hong Kong's innovation regime. Efforts toward building up Hong Kong's commercialization capacity are pointing in the right direction. Still, with the exception of the Jockey Club Institute of Chinese Medicine, life sciences industry, especially those sub-sectors that are unrelated to TCM, continues to be excluded from the ASTRI mandate. More can still be done.

Investment

The valley of death – the "challenges faced by would-be innovators seeking to make the transition from scientific breakthrough to market-ready prototype" – is a prominent reality in all technology innovation endeavors. The absence of institutional mechanisms promoting midstream R&D widens what Branscomb and Auerswald (2001: 11-12) refer to as the "research gap." Meanwhile, the "financial gap," or the absence of "investment funds [needed] to turn [an] idea into a market-ready prototype," is just as problematic for potential innovators. Risk and patient capital is needed. The US

biotechnology sector was fuelled primarily by competitive government R&D grants and a thriving venture capital (VC) sector. American-based biotech start-ups and small enterprises were also supported by investments from (and acquisitions by) the US' large pharmaceutical industry and firms. Enticing risk and patient capital is among the most significant challenges to growing a biotechnology industry. Regional competitors Taiwan, Korea and Singapore have all experienced the challenges of narrowing the financial gap. Simply put, finding risk and patient capital is difficult to do in an inherently uncertain industry such as biotechnology, particularly in countries that have little "track record" in the life sciences.

The problem in Hong Kong is not just about finding a critical mass of risk and patient capital, however; the challenge is identifying *any* sources of investment capital that are interested in the biotechnology sector. Private sector investment in biotechnology R&D is next to none in Hong Kong. In addition, there is no pharmaceutical industry in Hong Kong to make-up some of the financial gap. Some firms, such as CK Life Sciences, one of Hong Kong's most successful biotechnology firms, might benefit from an angel investor, who in the case of CK Life Sciences is Hong Kong billionaire Li Ka-Shing. Most firms, however, rely almost solely on personal out-of-pocket financing. Investable cash is in short supply in Hong Kong. Firms are thus constrained in how innovative they can be. The cash burn rate in biotech is uniquely high.

Hong Kong's VC sector is uninterested and thus inactive in biotechnology. Though Hong Kong is home to one of the world's most vibrant VC industries, only one investment fund, the Morningside Group, has invested substantially in Hong Kong biotechnology. Most VCs, if they are interested in biotech in the first place, tend to invest

in firms abroad, notably in China. But even Morningside's investment "commitment" to biotechnology in Hong Kong is relative. Morningside's biotechnology portfolio lists 30 invested firms. However, just one is clearly based in Hong Kong, though there are four additional TCM firms with potential ties to Hong Kong. The remaining biotech firms in the Morningside portfolio are based in either North America or China, with 17 firms in the US.[4]

There are several reasons why VCs have been slow to warm to Hong Kong biotech. First, the dearth of seed funding (both public and private) available for firms to demonstrate their commercial viability is a deterrent for otherwise interested VCs. As such, VCs in Hong Kong tend to be risk averse when it comes to biotechnology. Second, venture investors lack experience and the expertise to effectively execute the due diligence required to identify promising projects and firms. Investments also tend to be shorter term and thus less patient. The dot.com bust in the global IT sector of the early 2000s has altered investment strategies as VCs shy away from high risk, long term endeavors. Hong Kong-based VCs are waiting for a commercial "success case" in the local biotechnology sector (HKSTP biotechnology initiative, 2004). Third, government-funded VCs, such as the ARF, often "lead" new investments and in turn induce follow-on investments from investors in the private sector. Government leadership of this kind in places such as Taiwan, Korea and Singapore mitigates risk for follow-on investors. However, when the ARF ceased investing in new firms beginning in 2004, private sector investors have been without the assurances of government leadership in indentifying firms and projects. Investors have become even more risk averse.

[4] Data compiled from the Morningside Group website, www.morningside.com, accessed October, 2008. According to officials at the HKSTP, Morningside has funded three companies inside the Park, though they are not listed currently on the Morningside website.

And finally, there are few viable "exit mechanisms" for VCs, or the means by which investors can realize returns on their investments. Most notably, the second board of the Hong Kong Exchange, the Growth Enterprise Market (GEM) board, is roundly criticized for its poor levels of capitalization, competition from the main board for listings, and the lack of turnover in trading. Consequently, the GEM board is not viewed to be a particularly good exit mechanism for investors. In fact, its operation was suspended during the mid 2000s. Additionally the absence of critical mass of firms in Hong Kong's biotechnology sector means that there are few opportunities for mergers, acquisitions and other types of strategic alliances, all of which are considered to be viable exit strategies for venture investors.

Critical Mass

Innovation requires connectivity among actors. As discussed, the lack of midstream R&D mechanisms widens the gap among researchers and industry. There exists a financial gap in Hong Kong's biotechnology industry, as private sector investors are unwilling and unable to bring novel ideas downstream into industry due to financing constraints. Hong Kong's biotechnology sector also lacks a critical mass of firms, therefore constraining opportunities for inter-firm collaboration. Linkage among biotech firms – for instance, R&D collaboration and information sharing more generally, mergers and acquisitions, or the formation of strategic alliances – is critical to cutting-edge technological innovation. It is the basis of knowledge diffusion. Yet, as one bio-industry insider put it, "there are many biotech firms in Hong Kong, but there is no biotech *industry* in Hong Kong." Because of the reasons discussed above – the absence of

midstream institutions and the lack of risk and patient capital – new business creation in the biotechnology sector has been slow in Hong Kong

The lack of a biotechnology industry critical mass means that there are fewer firms able to receive technologies from further upstream. In other words, one of the main obstacles in the way of developing midstream R&D capacities in Hong Kong is the absence of firms that are capable of absorbing and assimilating new technologies. The technology licensing office at the CUHK, for example, tends to license-out its life sciences IP to foreign firms rather than the few local firms engaged in biotechnology R&D. Hong Kong's small biotech industry also means that firms have fewer opportunities to gain bio-industry experience. The movement of people and talent among firms is constrained in Hong Kong, though as Steven Casper describes in the case of the San Diego biotech cluster, it is precisely learning gained from the interaction of clustered firms which contributed to commercial success in US biotechnology.

Limitations in Hong Kong's biotechnology industry are not just rooted in the small number of firms, however, but also the weak bases of connectivity among them. Weak or non-existent inter-firm linkages constrain information exchange, learning as well as opportunities for partnering and R&D collaboration. According to most stakeholders, the Hong Kong Biotech Association has become very passive. Recent efforts by the HKSP have attempted to correct this. The HKSP hosted Hong Kong's inaugural Bio-Exchange partnering event in the spring of 2008, which attracted 180 attendees and 28 partnering initiatives; the significance, of course, is that the inaugural event took place just this past year.

5. LOOKING FORWARD

On balance, Hong Kong enjoys a sufficient though nascent base for growing a viable biotechnology industry over the long term. Basic and upstream research capacities in Hong Kong are quite strong in the life sciences. Hong Kong has been able to attract, and to a limited extent train, a high quality corps of life sciences researchers. With respect to biotechnology commercialization, renewed efforts in Hong Kong's biotech communities suggest some great potential. Hong Kong can – and should – take advantage of "low hanging fruit," leveraging its relationship with the mainland while also diversifying its existing industries (i.e. electronics, IT services) toward health technology applications. The biotechnology towers in the HKSP have quickly filled with both local and foreign-based tenants. The Hong Kong Biotechnology Association has also sought out a new leadership team in an effort to renew up- and downstream linkages. The HKSP has, just in the past year, hosted several investor forums for global and Chinese firms. The international community has begun to recognize these efforts. Hong Kong's nascent biotech sector has attracted interest from European investment consortia. As well, biotech "stars" from the US have created subsidiary R&D operations in Hong Kong, both drawing on and developing further local R&D talent.

Still, the reality is that Hong Kong's biotechnology base is small-scale, and as such, Hong Kong will continue to face several challenges as it looks to grow its biotech sector further downstream. One distinct advantage for Hong Kong, however, is that the China market looms large. Given its close proximity to and cultural, linguistic, economic and political "closeness" with the mainland, Hong Kong can take advantage of its relationship with the PRD and China more generally. Hong Kong ought to look beyond

the TCM sub-sector, and especially its past focus on manufacturing, if it intends to capture higher value-added gains in life sciences industry. Focusing solely on TCM will preclude the growth of new businesses, as the local TCM sector in Hong Kong is already quite saturated. In fact, it could benefit from some consolidation among firms, led by those with upgraded cGMP facilities.

The largest challenge facing Hong Kong's nascent life sciences sector is its weak capacities in midstream R&D and biotechnology commercialization. More specifically, Hong Kong faces serious "gaps" in translating upstream research to industry, in financing, and in inter-firm connectivity. The 2004 HKSTP biotechnology initiative internal report prepared by the Danish-Swedish Medicon Valley cluster stated that "*if Hong Kong wishes to do so*, it can now establish a biotech cluster that includes a biotech industry" (HKSTP, biotechnology initiative internal report, 2004: 5). The key point is the allusion to the political, economic and commercial will in Hong Kong needed to grow a viable local biotechnology industry. It will not be automatic. Hong Kong's biotechnology base, as it is today, is insufficiently developed. Gaps persist. Initiatives to narrow the "gaps" include the following:

1. <u>Regulation.</u> Hong Kong needs to leverage its proximity to the huge Chinese market. To facilitate that, the Hong Kong government should begin negotiations with the appropriate authorities in China to harmonize existing regulations and protocols governing clinical R&D, clinical data transferability and product registration. Where possible, the Hong Kong government should initiate negotiations to expand the scope of reciprocity regarding the direct transferability of data for clinical trials conducted in Hong Kong.

Existing agreements between the Hong Kong government and the Chinese SFDA regarding clinical trial data transferability should be implemented immediately. Even though the CEPA framework allows for tariff-free trade of health care products between Hong Kong and China, such trade will be severely mitigated if regulatory obstacles are not resolved.

2. Administration. The Hong Kong government should institutionalize a new life sciences industry steering committee, with membership comprising noted foreign experts from the academy and industry.

3. Midstream R&D Institution Building. An institutional equivalent of the ASTRI solely dedicated to biotechnology should be created and funded in part through public resources. The institute should be independent of the university sector, but should work closely with universities' IP offices in order to proactively identify and further develop promising technologies. The length of existing university research grants needs to be extended from the current standard of two to three years (Nature, 2001) to at least five years in order to allow researchers, if appropriate, the opportunity to develop new technologies further downstream. In South Korea, for instance, R&D grants from the Ministry of Science and Technology typically run up to ten years. Hong Kong, like Singapore and Taiwan, should also expend resources to actively recruit biotechnology talent from abroad, especially those with both life sciences research and industry experience. While the number of life sciences students (and graduates) at the undergraduate level is quite high in Hong Kong,

this talent pool cannot be expected to lead the growth of Hong Kong's biotechnology industry.

4. Investment. Due to market failure in biotechnological innovation and the inactivity of Hong Kong investors in the life sciences field, the government should revitalize the ARF, and establish as well as capitalize a dedicated biotechnology VC fund. The management of the fund should be left to private sector fund managers. And they should be longer term (i.e. considerably longer than previously managed by the ARF). Investments would encompass both local and international firms. International investment (i.e. into biotech firms in the US, Europe and Asia) will gain the Hong Kong fund managers investment experience in the sector and the expertise to identify promising projects and firms. This will also test the government's commitment to the biotechnology sector. As a point of reference, Singapore's Bio*One fund, the state's biotech VC, is capitalized at nearly $800 million US, of which most has been invested. Both the Taiwan and Korean governments have invested similar amounts into their respective VC markets.

5. Business Environment. Greater connectivity among firms needs to be encouraged. The Hong Kong Biotech Association should be revitalized and perhaps tied into the current biotechnology leadership at the Science Park. Due to the high cash burn rate in the life sciences sector, mergers and acquisitions as well as the formation of strategic alliances among firms should be normalized through less cumbersome legislation and rules and regulations. To encourage more R&D collaboration and to forge backward and forward linkages among firms and labs, government sponsored R&D projects should require that

principal investigators or corporate labs demonstrate the intent to collaborate with external units. In South Korea, for example, R&D grants provided by the Ministries of Science and Technology as well as Commerce and Industry stipulate that projects must involve inter-mural collaboration.

6. Government Attitude. The Hong Kong government adamantly maintains that it does not "pick winners." However, it needs to be emphasized that government intervention for the purposes of offsetting market failure in technological innovation is not the same as picking winners per se. Even "lean" states such as in the US invest heavily in inherently uncertain sectors such as biotechnology. The National Institutes of Health and the National Science Foundation allocate approximately $30 billion US each year for life sciences R&D. Decision-makers in Hong Kong must therefore understand that resources allocated for the purposes of facilitating midstream R&D and to seed industry investment are not equivalent to intrusive industrial policy. They are measures to reduce the vagaries of market failure. Additionally, the government must realize and in turn convey to stakeholders in Hong Kong that biotech innovation – as with any sort of cutting-edge innovation in any science-based industry – is necessarily long term and that progress and growth in such sectors cannot solely be evaluated by near term commercial returns. Rather, medium term achievements measured in terms of intellectual property generation, the inflow of foreign direct investment, the formation of transnational R&D partnerships, the completion of a phase 2 clinical trial, and so on, need to be understood as indicators of progress.

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