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DIVERSITY AND THE EVOLUTION OF A LIFE-SCIENCE INNOVATION SYSTEM: THE TORONTO REGION IN COMPARATIVE PERSPECTIVE

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INTRODUCTION

Despite many predictions to the contrary, knowledge-intensive economic activity has not become more widely distributed over time. If anything, the reverse appears to be true, and this seems especially evident for the most knowledge-intensive sectors. Life-science-based industries are a case in point. According to a widely cited study (Cortright and Mayer 2002), the US biotechnology sector is highly concentrated in a relatively small number of metropolitan regions. Moreover, this spatial concentration appears to have increased over the past 20 years and this trend is especially marked when one examines the most entrepreneurial components of this sector. Hence, although the spatial distribution of medical research grants from agencies such as the National Institutes of Health has increased over this period, the geography of new firm start-ups and venture-capital investment has moved sharply in the opposite direction.

While there are undoubtedly many ways to interpret this changing geography, there is emerging consensus that the characteristics of the local institutional environment are critical in supporting the emergence of life-science industries (Cooke 2004*b*). Moreover, “local” needs to be understood as the product of a multi-level process of governance, in which local, provincial/state, national, and supranational institutions and actors define a set of rules within which industries evolve over time (Gertler 2004).

In this chapter, we document the structure and recent evolution of the life-sciences complex in the Greater Toronto Area (GTA), one of North America's leading centres for biomedical research and commercial activity. As a regional-industrial concentration of economic activity, it possesses a number of distinctive features that make it particularly interesting. First, it has a large concentration of research-based, life-science organizations, including leading universities and teaching hospitals. Second, it is host to many pharmaceuticals producers, both "brand-name" multinationals and locally based generics. Third, it has been home to some of Canada's earliest and best-known research-based firms, and continues to generate new start-ups, although, at least according to some, in numbers that are not commensurate with the volume of university- and hospital-based research (Voyer 2001; Graytek 2004). Fourth, it has generated Canada's largest concentration of manufacturers of biomedical technologies, equipment, supplies, and assistive devices.

Another distinctive feature of the Toronto economy is its uncommonly diverse sectoral composition. It has developed a wide range of sophisticated service industries, including finance and professional/producer services, while retaining a strong manufacturing base in industries such as automotive, food products, electronics, specialized machinery, and aerospace (Gertler *et al.* 2000). As we shall argue below, this older, diverse economic base has provided many of the local assets (including diverse knowledge bases) upon which newer life-science industries have emerged.

We shall also argue that the evolution of life sciences in the GTA has been strongly shaped by the diversity of institutions that influence the practices of firms and the decisions of managers. These institutions span a range of spheres, including research, commercialization, finance, health care, and associative governance. We examine each of these in turn, considering their impact on the growth of local firms in biotechnology, pharmaceuticals, and medical and assistive technologies.

The following sections of this chapter focus primarily on how these life-science institutions have shaped and influenced the evolution of distinct groups of biomedical establishments in the Toronto region. Our findings are based on qualitative field research conducted in 2003 and 2004, in which close to 100 interviews were conducted with managers of biomedical firms, including dedicated biotechnology companies, medical and assistive technology producers, prescription drug-makers, and contract research firms. Over a dozen interviews were also completed with other local actors, including policymakers, financial

investors, university researchers, technology transfer specialists, hospital procurement managers, and industry association representatives. A close review of primary and secondary materials from other sources provided additional support for our interview findings, as did on-site observations at key industry events and government-sponsored networking sessions. In order to provide a useful benchmark, and to enable us to isolate more clearly the influence of *regional* institutional variables within a multi-level governance framework, we also review the recent experience of life sciences in Montreal, as documented in a variety of published articles and consulting reports.

TORONTO: A DECENTRED MEGACENTRE?

Toronto and Montreal have been identified as Canada's biomedical megacentres (Niosi and Bas 2003). In contrast to specialized biotechnology centres, which host dedicated biotechnology firms and medical research centres, megacentres are home to a wide range of firms located along the entire life-science value chain (Cooke 2004*b*). In Toronto and Montreal we find a critical mass of dedicated biotechnology firms (DBFs), as well as high numbers of contract research organizations, drug and device distributors and manufacturers, and related suppliers and professional service firms. In both regions, we also find a large number of reputable universities, teaching hospitals, and biomedical research centres, as well as a range of financial investment firms and funds: all of which provide research and commercialization support for early and late-stage biomedical firms.

Previous analyses focused on the structural similarities of these two regions to illustrate their relative advantage over specialized biotechnology centres in other parts of Canada, including Vancouver and Quebec City. In the next four sections, we look instead at the unique institutional systems that shape industry development patterns and reinforce inter-organizational and inter-firm relations *within* these two regions. While it is true that Montreal and Toronto share a very similar sectoral make-up, each has a distinct local system for organizing and coordinating life-science activity. In Montreal, government agencies — at both the provincial and municipal levels — have historically played a central role in industry development, using public research, marketing and financial support to motivate and direct firm strategy and when necessary, smooth tensions between diverse economic actors and interests. This centralized approach to industry development is not specific to the region's

biomedical industry, but rather crosses into other technology-intensive industries, including aerospace and information technology (Niosi 2005). It also reflects a larger, provincewide approach to industrial development and upgrading. It is not surprising then that scholars of regional innovation often describe Quebec's system as *dirigiste*, where "initiation of actions is typically a product of central government policies" (Cooke 2004a, p. 13).

In Toronto, however, government support is much more diffused and indirect and has been aimed at addressing weaknesses in individual organizations and agencies over time, rather than creating a coherent, regionwide plan or structured path for industry growth. As we shall see in a later section, private and civil sector actors, rather than government officials, often play a lead role in coordinating across and matching up different institutional and industry supports in Toronto. In the past, these actors concentrated on a specific life-science niche area, such as DBFs, big pharma, medical and assistive technology (MAT) sales (i.e., large, multinational firms) or indigenous MAT manufacturing. New competitive pressures have intensified intra-industry factions in recent years and have resulted in a growing commitment by these same actors to begin to forge strategic networks and alliances across distinct economic groups. Industry analysts routinely describe Toronto's life-science system as *laissez-faire* (Voyer 2001, p. 27). However, this characterization fails to capture the presence of less visible forms of intra-regional coordination. In particular, it overlooks the subtle yet important ways in which provincial and national government policies have shaped firm strategy in previous years, as well as recent efforts by government agencies to scale-up their involvement in intra-industry network formation.

These distinct systems, which we classify as *government-centred* for Montreal and *grassroots* evolving into *networked* for Toronto, to borrow Philip Cooke's terms (2004a), are reflected in four interconnected sets of institutions:¹ (i) research and commercialization systems, (ii) finance, (iii) health care (medicare), and (iv) industrial governance (associations). Each of these is reviewed in turn below.

RESEARCH AND COMMERCIALIZATION SYSTEMS

The GTA, along with Montreal, is a national leader in biomedical research and development in Canada. In 2000-2001, public funding for health sciences in Ontario was estimated to be over \$380 million, with the lion's share allocated

to GTA-based scientists and medical researchers (Ontario. Ministry of Economic Development and Trade 2004).² From 1996 to 2000, Ontario ranked first in the nation for health sciences publications, generating 41 percent of the nation's 6,827 scientific articles (Industry Canada 2004).³ Again, the majority of these articles were published by scientists and medical professionals associated with GTA-based universities and research centres. Life-science research takes place at the University of Toronto's (UofT) three GTA campuses, as well as its nine fully affiliated and 11 partially affiliated teaching hospitals (University of Toronto. Faculty of Medicine 2004).⁴ The university receives the largest share of national funding from both the Canadian Institutes of Health Research (CIHR) and the National Sciences and Engineering Research Council (NSERC) (CIHR 2004; NSERC 2004; University of Toronto. Office of the Vice-President, Research and Associate Provost 2004). It is estimated that the university spends close to \$2 million each day on research activities, with roughly half of these funds allocated to life-science-related projects (Innovations Foundation 2005). York University in the northern region of the GTA also conducts biomedical-related research, and has strong research programs in sensory science and mass spectrometry (Strategic Health Innovations 2004).

In addition to providing research support, the University of Toronto continues to play a central role in biotechnology firm formation. University-affiliated Connaught Laboratories was directly involved in the creation of Canada's first two DBFs in the early 1980s: Allelix and Cangene. Connaught Laboratories was a commercial research centre established in 1914 and later sold to the French pharmaceutical firm, Institut Mérieux in 1989; Mérieux eventually merged with Aventis Pasteur. A recent industry history described the early working relationship between the three organizations — Cangene, Allelix and U of T's Connaught Labs — as a “revolving” research door (Kuyek 2002, p.10).⁵

Allelix was established in 1981 in downtown Toronto with start-up financing from the Canadian Development Corporation, the Province of Ontario, and John Labatt Ltd. Initially, the firm concentrated on agricultural biotechnology and was successful in its early use of cell-fusion technology to develop a new variety of Canola seed in the mid-1980s (Warden 1986). Revenue generated from national and international seed sales and contract research for large agri-business interests in the United States provided additional working capital for the firm and helped finance start-up research in biopharmaceuticals. In 1988, the firm sold its agricultural division, Allelix Crop Technologies, to Pioneer Hi-Bred, a plant genetics research operation in Des Moines, Iowa (Ansoorge

et al. 1990). In the late 1980s and early 1990s, Allelix Biopharmaceuticals worked closely with multinational pharmaceutical firms, including Glaxo Canada and Eli Lilly & Co., and University of Toronto scientists to develop treatments for osteoporosis and nervous systems disorders (Chamberlain 1994). In 1999, the company merged with NPS, a mid-stage biotechnology firm from Salt Lake City, Utah. NPS-Allelix continues to perform research and development activities from its Mississauga operations on the western side of the GTA. Canada's second biotechnology firm, Cangene, was established in the western GTA in 1984. The company continues to conduct research in Mississauga, despite moving its national headquarters to Manitoba in the early 1990s.

In its last comprehensive national survey in 2001, Statistics Canada identified 55 dedicated biotechnology firms in the GTA. The University of Toronto has played a central role in the formation of 44 of these firms (University of Toronto. Office of the Vice-President, Research and Associate Provost 2004). In 2003, 42 of these firms remained active with 1,355 employees and a combined annual revenue of approximately \$270 million (Strong 2004).⁶ The University of Toronto uses specialized CIHR, NSERC, and provincial Community Small Business Investment grants to provide early-stage financing for university spinoffs, and in the process encourages biomedical scientists to commercialize their research. Recent U of T life-science start-ups include Innova LifeSciences Corporation, Interface Biologics, InSception Biosciences, Rimon Therapeutics, and Trillium Technologies. In addition to these entrepreneurial successes, the university generates licensing revenues from life-science-related technologies. Recent licencees include Eli Lilly, Neurochem (based in Montreal), Aventis Pasteur, NPS Pharmaceuticals, and QLT (in Vancouver).

Historically, the GTA has led the nation in biotechnology start-ups. However, as we shall demonstrate in the next section, Montreal's financial stability — itself a reflection of the province's centrally-managed innovation system — not only enabled the region's biotechnology "cluster" to withstand the global venture-capital crisis at the start of the decade, but allowed it eventually to overtake the GTA in new firm start-ups. In recent years, Quebec's provincial government has also increased its support for health-sciences research. While Toronto-based universities received the largest share of CIHR grants from 2002–2003 (\$130 million, compared to Montreal's \$125 million), Montreal's year-to-year increase in CIHR grants was significantly higher during this period (Holbrook and Clayman 2003). Similarly, Montreal-based universities received a higher share of NSERC life-science grants during the

2002–03 period: \$84 million, compared to \$60 million for Toronto. Researchers in Montreal are able to secure grants through their own universities, as well as through the city’s Biotechnology Research Institute, one of five biotechnology research centres created by the federal government’s National Research Council. Today, the Biotechnology Research Institute (established in 1983) is the largest single biomedical research and development (R&D) centre in Canada with over 800 personnel, guest workers, students, and industry scientists (National Research Council of Canada 2003). With the exception of the now disbanded Connaught Laboratories, no single centre of equivalent size exists in Toronto. Rather, biotechnology-related research and commercialization activities are dispersed across the city’s numerous research laboratories and U of T-affiliated teaching hospitals.

It should be noted here that the GTA is also home to roughly half-a-dozen start-up hybrid operations that are not easily categorized as dedicated biotechnology operations. Hybrid firms pursue “convergent” strategies by working at the interface of distinct technology areas. In life sciences, this often involves combining capabilities in material sciences or information technology with novel science in biology and biotechnology. A fast growing group of GTA hybrids includes firms that manufacture drug delivery and surgical devices that are used in conjunction with drug therapies. Examples include Interface Biologics, Delex Therapeutics, Rimon Therapeutics and TM Biosciences. The GTA’s national lead in mixing life-science and physical-science activities reflects its diverse research strengths in multiple disciplinary fields, as well as national and provincial support for interdisciplinary research projects at the University of Toronto. A new generation of venture fund managers and technology-transfer agents from the Toronto area are also actively working to extend this interdisciplinary tradition (Delex Therapeutics Inc. 2003).

Technology Transfer

In addition to having decentralized research support, the GTA has one of the nation’s most fragmented systems for translating health-science research into commercializable technologies. At least five independent technology-transfer operations exist within the University of Toronto’s health-sciences network alone. The largest operation is the Innovations Foundation at the university’s downtown campus. A small number of U of T-affiliated hospitals, including Sunnybrook and Women’s, license non-rehabilitative medical technologies

through the Innovations Foundation. Others, like the University Health Network, Hospital for Sick Children, Bloorview MacMillan Children's Centre, and Centre for Addiction and Mental Health, prefer to use their own technology-transfer systems. In recent years, separate technology-transfer operations have also been created to target faculty and students in related medical fields or disciplines. U of T-affiliated researchers working on rehabilitative technologies, for example, are encouraged to license their products through the Ontario Rehabilitation Technology Consortium, headquartered at Toronto's Bloorview MacMillan Children's Centre. Other consortium members include U of T's Sunnybrook and Women's and Centre for Studies in Aging, and non-GTA organizations, including the University of Waterloo, the University of Western Ontario, and West Park Healthcare Centre (Canadian Technology Network 2004). York University also has a separate technology-transfer system, which is managed through the university's Office of Research Services (York University. Office of Research Services 2004).

In other biomedical regions in Canada, including Montreal, individual universities and their affiliated hospitals typically share a single technology-transfer office. Furthermore, in cases where research crosses university boundaries, technology-transfer centres work closely together to determine jurisdictional authority over intellectual property. At Montreal's McGill University for example, the Office of Technology Transfer (OTT) controls *all* licensing agreements at both its downtown and Macdonald campuses, as well as at six fully affiliated teaching hospitals: Montreal General, Montreal Children's, Montreal Neurological Institute, Royal Victoria, Jewish General and Douglas Hospital (McGill University. Office of Technology Transfer 2004). A satellite office of OTT is located at McGill's largest teaching hospital, Montreal General, and is staffed by a technology-transfer specialist who represents hospital-based researchers within the university's extensive health-care system (ibid. 2004). Montreal has also earned a reputation for its strong interuniversity coordination. McGill, Concordia, University of Quebec-Montreal, University of Montreal, and two Montreal polytechnics coordinate technology licensing through the Montreal division of the Bureaux de Liaison Entreprises-Universités des Universités Québécoises (BLEUs) — a government-created and financed network of university technology-transfer offices established in 1987. Quebec's Ministries of Education and Science, Research and Technology play an active role in facilitating interuniversity coordination and provide the BLEUs network with clear policy guidelines for assigning

ownership in the case of jointly developed technologies (T3 2001; Navarre 2002). The provincial government also provides additional financial support for sub-network formation through its Valorisation-Recherche program. Included here are four value-enhancement corporations that represent and coordinate among subgroups of Quebec universities. The largest corporation, the MSBi, was initially developed in 2001 to finance start-up firms at McGill, Sherbrooke, and Bishop's Universities (Bishop's University. University Industry Liaison Office 2005). Today, Quebec's four value-enhancement corporations, including MSBi, are used to launch other provincewide initiatives, including a government-sponsored internship program designed to train future technology-transfer specialists (Canada News Wire 2003).

In comparison, inter- and intra-organizational coordination in the GTA is rather limited. Instead, academic researchers-turned-inventors within the University of Toronto system have considerable freedom in selecting their commercialization path. As noted above, they can choose to work with technology-transfer agents at their affiliated teaching hospital(s), with those from the Innovations Foundation or, depending on the area of expertise, with specialized intellectual property offices that span Ontario's health-care system. Given the size and geographic reach of Toronto's health-care system, there are benefits to this overlapping mandate of commercialization organizations. Primarily, it ensures that diverse researchers — from tenured faculty to research associates and graduate students — across a wide range of research institutions have equal access to commercialization centres and supports.

A major disadvantage, however, is the lack of consistent technology-transfer rules and protocols, which lead to inconsistencies in the "signals" sent to researchers, and wasteful competition between organizations. The system can be characterized as a "patchwork quilt" with potentially conflicting commercialization incentives for university researchers. Furthermore, individual technology-transfer operations are often understaffed and overworked. Their isolation from other organizations, as well as their need to duplicate services and promotion work, is often viewed by their target audience as a source of organizational weakness. Related to this, older technology-transfer offices often have a hard time competing with newer operations and suffer significant first-mover disadvantages. The Innovations Foundation, for example, the oldest technology-transfer operation in Canada, has faced considerable difficulty shaking its earlier reputation as a university profit-seeker, rather than researcher-ally and small business nurturer. Owners of start-up firms with earlier, formal

links to the foundation remain highly critical of the organization, despite ongoing efforts by its directors and staff to improve its outreach services and support.⁷ Perceptions of its limited effectiveness continue to circulate within the GTA health-sciences community. In an attempt to improve its public image, as well as increase its involvement in the current round of health-science start-ups, the foundation has recently partnered with a Toronto-based life-science, venture-capital firm. The details of this working relationship, including its role in a region-wide movement to encourage greater institutional coordination and networking, are described in a later section.

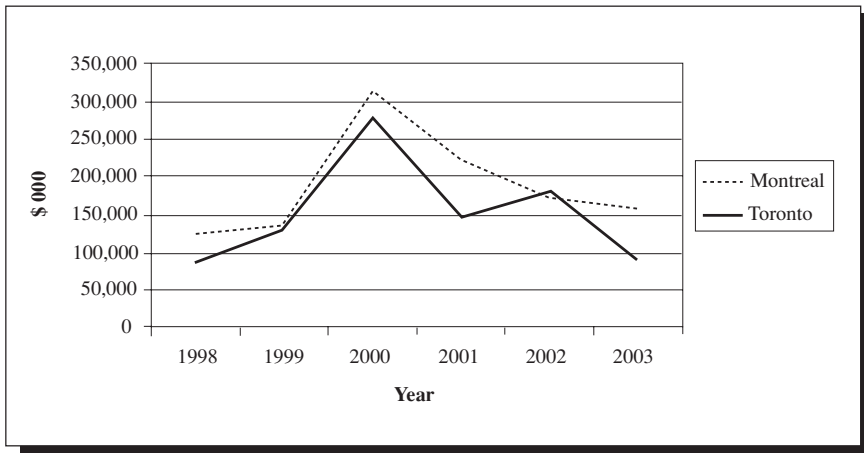
FINANCIAL MARKETS

The second set of key institutions are those associated with finance. As mentioned above, dedicated biotechnology firms receive early-stage financing for drug-discovery work from government funding agencies, including CIHR, NSERC, and the Ontario Research and Development Challenge Fund. In some cases, firms also receive support from GTA-based “angel” investors, many with formal connections to the Toronto Angel Group. In contrast, most mid-to-late stage biotechnology firms in the GTA rely almost exclusively on venture-capital markets to finance drug-discovery research. Exceptions are the hybrid firms that generate additional revenues through device sales and in some cases, contract research work. A very small number of GTA biotechnology firms are publicly traded. GTA-based dedicated biotechnology firms that trade on the Toronto Stock Exchange include Biovail, Microbix, Viventia, TM Bioscience Corporation and YM BioSciences Inc (Toronto Stock Exchange 2004).

In 2003, venture financing for dedicated biotechnology firms in the GTA totaled \$95 million (Macdonald & Associates 2004a). In most years since 1998, the city’s biotechnology industry has received substantially less venture-capital financing than Montreal. In 2001, for example, Montreal biotechnology firms received \$255 million, whereas Toronto firms only received \$150 million. In 2003, dedicated biotechnology firms in Montreal received \$160 million more in venture financing than their counterparts in Toronto (Figure 1).

A second major difference between the two cities relates to the degree of government involvement in early-stage and late-stage venture-capital markets. While available data is aggregated across all venture-capital activities and is reported at the provincial level, detailed comparisons of Montreal and Toronto also indicate notable differences in government involvement in

FIGURE 1
Life-Science Venture Capital for Montreal and Toronto, 1998–2003



Source: MacDonald & Associates (2004a).

biotechnology industry development (Niosi and Bas 2003). In 2003, over 30 percent of all venture-capital financing in Quebec came from government-owned firms or institutions, including university venture-capitals funds, like MSBi mentioned above (Macdonald & Associates 2004b).

Union and professional pension funds controlled an additional 31 percent of Quebec's venture-capital market, with the majority of this financing managed through quasi-public agencies such as Quebec's Federation of Labour. In other words, close to 60 percent of the venture financing in Quebec is provided by government-owned or government-backed agencies. In Ontario, the government plays a limited role in venture-capital markets, with only 11 percent of venture financing controlled by government-owned firms or institutions. Instead, 47 percent of financing comes from private or corporate sources, with half of these funds provided by foreign-owned venture-capital operations (only 9 percent of Quebec's venture financing is from foreign-owned sources). An additional 34 percent of Ontario's venture financing is from professional and union pension funds. However, in contrast to Montreal, these funds are managed by private investment firms. In life sciences, private fund managers include GTA-based MDS Capital, Vengrowth, and Genesys. All told, private

interests control 80 percent of Ontario's venture-capital market, with 23 percent foreign-owned.

Analysts argue that the dominance of government venture-capital funding in Montreal has made it possible for local policymakers to react quickly to shifting market conditions by coordinating across local and provincial financial agencies that are already sympathetic to the needs of home-grown biotechnology firms (Boake 2004). In contrast, the large presence of private, globally connected financiers in Toronto has made it harder for policy actors and industry advisors to rally the city's investment community to develop and support a cohesive, locally oriented strategy. It has been especially problematic in light of the recent global venture-capital crisis (*The Economist* 2004; Pollack 2004; Mendelein 2004). As one GTA firm owner explained, since 1999 there has been a shift "to the right" by venture capitalists, which has created a financial gap at the mid- or intermediate stage of drug development. This shift has also affected early-stage financing, insofar as expectations of later financial shortages have altered the investment environment for new start-ups. A further challenge relates to increased competition for financing from US biotechnology firms. In recent years, a number of established venture-capital firms in the GTA, including MDS Capital, have substantially increased their investments in later-stage firms in the United States. At the same time, the IPO (initial public offering) market in life sciences in both Canada and the United States has remained dormant since 2001, making it difficult for maturing firms to use the New York or Toronto stock exchanges as alternative sources of revenue generation.⁸ The results of Statistics Canada's 2001 Canadian biotechnology survey, which indicated that Montreal had supplanted Toronto as home to Canada's largest number of DBFs, may indeed reflect the relative ease of gaining access to finance in each region, and especially the recent financing challenges confronting DBFs in the Toronto region.

HEALTH-CARE SYSTEM

Up to this point, we have focused on the experiences of dedicated biotechnology firms. In this section and the next, we introduce two more groups of life-science firms that operate in the GTA, medical and assistive technologies (MAT) manufacturers and pharmaceutical drug-makers. As we indicated in the introduction, MAT and pharmaceutical firms are key players in the GTA biomedical complex. Like dedicated biotechnology firms, their evolution has been

shaped by life-science support institutions in the region. However, important differences exist between these groups and dedicated biotechnology firms that shape the kinds of support institutions that are central to their development.

First, MAT firms and drug-makers are suppliers of goods and services to teaching hospitals and medical practices in the GTA and therefore are most directly affected by policy decisions related to health-care provision and spending. In contrast, a large number of the region's DBFs are still at the early stages of product development and as such have no products or technologies to sell to health-care providers. Even for mature biotechnology firms in the region, direct sales to hospitals, both inside and outside the region, remain limited. Rather, revenues are typically generated through licensing agreements with the global headquarters of pharmaceutical firms in the United States or Europe. Related to this, a high priority for DBFs in the GTA is securing drug approval in the United States and Europe. Therefore, we can include agencies like the Food and Drug Administration in the United States in our institutional analysis of dedicated biotechnology firms in the GTA, and for that matter, a large number of home-grown MAT firms. Similar cross-border connections exist between GTA biotechnology firms and university research institutions in the United States and Europe that serve as key centres of knowledge production.

A second difference relates to financing. As mentioned earlier, DBFs rely extensively on seed and venture capital to finance risky *de novo* drug-discovery work. In contrast, MAT and pharmaceutical firms in the GTA depend almost exclusively on product sales to generate working capital. For Canadian divisions of multinational pharmaceutical firms, as well as home-grown generic pharmaceutical firms, sales to GTA-based hospitals are especially important. MAT firms, particularly those that are locally owned, generate additional revenue through product sales in the United States and Europe. Still, as we shall see below, face-to-face interaction with hospital practitioners (i.e., doctors, nurses, technicians, and physical therapists) in the GTA remain a key source of innovative ideas, although this form of knowledge-sharing usually results in incremental product development and modification. Furthermore, this exchange usually takes place within a hospital rather than a university setting, leading some industry analysts to describe the relationship as "little r, big D," that is, development rather than research-intensive.⁹ This is quite different from the relationship described above involving university researchers and dedicated biotechnology firms. DBFs, laboratories and research centres located within the university setting play a central role in *de novo* drug-discovery

work, that is activities that are “big” on the R (i.e., research-intensive). Here too we find greater use of formal commercialization supports at both the university and hospital levels when compared to the MAT sector.

The Purchasing Power of Ontario's Hospitals

The GTA is home to over 20 publicly funded and managed teaching hospitals. This includes, among others, the three-hospital University Health Network (Toronto General, Toronto Western, and Princess Margaret), as well as Sunnybrook and Women's, Sick Children, and St. Michael's. In addition, there are a large number of public and private community clinics and regional health-care centres, over 50 at last count (Greater Toronto Marketing Alliance 2003). Combined, these facilities help to make the GTA the largest health-care centre in Canada and fourth largest in North America (Niosi and Bas 2003). In addition to helping improve the quality of life for GTA residents, the region's health-care institutions also play an important role in the regional economy insofar as they annually purchase more than \$500 million in medical equipment and related inputs (excludes prescription drugs) (Goodhand 2005).

Two sets of MAT firms reside in the region to meet local demand for non-therapeutic technologies.¹⁰ The first group, large multinational MAT firms, including Baxter, Johnson & Johnson, Medtronic, Agfa and GE, focuses on high-end, bulky machinery, and non-specialized or standardized goods such as intravenous drips, syringes and basic surgical instruments. Until the 1990s, multinational MAT firms manufactured medical technologies in the GTA. Many originally opened branch plants in the region in order to benefit from Canada's access to protected Commonwealth markets, including the United Kingdom. Trade liberalization and the search for lower-cost production sites, however, resulted in the closure of many of these Canadian manufacturing operations. Today, the GTA instead serves as a Canadian sales and distribution base for most of these firms. For a growing number of firms, it is also the North American centre for product testing, clinical trials, and modification, due in part to the high density of teaching hospitals and frequent, almost daily, interaction between technology users and health-care researchers.¹¹ Today, there are 98 multinational MAT firms in the GTA, employing approximately 9,000 workers (Health Technology Exchange 2004a).¹²

Procurement officers at Toronto area hospitals, under strong pressure to constrain costs at a time when medicare budgets are under intense pressure,

tend to favour contracts with multinational companies (MNCs) as these firms offer volume discounts and bundles of products in exchange for long-term contracts. Policy analysts have grown increasingly critical of this development, arguing that the overwhelming focus on cost containment in hospital purchasing (and the resulting dominance of MNC suppliers) is limiting sourcing opportunities for a second category of GTA MAT firms: small, home-grown or “indigenous” operations (see, e.g., Martin 2003). Our interviews do reveal a strong purchasing bias toward foreign-made and imported technologies by the GTA’s hospital procurement offices. They also suggest a conscious move by MNCs to strengthen their position in regional markets by offering additional discounts to regional hospitals that use their e-business and e-cataloging systems and logistics and warehousing partners.

Despite these efforts, however, the region’s hospital-procurement system still remains *porous* enough to allow for and encourage considerable local product penetration. While bulky and standardized goods continue to be centrally purchased, specialty and customized products are ordered on request by front-line medical practitioners and professionals. According to one industry expert, even in the case of the GTA’s University Health Network, considered the most centrally coordinated purchasing systems in the region today, approximately 50 percent of all products are still purchased on request by practising physicians, nurses, and occupational therapists.

This bifurcated purchasing system has not gone unnoticed by smaller, indigenous manufacturers in the GTA, a group that today numbers over 180, making this the largest concentration of device manufacturers in both Ontario and Canada (Health Technology Exchange 2004a; Goodhand 2003, 2004). Owners of these firms take advantage of decentralized procurement channels not only to distribute imported niche products but, more importantly, to identify and respond to local demand for specialty manufactured goods and customized equipment. Many of these firms started out as health-care product distributors, medical equipment repair and maintenance shops or contract manufacturing operations (in some cases with earlier links to Ontario’s automotive and information technologies industries) before moving into medical product manufacturing and design. In contrast to MNCs, these firms have limited formal contact with senior hospital executives and procurement officers. Rather, sales and product development decisions reflect ongoing, in-person exchanges with front-line health-care practitioners and technology users. While MNCs also benefit from regular contact with front-line practitioners, exchanges

between these groups are often brokered through and mediated by senior hospital administrators. In contrast, smaller, indigenous firms tend to build on existing, informal personal and professional networks in order to develop and retain their local customer base.

Interestingly, many indigenous MAT firms from the GTA claim they have had an easier time accessing formal procurement channels in Montreal than in their home market. This is likely a reflection of Quebec's decision to extend the life of an earlier federal requirement that encouraged hospitals to purchase Canadian-made technologies, an additional example of Quebec's *dirigiste* or government-centred system. While local content requirements were recently discontinued in the province (due in part to international trade regulations), their prolonged use enabled older, home-grown firms to negotiate additional, high-volume orders with Quebec hospitals and, in the process, establish a local reputation for quality production and customer service at an early stage in this relationship. At the same time, they likely created opportunities for these same firms to identify and approach higher-level policy advocates and sympathizers. Finally, provincial language requirements have led many GTA-based MAT firms to establish satellite sales and repair operations in Montreal. In contrast, multinational MAT firms have been more successful in their efforts to recruit qualified, bilingual staff to Ontario and therefore have preferred to service French-language markets from their GTA base. The fact that Montreal is home to fewer multinational MAT operations than Toronto has only helped to increase the visibility and relative bargaining power of smaller, home-grown medical technology firms in that market.

While emphasis on front-line exchanges by these same firms has undoubtedly helped to foster client loyalty in the GTA, it has also acted to reinforce their isolation from higher level decision-making circles, including those involving senior hospital administrators, strategic planners and health-care ministers. This poses an additional challenge when we consider a recent decision by Ontario hospitals to partner formally with MNCs in order to coordinate purchasing of both standardized and customized medical products. These efforts are explicitly designed to target front-line practitioners, not just high-level administrators, by using "educational" support and sessions to convince doctors and nurses of the benefits of systemwide coordination of product purchasing and product information exchange, including sharing knowledge about specialty products and producers (GHX 2002). This development is itself part of a grass-roots effort to develop a regional governance structure or network. In contrast

to other provinces that use provincial health-care authorities to manage hospital buying centrally on a regional basis (e.g., Quebec, Alberta, British Columbia, and the Maritimes), Ontario's regionalization efforts have been spearheaded by urban-based hospitals, including the GTA's University Health Network, with support from large private sector firms, such as GTA-based multinational MAT operations and "global" e-business solution centres (King 2004). The Ontario government supports this hospital-driven solution, in part because it is designed to reduce provincial health-care costs by enhancing the efficiency of hospital purchasing. This bottom-up initiative also allows provincial authorities to avoid imposing regionalization, an earlier, controversial policy recommendation that encountered considerable resistance from the Ontario Hospital Association.

The challenge now is for smaller, home-grown firms to find a way to use their existing front-line contacts to access these regional buying networks or "clubs." Realistically, success in this area will require greater collective action, including deliberate measures by the provincial government to ensure equal access by smaller, indigenous firms. Without this, there is a high probability that MNCs will align themselves with customized product manufacturers from outside Canada to fill out their product lines. As we shall see below, this challenge has not gone unnoticed by key industry representatives and especially, small-firm advocates from the GTA.

INDUSTRIAL GOVERNANCE

The high visibility of multinational MAT firms is reinforced through GTA-based industry associations. MEDEC, a national association of medical device technologies firms, has long been the preferred lobbying organization for most Canadian-based MNCs. The association was founded in 1973 by Alan Tuxworth, also its first executive director (MEDEC 1998). Active governing board members today include executives from global MAT giants, Johnson & Johnson, Baxter, Alcon, Guidant, Bayer and Medtronic (ibid. 2004). The organization has one Canadian office, located in downtown Toronto.

Smaller, home-grown MAT firms do participate in the organization and in recent years, a handful of these firms, including Baylis and TM Biosciences, have managed to secure seats on MEDEC's governing board. In general, however, smaller member firms are less active (and less vocal) in the association. Unlike their larger, foreign-owned counterparts, these firms often lack the resources (both time and money) and personnel to attend all informational and

networking events and strategic planning sessions. Rather, they pick and choose those activities and gatherings that most reflect their immediate concerns and needs. In some cases, smaller firms also limit MEDEC membership to years immediately following periods of high growth and/or financial stability.

Home-grown firms in the GTA are more likely to be active members of the Association of Ontario Medical Manufacturers (AOMM), a provincial association created in 1995 to represent smaller-sized, Canadian-owned medical technologies producers (AOMM 2005). Group meetings and events are scheduled to reflect financial and staffing constraints of its 60 or so member firms. Informal peer support and mentoring sessions are organized to encourage inter-firm and inter-organizational exchanges in-between quarterly networking events. While AOMM provides some lobbying support, its central mission is to help facilitate firm growth. It does so by assisting its members with trade-show planning, as well as brokering exchanges between member firms and federal research and technical assistance agencies. One example is a joint technology seminar with the National Research Council's Industrial Materials Institute that was held in July 2004 (*ibid.* 2004).

AOMM offices are based in Markham, in the northern "905 belt" of the GTA. Association officials often promote the organization as a small-firm alternative to MEDEC. However, our interviews indicate that member firms tend to view these two organizations as complementary, rather than in conflict. Participation in MEDEC, even for short periods of time, allows small firms to keep track of changing industry regulations and policies, at both the national and international levels. Information on US regulations is especially valued, as many home-grown MAT manufacturers from Ontario also sell their products to US-based hospitals and health-care clinics.¹³ For more active home-grown members, MEDEC also offers a direct communication to key provincial and federal agencies.

The willingness by smaller MAT manufacturers to view co-existence with MNCs as beneficial partly reflects the origins of many home-grown GTA operations. Of the 35 home-grown firms we interviewed, six were started by former MNC employees. In most cases, firm owners gained valuable knowledge of the industry through this earlier experience and, in an effort to deepen their knowledge of market and regulatory trends, have worked hard to maintain relationships with current MNCs executives and employees. In some cases, restructuring efforts by their former employers have also opened up opportunities for home-grown firms to absorb specialized manufacturing and

service divisions being hived off from the MNCs. Similar positive spillovers have been identified by MAT repair and maintenance operations in the region. Here again, corporate restructuring across the MNC community has enabled these service firms to integrate backwards into product manufacturing and by “picking up” previous MNC clients (and, in some cases, skilled workers) in the GTA.

As new industry challenges emerge that threaten to destabilize both home-grown and multinational MAT subsectors in the GTA, strategic actors from the region are taking steps to formalize intra-industry relations. To use a biological metaphor, these actors are essentially shifting the terms of the relationship from one of “commensalisms” — whereby small, home-grown firms are simply feeding off the scraps of large MNCs — to one of mutually beneficial interdependence. One way they are doing so is by convincing Canadian-based MNC executives that local partnering is not only useful for product modification and new client service development but, more importantly, can be used to send a powerful message to global headquarters that Canadian operations are valuable and worth maintaining, especially during the next wave of corporate restructuring.

Big Pharma’s Canadian Battleground

The GTA not only hosts the largest number of brand-name pharmaceutical firms in Canada (23 firms according to one industry source), but almost two-thirds of Canada’s generic drug-making operations as well. This second group includes Canada’s two largest generic drug manufacturers: Apotex, a home-grown firm established in the GTA in 1974, and Novopharm, another home-grown establishment, founded in the late 1960s and recently acquired by Israel’s Teva Pharmaceuticals. Other important generic manufacturers in the region include Israel’s Taro Pharmaceuticals, which opened facilities in the GTA in 1984, ratiopharm, a GTA-based subsidiary of Europe’s ratiopharm GmbH, and Cangene, a Manitoba-based firm with research, manufacturing, and marketing facilities in the GTA. Brand-name pharmaceutical firms in the Toronto area include foreign-owned giants, AstraZeneca, GlaxoSmithKline, Eli Lilly, Bayer, Amgen and Roche, as well as home-grown biopharmaceutical firms: Biovail, Hemosol, and Lorus Therapeutics Inc.

Montreal is also a major centre of pharmaceutical research and manufacturing. It is a close second to the GTA, hosting 18 brand-name drug-makers in Canada. Where it differs from Toronto, however, is in the area of generic

drug-making. The GTA is home to 12 generic pharmaceutical firms and related suppliers. In contrast, only five of these operations exist in Montreal. The GTA's locational advantage is not simply a result of its larger health-care system, but also Ontario's drug formulary or government-managed drug reimbursement program. In contrast to Quebec, Ontario's health-care agency required medicare patients to purchase generic substitutes as early as the 1970s (Gorecki 1993; Jenish 2003). This provision was used to garner political support for extending universal health-care coverage to the province in the 1970s and by illustrating the provincial government's serious commitment to lowering public health-care costs.¹⁴ Quebec's drug formulary has instead favoured prescription drug-makers, a deliberate strategy used by policymakers to attract large pharmaceutical research and manufacturing facilities to the region. Until this year, brand-name drug-makers have enjoyed a captive market in Quebec thanks to the province's "15-year rule." Under this policy, brand-name drugs are guaranteed medicare approval for 15 years, regardless of the existence of a generic substitute (Dougherty 2002). Patients with medicare drug coverage in Quebec are permitted to use generic drug substitutes. Brand-name drug-makers, however, benefit from patient inertia, as well as the public perception that generic drugs are unsafe or inferior. Brand-name drug-makers have also benefited from Quebec's more generous tax exemptions on research activity and job-creation.

In contrast to the MAT sector, the co-existence of these two sets of drug-makers in the GTA, brand-name and generic, is more adversarial in nature, with inter-group tensions and rivalries visible at the associational level. The GTA is home to the national headquarters of both Canada's generic *and* brand-name pharmaceutical associations. Rx&D, the country's brand-name pharmaceutical association, was established in 1914 under the original name, Canadian Association of Manufacturers of Medicinal and Toilet Products. Today, the organization represents over 50 brand-name drug-makers and related suppliers throughout the country (Rx&D 2004). Its rival organization, the Canadian Generic Pharmaceutical Association (CGPA) was founded in the 1980s to represent Canada's growing generic drug-making industry. Today, CGPA represents 12 generic pharmaceutical firms in Canada, as well as nine input suppliers, and contract research and manufacturing operations.

Both organizations use their GTA offices to launch aggressive lobbying and public awareness advertising campaigns. Rx&D, for example, emphasizes the research investments of its member firms, as well as their commitment to creating high-paying research and manufacturing jobs in Canada. In contrast,

CGPA focuses on the cost savings that its member firms provide provincial governments and Canadian taxpayers, as well as public awareness campaigns on generic drug safety and efficacy. In recent years, the CGPA has also emphasized the generic sector's growing research commitment, including Apotex's endowment of \$2 million in December 2004 (\$7 million in total pledged as of 2004) to the University of Toronto (Kelly 2004) and the firm's ongoing drug discovery work in hematology and skin replacement (Apotex Inc. 2004). Despite this sometimes bitter public battle for the attention of policymakers, unexpected overlaps do exist between these two groups. Ratiopharm, an active CGPA member, is a subsidiary of brand-name giants, Roche and GlaxoSmithKline, and was acquired in the 1990s to manufacture generic versions of brand-name drugs with soon-to-expire patents (ratiopharm 2005). In 2003, ratiopharm's president was appointed chair of the CGPA (CPGA 2003).

As in the case of drug-makers and medical device manufacturers, dedicated biotechnology firms also have considerable choice when it comes to formal networking and lobbying support. A significant number of the city's 60 or so DBFs participate in the Toronto Biotechnology Initiative (TBI), an industry association created in 1989 to facilitate inter-firm and inter-organizational networking. In order to encourage participation by early-stage biotechnology start-ups and other firms that have limited financial resources and personnel, many TBI events are also open to non-member firms. Early-stage start-ups instead have strong initial ties to specialty medical associations, a decision that often reflects their founders' existing connections to specific medical disciplines or areas of health-science research, like oncology, dermatology or neurology. In contrast, later-stage biotechnology firms in the GTA tend to have multiple affiliations with local and non-local associations. In some cases, late-stage firms also belong to region-specific trade groups that are not focused on the life sciences. This is especially true for biotechnology firms in the western GTA, many with formal membership ties to the Mississauga Board of Trade. These associations play an important role in industry-wide coordination efforts and in representing their member firms at key policy and strategic planning events at both the municipal and provincial levels.

DIVERSITY: ORGANIZED OR NOT?

As we have seen in the previous sections, Toronto's life-science complex includes not only a diverse array of subsectors and firms, but also a diverse set of

institutions and institutional actors. This institutional diversity has helped to jump-start the region's life-science industry, with the city's high concentration of hospitals attracting a critical mass of big pharma operations (both brand-name and generic), clinical trial specialists and laboratory service firms throughout the second half of the twentieth century. In the past two decades, this has also opened up growth opportunities for more research-intensive, smaller operations in biotechnology, and medical and assistive devices. Interestingly, the contribution of institutional diversity to the development of the region's life-science industry has not been fully explored or recognized by industry analysts. In fact, it is often viewed as a major hindrance to sustained industry growth, as it results in a lack of "clear focus" for the region (Voyer 2001). This perspective is reiterated in numerous case studies and analyses of Toronto and often reflects comparative studies that not only highlight the benefits of Montreal's style of economic development, that is, well-coordinated and centrally-managed, but encourages its diffusion to the GTA (Graytek 2004; Mendelein 2004).

Like life-science clusters everywhere, Toronto's life-science complex is subjected to challenges that reflect larger macro events and global shifts. The region's highly diversified institutional environment fosters institutional fragmentation and decentralization that have made it increasingly difficult for governance leaders to identify and rank areas of weakness that need greater policy attention. This fragmentation has also made identification and "scale-up" of successful local solutions a slow-moving process. Still, calls for a clear, focused, and immediate policy response and specifically, the adoption of Montreal's centralized model of institutional governance, ignore the fact that initial moves toward centralization have demonstrably worked against smaller, home-grown firms and in favour of Toronto-based MNCs: as we have indicated above, the latter are more organized and have been more effective in shaping the discussion about health-care reform and coordinated hospital procurement. Also overlooked is the emergence of a new set of strategic actors (described below) that are not only aware of the schism (and power imbalance) between MNCs and indigenous firms, but are actively creating opportunities for small-firm representation by breaking down existing institutional boundaries and, in the process, building networked forms of industry support. What makes these emerging support networks so unique is their growing use by *multiple* categories of firms, large and small, foreign and domestic, and more specifically, their success in facilitating inter-group dialogue and collaboration.

As we shall see below, network promoters include a former director of MEDEC, a research scientist with formal connections to brand-name pharmaceutical firms and a new generation of life-science investors who learned their trade as former employees of established investment firms. These actors use their first-hand knowledge of existing institutional supports to design and promote bridging structures that appeal to a wide range of life-sciences firms. At the same time, they leverage their credibility within the large firms and financial communities to advocate for more inclusive forms of institutional support.

Equally important is the ability of these same actors to devise networking strategies that complement, rather than clash with, Ontario's existing business culture. Obstacles to collective action, especially among smaller, indigenous firms, have been identified in earlier studies of the region and include a local business culture that is "dominated by the ideal of rugged individualism, self-sufficiency and competitive rivalry" (Gertler and Wolfe 2004, p. 114). This business "ethic" is not only common among smaller life-science firms, but is shaped by and acts to reinforce institutional fragmentation in the GTA. To use Albert Hirschman's (1970) terms, small life-science firms in the city prefer to use an "exit" rather than "voice" strategy when encountering less than satisfactory forms of support — be it research-related, marketing-based, financial or associational. It is not surprising then, that these same firms also prefer the option to mix-and-match their institutional supports and when necessary, disengage from a given institutional environment altogether.

In this light, networking structures are designed to monitor firms more effectively as they move in and out of this institutional environment. At the same time, they work to facilitate greater institutional "loyalty" by encouraging smaller firms to vocalize their concerns about a given set of supports and in turn, become more active in the process of institution-building and strengthening. For networking alternatives to be attractive to home-grown firms, however, their promoters have had to convince business managers that their participation is a logical extension of individualism. Montreal-style industrial planning and upgrading —imposing inclusion from above through strong government involvement — are not likely to work in the Ontario environment and may actually risk driving away or alienating the very industry sub-groups they seek to support.

This is not to say that policymakers in Ontario are absent from the process of life-science network formation. In fact, quite the contrary, as we shall see with the BCIP initiative mentioned below. Rather, their initial approach

has been more cautious and reflects a series of formal discussions on how to facilitate and enhance life-science innovation in the region. This has opened up the possibility for network promoters to gain access to key policy-making circles and in the process, encourage institutional actors to consider new and novel ways to facilitate interaction across subcategories of firms. At the same time, the initial hesitation by local policymakers to adopt a single, unified plan of action has also created opportunities for network promoters outside government to allow small firms into the formal discussion, by illustrating the ways that their participation can help direct and shape the policy-making process and, ultimately, create the conditions for sustained, firm-level growth.

While a detailed review of network formation is beyond the scope of this chapter, three examples are presented here. The first is Health Technology Exchange (HTX), a non-profit, member-based organization that was established in 2001 to help develop and promote Ontario's home-grown MAT industry (Health Technology Exchange 2004*b*). HTX has strong links to Toronto-based hospitals and was originally housed at York's Bloorview MacMillan Hospital. The organization receives financial and institutional support from Ontario's Ministry of Economic Development and Trade (MEDT), as well as Ontario's MAT industry associations, MEDEC and AOMM. HTX provides a Web-based "match-making" service that member firms use to identify local area consultants, input suppliers, and industrial designers and engineers. HTX also circulates information about industry trade shows, funding sources and health-care and procurement policies. Member firms are encouraged to use the HTX Web portal to develop strategic alliances with other MAT firms in related technology areas. Related to this, HTX mediates exchanges between home-grown firms and Ontario-based MNCs. The idea for using the organization to bridge these two communities initially came from HTX's founder, Peter Goodhand, and reflects his earlier connections to MEDEC and the MNC community. In a recent HTX-brokered exchange, a home-grown, Toronto-based endoscope repair shop negotiated a deal to acquire a specialized production facility from a local division of a multinational MAT firm. The MNC was looking to divest itself of its Canadian endoscope division as part of a global restructuring effort. The local repair shop benefited greatly from having the option to absorb skilled endoscope manufacturers from the MNC and also continue to service the MNC's Canadian clients, including large Toronto-based hospitals.

A second example is the Western GTA Biotechnology Consortium (WGBC). WGBC was established in 2001 to create a strategic development

plan for the region's life-science industry. The organization is made up of key representatives from industry, university, and government (both local and provincial) and is one of 11 regional consortia that participate in MEDT's Biotechnology Cluster Innovation Program (BCIP). BCIP was initiated in 2003 to identify opportunities for government involvement and investment in Ontario's life-science industry. WGBC stands out from other BCIP consortia in its attempt to use the strategic planning process to forge alliances between two categories of life-science actors: home-grown biotechnology firms on the one hand and MNC pharmaceutical firms on the other. The idea to formally link these two groups of life-science firms grew out of an earlier discussion by WGBC advisory board members — a diverse group that includes executives from two home-grown biotechnology firms (Biovail and NoAb Biodiscoveries) and two MNC pharmaceutical operations (AstraZeneca Canada and Merck Frosst Canada). The consortium's founder and director, Ulli Krull, has helped to translate this shared goal into formal bridging mechanisms by drawing on his own connections to both communities: currently he is director of the University of Toronto's biotechnology Master's program and holds the AstraZeneca Chair of Chemical and Physical Sciences at the University's Mississauga campus. Mid-stage biotechnology firms have initiated the alliance-formation process by providing contract research services to locally-based MNC pharmaceutical firms. For their part, large pharmaceutical firms in the western GTA are starting a search for local biotechnology partners and are actively promoting the concept of Canadian partnering to their global headquarters.

A third and final example involves a GTA-based venture-capital firm. The firm was founded in the late 1990s to focus on the life-science industry and is staffed by fund managers who have earlier employment experience at older venture-capital firms in the region, including MDS Capital. These second-generation fund managers have been instrumental in forging connections across academic disciplines and by encouraging U of T scientists to draw on diverse areas of expertise to create biotechnology-MAT hybrid firms. Related to this, the venture-capital firm is working to strengthen some of the existing institutional supports in the region by acting as a mediator between key institutional and industrial actors. One example includes recent efforts to elevate the status of U of T's Innovations Foundation within the local life-science community. The venture-capital firm is doing so by inviting technology-transfer officers to attend monthly networking events that target university scientists interested in identifying commercial uses of applied research. During these

events, technology-transfer officers have an opportunity to share information about their ongoing efforts to improve their commercialization system and also to feature successful life-science firms that have benefited from their support. As mentioned earlier, the Innovations Foundation has not only struggled to overcome its past reputation, but it now competes with new technology-transfer operations that seem to benefit from local knowledge of the organization's past mistakes. By participating in this networking event, the foundation benefits from having regular access to university researchers and future life-science inventors.

CONCLUSION

We began this chapter by noting the distinctive geography of innovative economic activity in the life sciences, suggesting that local institutions play a key role in shaping this evolution. In the subsequent analysis of the GTA, we have argued that this institutional architecture is strongly distinct from that of Canada's other biotechnology clusters, most notably the Montreal region. In comparison to Montreal, Toronto's multi-level institutional architecture is fragmented and decentred, producing a diversity of sometimes competing, sometimes complementary organizations. While this regional innovation system has been successful in some ways, yielding Canada's largest concentration of economic activity in life sciences, it has performed less well in other aspects: most notably in its smaller volume of entrepreneurial start-up activity in DBFs compared to Montreal. We have also documented the recent emergence of a new generation of local institutions for associative governance of this diverse set of economic activities. Many of these have been established with the goal of enhancing the local support structure for commercialization and entrepreneurial start-ups, as well as encouraging closer collaborative research between large MNCs and home-grown firms. As such, this institutional evolution represents something of a "turn" in the region's recent economic history. While hopes remain high that this new level of activism and civic entrepreneurship will bear fruit quickly, experience in other settings suggests that such change will come slowly, and will be contested and unpredictable. Twenty years from now, the current era may be viewed as a watershed in the region's evolution, or a period of interesting but short-lived experimentation. We look forward to future analyses with considerable interest.

NOTES

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¹We use Friedland and Alford's definition of institutions here, as the "supraorganizational patterns of activity through which humans conduct their material life in time and space, and symbolic systems through which they categorize that activity and infuse it with meaning" (Friedland and Alford 1991, p. 232).

²This is based on Ontario health research funding that includes CIHR, selected categories of CFI, NSERC, and ORDCF, OIT (estimated), Genome Canada (Round 1), and 2000 NIH funding in US dollars.

³Quebec-based scientists published 2,000 biotechnology related articles during the same period, accounting for 28 percent of the national total. Percentages for British Columbia and Alberta were 14 and 12 percent respectively (Industry Canada 2004).

⁴These include: Baycrest Centre for Geriatric Care, Bloorview MacMillan Children's Centre, Centre for Addiction and Mental Health, Hospital for Sick Children, Mount Sinai Hospital, St. Michael's Hospital, Sunnybrook and Women's College Health Sciences Centre, Toronto Rehabilitation Institute and University Health Network, which includes Toronto General, Toronto Western, and Princess Margaret Hospitals.

⁵Allelix founders and former executives continue to play a lead role in the development of the GTA biotechnology industry through their active participation on industry task forces and advisory committees. They were instrumental in creating early linkages between industry representatives and key provincial and federal policymakers and also helping to mobilize industry-wide support for the MaRS project, a life-science convergence centre located in downtown Toronto. Interestingly, the initial impetus for the MaRS project came from Allelix' earlier failure to locate affordable, downtown laboratory space following its merger with NPS Pharmaceuticals (Voyer 2001).

⁶This information was provided by the Office of Technology Transfer at the University of Toronto and is based on a 2003 survey of U of T-affiliated biomedical start-ups.

⁷Based on our interviews with firm owners.

⁸There are recent signs that the IPO market may again be open to biotechnology firms. According to financial analysts, 11 biotechnology firms filed initial public offerings with the US Securities and Exchange Commission in September 2003. An additional six firms were expected to follow their lead. While most of these operations are based in the US, Neurochem—a Montreal-based firm with financial ties to BioChem Pharma—is included on the list (Webb 2003).

⁹A recent study of Waterloo's ICT industry has identified a similar process of incremental product development resulting from ongoing client-supplier or technology "user-producer" interaction. See Bramwell, Nelles and Wolfe (2004).

¹⁰Prescription drug-makers will be introduced in the next section.

¹¹This development also reflects a Canadian advantage over the US, where HMO-style health care encourages greater distance between health-science research and medical practice.

¹²Employment figures are approximate and based on the mean number provided in the HTX database for each firm.

¹³MEDEC-sponsored workshops on Canadian and US regulations also reflect MNC interest in having policy convergence or “standardization” across North America.

¹⁴In the 1970s, Ontario had one of the more successful private health-care systems in Canada, including widespread private insurance coverage. The success of this private model created additional challenges for justifying greater government involvement in provincial health care. Generic drug purchasing was a central part of the government’s campaign to assure Ontario residents that health-care costs (and thus provincial tax rates) would be carefully monitored and managed.

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