

EVERY DAY WE ASK OURSELVES WHAT IF?

COLLABORATE AND DISCOVER: ONTARIO'S BIOPHARMA CLUSTER



ONTARIO'S TRACK RECORD OF DELIVERING INNOVATIVE ANSWERS TO 'WHAT IF' QUESTIONS IS ENVIABLE. TODAY WE ARE SETTING THE PACE THAT IS PRODUCING ANSWERS TO NEW 'WHAT IF'S' – ANSWERS THAT WILL CHANGE THE GLOBAL INDUSTRY OF DELIVERING TREATMENTS AND CURES TO PEOPLE AROUND THE WORLD.

THE KEY TO ONTARIO'S SUCCESS?
COLLABORATE AND DISCOVER.

WHAT IF ONTARIO RECEIVED GLOBAL RECOGNITION FOR ITS CAPACITY TO COLLABORATE? WE DID.

In spring 2008, the Ontario Institute for Cancer Research (OICR) was selected to coordinate the ambitious agenda of the International Cancer Genome Consortium (ICGC). This international effort, on the same scale as the Human Genome Project while producing 25,000 times more data, will bring together researchers from 10 countries to explore the genetic mutations that underlie 50 types of cancer. The hope is that a global assault will halt the world's leading killer by discovering new ways to diagnose, treat and prevent the disease.

As the only sub-national member of the consortium, Ontario's proven capacity for collaboration won the day for this high-profile assignment.

A PERSONAL MESSAGE FROM THE PREMIER OF ONTARIO



On behalf of the Government of Ontario, I am delighted to extend warm greetings to the readers of the Biopharma Cluster Report.

As Premier of a province that enjoys a distinguished history of innovation, I am proud to introduce this report — one that flows from a fruitful collaboration between the Government of Ontario and the MaRS Discovery District, a unique community representing the best and brightest minds in research and innovation.

Ontario is home to a thriving biopharmaceutical economy — one that attracts researchers, investors and scientists from all over the world. And our government remains committed to delivering an integrated innovation strategy, to supporting researchers and their drive to succeed, and to ensuring that innovative ideas become a reality.

One of our most recent success stories is the International Cancer Genome Consortium — one of the largest global research efforts yet — which will work with the Ontario Institute for Cancer Research to collect and share research data with scientists around the world. Ontario's role in co-ordinating this important work is a reflection of the world-class expertise we possess, and our ability to push the boundaries of knowledge to develop new technologies and therapies.

Many companies have already discovered that Ontario offers a highly cost-competitive growth environment for biotechnology. A robust economy and a strong and dynamic life sciences sector are attracting businesses and investors who see the value in supporting the work of our leading-edge researchers and scientists.

I am pleased to share this report showcasing Ontario's strengths, vision and leadership in life science. Working with partners around the world, we are developing the breakthroughs that are transforming the world's biopharmaceutical industry.

A handwritten signature in black ink, reading "Dalton McGuinty".

Dalton McGuinty, Premier of Ontario

A MESSAGE FROM THE MINISTER OF RESEARCH AND INNOVATION

Ontario is home to the fastest growing biomedical cluster in the world.

In every field – cancer research, stem cells, diabetes, cardiovascular disease, and more — Ontario is leading the way by attracting world-class researchers, key investors, and innovative companies to help turn research into reality.

Multinational biopharmaceutical firms currently invest about \$550 million annually in research in Ontario, and we are actively partnering with industry to grow that investment even further. Through our recently announced Ontario Innovation Agenda, our province has provided a blueprint for strategic government investments so we can act as a catalyst for innovation and commercialization. Our plan to seize global opportunities is based on proven business practices, and was created with assistance from leaders in industry, research institutions, hospitals, academia and the investment community. That is how we are making Ontario the number one place to invest in the world's bioeconomy.

The Government of Ontario's \$150 million Biopharmaceutical Investment Program is an economic development initiative focused on increasing the amount of biopharmaceutical research and advanced manufacturing activity that is happening in our province. It is the first component of our \$1.15 billion Next Generation Jobs Fund strategy, and is aimed at attracting new or enhanced biopharmaceutical investments in Ontario. By reducing the risks involved in research and development or advanced manufacturing our Biopharmaceutical Investment Program will help make Ontario a choice for innovation-driven companies.

We are also helping to strengthen the atmosphere for innovative businesses here in Ontario. We are doing this through enhanced tax exemptions and credits for scientific research, experimental development, and the commercialization of intellectual property. Our ultimate goal is to build an economy that delivers market-driven product, by creating a favourable environment for collaboration, innovation and investment.

Ontario has a proven plan to develop and deliver biopharmaceutical opportunity. We have committed the resources to making this vision a reality. Simply put, there is no better place in the world to do business than Ontario.



John Wilkinson, Minister of Research and Innovation



A MESSAGE FROM THE MINISTER OF ECONOMIC DEVELOPMENT AND TRADE



For years, Ontario has been an economic leader, with a long history of strategic government partnerships with industry. Manufacturers initially come to Ontario for our access to market and our business climate; they stay because of the quality that is achievable in products and customer service.

The Ontario government places great importance on 'value-added' manufacturing leadership. Our commitment to helping Ontario's manufacturing industries grow and compete internationally is demonstrated in several strategic investment programs. These include our Advanced Manufacturing Investment Strategy, the Next Generation Of Jobs Fund (NGOJF), and new corporate tax breaks announced in January 2008.

Ontario is partnering with companies that invest in people and in innovation capacity as a competitive strength and as an enabler of long term sustainability. Our Next Generation Of Jobs Fund is taking this to a new level by acknowledging the role of innovation as a key economic driver of today and the future.

Sustainability also applies to environmental practices. Responsible industries want to conduct operations using cleaner technologies and in jurisdictions that support efforts to manage environmental footprints and energy consumption. This is a central element of Ontario's NGOJF.

Ontario has chosen to focus on a few key areas to drive innovation, develop our economy and lead the world in the bioeconomy. Some of our focus areas include clean technologies, such as fuel cells. Other areas include digital media and advanced health technologies, including cancer research, stem cell discoveries and degenerative diseases.

Sincerely,

A handwritten signature in black ink that reads "Sandra Pupatello". The signature is written in a cursive, flowing style.

Sandra Pupatello, Minister of Economic Development and Trade

WHAT IF WE COULD CREATE A LAUNCH PAD FOR COLLABORATION AND INNOVATION? WE HAVE.

Ontario, Canada is well positioned to become one of the most innovative economies in the world. We offer a creative environment, a diverse culture, a highly skilled workforce and a strong track record of research and commercial success.

Year after year, Canada has consistently been ranked by the United Nations and others as one of the top 10 countries in the world to live, work and prosper. As Canada's largest province, and home to its largest city (Toronto), the Province of Ontario is a magnet for world-class talent, and innovative companies.

ONTARIO'S INNOVATION AGENDA

While much of Ontario's past economic success points to a history of innovative thinking and practices, we are not resting on our laurels. Aggressive strategies, and a relentless need for focus, are critical in today's hyper-competitive global economy.

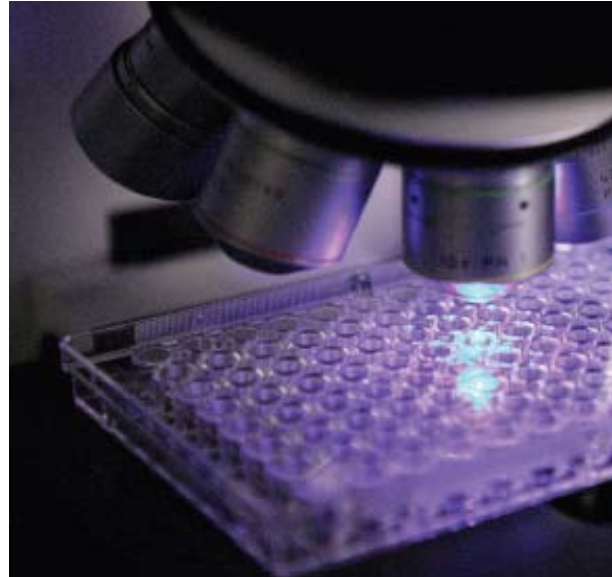
Supported by close to \$3 billion in spending over eight years and a focus on seizing global opportunities where Ontario can compete and win, we have launched the Ontario Innovation Agenda. The Ontario Innovation Agenda will support continued growth and prosperity through a renewed focus on commercialization; in large part by forging new strategic partnerships with industry.

The foundation for the Ontario Innovation Agenda is our ongoing commitment to supporting excellence in world-class basic and applied research.

Ontario is now in the process of reviewing all of our funding programs to ensure they deliver on our Innovation Agenda. Working at the speed of business means having programs that are focused, streamlined and easy to understand and access.

At the same time, Ontario remains committed to enhancing our already competitive tax environment, and to modernizing and streamlining our regulatory system.

Ontario's Innovation Agenda speaks to global industry and all its stakeholders with a voice that is committed and collaborative. We believe it delivers a practical vision of continuous innovation, recognizing it as the only real pathway to sustainability in today's global economy.



WHAT DOES THIS MEAN FOR THE BIOPHARMACEUTICAL INDUSTRY?

A cornerstone of the Ontario Innovation Agenda is the \$1.15 billion Next Generation of Jobs Fund — a five-year program designed to support strategic, industry-led projects in a handful of identified areas where Ontario can compete and win globally.

Under the auspices of the Next Generation of Jobs Fund, Ontario has launched a targeted Biopharmaceutical Investment Program (BIP), which is adapted to the unique business needs of the biopharmaceutical industry as a priority area of focus.

It is only natural for Ontario to focus on tapping the potential of our biopharmaceutical cluster as a key engine for growth in the 21st Century:

- With 25 research and academic hospitals employing 10,000 scientists, clinical investigators and other researchers conducting \$850 million in research annually, Ontario is the largest hub of biomedical activity in Canada and the third largest biomedical research centre in North America.
- Ontario is globally recognized for our research excellence in genomics, cancer treatment, regenerative medicine, clinical trials, bioinformatics, medical imaging and infectious disease prevention and control.
- As the central hub of Ontario's biopharmaceutical cluster, the City of Toronto has reached a "critical mass" worthy of global attention. Toronto's Discovery District, which encompasses the MaRS Centre, the University of Toronto with the third most life sciences publications in the world, six research hospitals, approximately 5,000 top scientists and over 2.4 million sq. ft. of new research space since 2005 with 2.2 million sq. ft. in planning and early construction stages.
- Ontario's life sciences industry employs more than 40,000 people at more than 800 companies which generate more than \$11 billion in annual revenues.
- Ontario has the highest level of post-secondary graduates in the G7, graduating more than 29,000 new post-secondary graduates every year in mathematics, science, and engineering.



R&D TAX INCENTIVES AVAILABLE TO BUSINESSES IN ONTARIO CAN REDUCE THE AFTER-TAX COST OF \$100 IN R&D EXPENDITURES TO LESS THAN \$36.

ONTARIO'S NEW BIOPHARMACEUTICAL INVESTMENT PROGRAM MAY REDUCE BUSINESS COSTS EVEN FURTHER BY CONTRIBUTING UP TO 20% OF ELIGIBLE PROJECT COSTS.

ONTARIO IS READY TO COMPETE AND WIN IN THE 21ST CENTURY. WE ARE ACTIVELY SEEKING NEW PARTNERS IN THE BIOPHARMACEUTICAL INDUSTRY WHO ARE READY TO DO THE SAME.

HOW DOES THE BIOPHARMACEUTICAL INVESTMENT PROGRAM WORK?

Ontario's Biopharmaceutical Investment Program (BIP) was developed in collaboration with the innovative pharmaceutical industry to ensure government policy-makers were fully apprised of the challenges and opportunities facing the industry today.

BIP has three main objectives:

- Increase the level of new biopharmaceutical research and development and advanced manufacturing in Ontario;
- Expand companies' local footprints, and create a new generation of high value jobs for Ontarians;
- Increase 'deal flow' within Ontario's growing biotechnology cluster, and build collaborations with public research institutions.

Through BIP, the Government of Ontario seeks to partner with eligible companies, and share financial risk by providing conditional grants of up to 20% of eligible costs associated with eligible R&D or advanced manufacturing projects.

Additional details on Ontario's Biopharmaceutical Investment Program are available on the Ministry of Research and Innovation's website, www.ontario.ca/innovation.

In addition to BIP, Ontario is also making R&D dollars go further through generous tax incentive programs, by fostering linkages that spur collaboration and commercialization, by leveraging a world-leading R&D capacity, and by continuing to make Ontario a great place for innovative companies to do business.

ONTARIO INTRODUCES NEW PROGRAMS FOR EARLY STAGE INNOVATIVE COMPANIES:

Announced in March 2008, Ontario's 10-year income tax exemption is available to new corporations that commercialize intellectual property developed by Canadian universities, colleges or research institutes.

Announced in November 2007, the Ontario Venture Capital Fund provides access to capital for innovative, Ontario-based companies to ensure that emerging companies can grow, create new jobs, and build their business in Ontario.

GROUND-BREAKING CELEBRATED FOR NEW \$100M CENTRE FOR VACCINE RESEARCH



WHAT IF ONTARIO'S BIOPHARMACEUTICAL INVESTMENT PROGRAM ATTRACTED ITS FIRST INDUSTRY PARTNER? WE HAVE.

Sanofi Pasteur, the vaccines division of Sanofi-Aventis Group, broke ground in April 2008 on a new, \$100 million state-of-the-art vaccine research facility at the company's historic Connaught Campus in Toronto. The total includes \$80 million for construction of the facility, plus the purchase of specialized research and development equipment, and the support of high-value R&D jobs over the next five years. The company says the centre is expected to attract 30 new R&D jobs, at the same time that it enables the retention of 900 jobs — including 312 researchers.

For this project, Sanofi Pasteur partnered with the Government of Ontario, which will contribute \$13.9 million through the Biopharmaceutical Investment Program (BIP).

“This new facility demonstrates Sanofi Pasteur’s commitment to growing research and development capabilities in Canada for new and innovative vaccines that will help protect the health of people worldwide,” said Wayne Pisano, President and Chief Executive Officer of Sanofi Pasteur.

Construction of the 165,000 square-foot facility will begin in 2008 and is projected to be ready for occupancy in 2010. This significant investment aims at accelerating Sanofi Pasteur’s ongoing research activities based in Canada.

Research at the new facility will help support the company’s global research and development efforts to improve existing vaccines and create new vaccines. Research targets will include pediatric combination vaccines, pneumococcal protein vaccines and cancer vaccines.

In addition to being a state-of-the-art vaccine research and development facility, the new R&D facility will incorporate a number of new technologies to reduce environmental impact. This includes using the company’s natural gas-powered cogeneration system for the facility’s electrical and steam requirements.

Sanofi Pasteur has a tradition of more than 90 years of protecting and safeguarding the public health of Canadians. Currently, Sanofi Pasteur supplies the only conjugate vaccine in Canada that protects against four of the five strains of bacteria that cause meningococcal meningitis.

ONTARIO HAS PRODUCED GLOBAL LEADERS IN BIOPHARMACEUTICALS (I.E. COMPANIES WITH GREATER THAN \$100 MILLION IN ANNUAL SALES AND WHICH ARE IN THE TOP FIVE OF THEIR NICHE GLOBALLY):

MDS Inc. (contract research organizations
and medical isotopes niches)

Patheon Inc. (drug development and
manufacturing services niches)

TLC Vision (laser vision correction niche)

Source: Assessing the Strength of the Toronto Biopharmaceutical Cluster by Roger L. Martin, Dean, Joseph L. Rotman School of Management, University of Toronto; James Milway, Executive Director, The Institute for Competitiveness & Prosperity

September 2004

WHAT IF ONTARIO'S ADVANTAGES COULD ATTRACT NEW INVESTMENT? THEY DO.

GlaxoSmithKline (GSK) is Canada's largest research-based pharmaceutical company devoted to discovering and developing new and innovative medicines, vaccines and health-care products for Canadians and people around the world.

GSK is a top 15 Canadian investor in research and development, contributing more than \$176 million in Canada in 2006 alone. Key products target five major disease areas — respiratory illnesses, diabetes, viral control, infections, and central nervous system disorders. GSK is also a leader in the important area of vaccines & pandemic preparedness, and is developing new treatments for cancer.

Paul Lucas, President and CEO of GSK Canada, shared his thoughts on the global investment climate for pharma and the Ontario advantage.

Q: What are some of the advantages that brought GSK to Ontario?

Paul Lucas: In 1987 and 1992, the Federal Government restored intellectual property protection and developed a collective agreement with the pharmaceutical industry, which was designed to bring investment to Canada.

We also saw an opportunity to benefit from Ontario's highly skilled workforce, and proximity to the US market, and in response, the GSK leadership team set out to create a robust physical presence in Ontario.

Our Canadian executive team is focused on securing investment from our global company, because we value the opportunity created locally for research and innovation in health sciences leading to earlier access to new medicines for patients, world leading clinical trials headed by local doctors and creating quality science-based jobs.

For example, our investment in Ontario has enabled us to create a highly specialized manufacturing and development facility that produces more than 75 different products for more than 100 markets worldwide. In 2005-2006, we secured an additional 23 new manufacturing mandates, resulting in a capital investment of \$55 million and 230 new job opportunities.

This is the clearest proof that government policy continues to make a definite difference in determining where a company chooses to locate its offices and invest its resources.

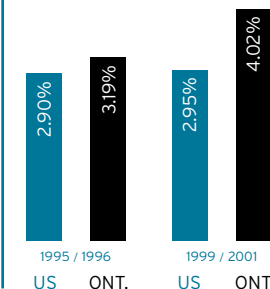


Paul Lucas, President and CEO of GSK Canada.



STOCK OF SCIENCE AND ENGINEERING UNIVERSITY GRADUATES

(% of population 20 and over)



Source: Statistics Canada; Cansim II; National Science Foundation

ONTARIO IS ABLE TO OFFER A HIGHLY SKILLED POOL OF ENGINEERS, CHEMISTS, PHYSICISTS, MBAS AND PHDS TO HELP US WIN AND MANUFACTURE INNOVATIVE PRODUCT MANDATES.

Q: How has the environment evolved for pharma investment and what are some of the global factors at play?

PL: The reality is that competition for R&D investment takes place on a global scale, and countries around the world are competing with each other to attract R&D and to drive their knowledge-based economies.

Through the creation of the Biopharmaceutical Investment Program (BIP), the Government of Ontario has signaled its desire to bring our high value, highly skilled jobs to Ontario. This investment by the government is helping to attract the jobs of the future. Taken together with the Federal SR&ED program, the BIP will help make Ontario more attractive for biopharmaceutical investment.

We are also pleased that the Ontario Ministry of Research and Innovation has announced its Innovation Agenda, which clearly recognizes the biopharmaceutical industry as a key partner, and speaks to recognition of the need to reduce regulation, align procurement with sector policies and establish metrics for monitoring.

Q: For the talent that GSK is looking to attract, how do the Ontario advantages stack up, in your view, compared to the global landscape?

PL: Ontario is able to offer a highly skilled pool of engineers, chemists, physicists, MBAs and PhDs to help us win and manufacture innovative product mandates.

Our 250,000 square foot manufacturing and development facility in Mississauga is a highly-specialized, state-of-the-art facility that uniquely co-locates product development and manufacturing in the same building, and is capable of taking a drug from early development through clinical trials to full manufacturing. The facility is also seen as a leading site for the manufacture of difficult and hard to produce products. In fact, it is the single global site for a number of GSK oral liquid products, including products for HIV/AIDS and oral solutions for nausea in patients undergoing chemotherapy and radiotherapy.

This means that a highly skilled workforce is critical for GSK to maintain and grow our manufacturing facility here.

Q: If you had a prescription for Ontario to continue to maintain its advantage, what would it be?

PL: Ontario's Premier and government should be commended for recognizing the importance and opportunity within the life sciences industry, and specifically the biopharmaceutical industry.

Developing a life sciences industry cluster is a long-term proposition that requires collaboration between industry and government. While there are still challenges that we are addressing in the province and at the federal level, by the federal and provincial governments working together with industry, we can compete and win.

The ultimate result of our commitment to innovation is new vaccines, medicines and better quality of lives for Canadians. This is important to me personally. I chose to remain here in Canada because I wanted to see this industry grow locally. I believe that there is hope, and that all of us working together can achieve it.



WHAT IF WE DELIVERED ON BANTING'S VISION? WE ARE.

Ontarians have a deeply personal and historical relationship to drug discovery, development and commercialization.

If there is one thing that citizens of the province identify as their contribution to the world it is the discovery of insulin in 1921 at the University of Toronto by Frederick Banting, Charles Best, John Macleod and James Collip. Indeed, when the Canadian Broadcasting Corporation did a Canada-wide survey in 2007, insulin was seen as the country's greatest invention.

But the story that students learn in middle school is not simply about discovery, but how the University of Toronto trio teamed up with the American drug company Eli Lilly to commercialize the product. How the university researchers who took out the patent needed the development savvy and production capacity of Eli Lilly to bring their discovery to market, and how the future Nobel Prize winners were insistent that partnering with reputable pharmaceutical houses was necessary to ensure the purity and potency of insulin.

The work with Eli Lilly was done in conjunction with Connaught Laboratories, a University of Toronto spin-off company created to produce the diphtheria and then tetanus anti-toxins. Some of the royalties from insulin were designated for medical research, and helped establish the first research-supported infrastructure in Canadian universities. When Connaught was sold in 1972, \$25 million was used to set up the Connaught Fund, which still supports the research of University of Toronto faculty and graduate students.

We mention our intrinsic relationship to insulin because it brings up three points. The first is that we recognize that, as a society, we haven't been diligent enough in translating the brilliance of basic medical science in the province into the next insulin. "We need more Bantings, strings of Bantings. We need to make our past our future," says Dr. Aled Edwards, who heads up the Structural Genomics Consortium (which has identified one quarter of the human protein structures in the world).



Charles Best and Frederick Banting, circa 1924.

A TRADITION OF SEEKING SOLUTIONS

1914 - Dr. John FitzGerald founds Connaught Laboratories in partnership with the University of Toronto, where he personally manufactures the first safe, effective, Canadian-made rabies vaccine and diphtheria anti-toxin. (Toronto)

1916 - Norman Bethune receives his M.D. (Toronto), launching a career that defines the battlefield surgeon with the development of new surgical instruments and first mobile blood bank among his key innovations. A doctor to the very end, Bethune died of blood poisoning in 1939, while ministering to the Chinese Army.

1921 - Dr. Frederick Banting and his assistant Charles Best discover insulin as a treatment for diabetes with the aid of J.B. Collip and J.J.R. Macleod (Toronto). Banting and Macleod later win the Nobel Prize in Medicine for their discovery. Treatment for children begins the following year at SickKids; 10-year mortality drops 50 per cent.

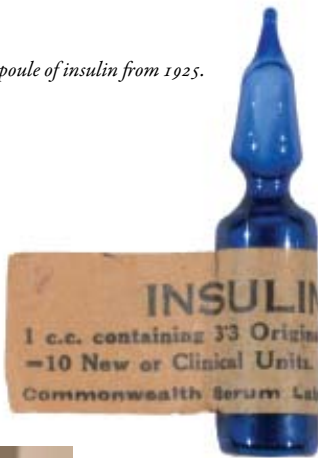
1930 - Nutritional research by Drs. Alan Brown, Fred Tisdall and Theo Drake at The Hospital for Sick Children leads to the development of a new quick-to-prepare, low-cost cereal that later becomes famous the world over as Pablum. (Toronto)

1935 - Dr. Gordon Murray conducts first human trials of heparin as a blood thinner. (Toronto) By 1937, it is clear that heparin is a safe, easily available and effective blood anticoagulant.

1946 - Dr. Gordon Murray performs North America's first kidney dialysis, using a machine he co-invented. (Toronto)

Sources: Canadian Medical Hall of Fame, Stem Cell Network, The Hospital for Sick Children

Ampoule of insulin from 1925.



And thus we are actively striving in a number of ways — massive investment in research infrastructure, tax incentives, recruitment of great scientists from all over the world — to bring forth more Bantings.

But beyond this there is an instinct for collaboration in the discovery and commercialization of insulin that is almost our defining provincial trait. And there is no better example of how we value working with people from everywhere than the fact that today Toronto is almost certainly the most culturally diverse of all big cities in the world.

And finally, Banting understood that insulin was not a complete cure for diabetes and left a note in his will that a light should burn in the house he was born in until such a cure is found. That too is our modern Ontario vision. Already Dr. Tony Pawson, Senior Scientist at Mount Sinai Hospital, has been able to explain what Banting couldn't: How insulin interacts with cells in the body. But there is more. As perpetrators of Banting's greatness, Ontario researchers want to extinguish the lights which are still burning for any number of human diseases. By collaborating with others with the same vision, we want to live up to Banting's vision of research that only ends with a true cure.



“HERE IT'S ALL RIGHT IN ONE PLACE, AND THAT'S A HUGE, HUGE ADVANTAGE, ESPECIALLY WHEN IT COMES TO INTERACTIONS BETWEEN DISCIPLINES SUCH AS CHEMISTRY AND PHYSICS AND COMPUTATION AND BIOLOGY.”

DR. TONY PAWSON, SENIOR SCIENTIST, MOUNT SINAI HOSPITAL



1947 - Dr. Wilfred Bigelow begins experiments with lowering body temperature to reduce blood circulation and allow surgeons time to operate cleanly on the heart. By 1960, he had performed 50 “deep-freeze operations” using blankets with cold-water cooling coils. (Toronto)

1947 - Dr. Marion Hilliard and colleagues develop a simplified method for detecting early symptoms of cancer, particularly of the cervix. (Toronto)

1948 - Later nominated for the Nobel Prize, Dr. Murray Barr discovers the sex chromatin body now known as the Barr body, initiating a new era of research and diagnosis of genetic disorders. (London, ON)

1949 - Dr. William Mustard is one of the first to perform open-heart surgery. He developed two operations named for him: the Mustard operation in orthopedics used to help hip use in people with polio and the Mustard cardiovascular procedure used to help correct heart problems in “blue babies,” which has saved thousands of children worldwide. (Toronto)

1950 - Dr. Wilfred Bigelow, Dr. John Hopps, and Dr. John Callaghan build the world's first pacemaker for continuous clinical use. Duplicating the normal stimulation of body nerves without damaging muscles or nerves, the design is not unlike that of modern pacemakers, except for its size. This collaboration is considered to be the dawn of bioengineering and Hopps the father of that field. (Toronto)

1950 - Based on the work of Dr. Gordon Richards, Dr. Vera Peters demonstrates that Hodgkin's disease is curable with high-dose radiotherapy. (Toronto)

1954 - Dr. Robert Noble, Dr. Charles Beer and their teams isolate and purify a potent alkaloid extract from periwinkle tea leaves (London, ON); called “vinblastine”, it's the first major advance in chemotherapy originating in Canada.

WHAT IF THE STEM CELL REVOLUTION BEGAN HERE? IT DID.

Every year when the Nobel Prizes in Medicine are announced, scientists in the know do a quick scan to see if James Till and Ernest McCulloch have been declared winners.

This is because between 1961 and 1963, Till, a physicist by training, and McCulloch, a medical doctor, brought their disparate talents together at the Ontario Cancer Institute in Toronto and discovered that seminal element of body biology: the stem cell.

It is a discovery that has already seen McCulloch, 82, and Till, 76, win both the Lasker and Gairdner Prizes, awards that have generally served as precursors to the Nobels. Breakthroughs since then — many cementing Ontario's continued prowess in this field — have generated a tidal wave of research as scientists seek to harness the therapeutic potential of these self-renewing cells capable of producing a variety of different tissues.

What first brought Till and McCulloch together wasn't the search for stem cells but an attempt to understand what happened in the blood when bodies were subject to large doses of radiation.

Their experiments were testing whether it was possible to protect against radiation-induced death by injecting various numbers of bone marrow cells into mice. One Sunday, McCulloch came in to the laboratory to prepare mice for autopsy and noticed they had bumps on their spleens. Others had seen this phenomenon before but had assumed it was a local growth of cells. McCulloch, with a background in cell biology, had a Eureka moment: Perhaps it was a colony of cells derived from the much theorized, but until then never seen, stem cells.

And then the hard work began...

ALBERT LASKER MEDICAL RESEARCH AWARDS – ONTARIO-BASED WINNERS

2005

Ernest McCulloch and James Till
University of Toronto
Ontario Cancer Institute

"For ingenious experiments that first identified a stem cell"

1998

Yoshio Masui
University of Toronto

"For pioneering genetic and molecular studies that revealed the universal machinery for regulating cell division in all eukaryotic organisms, from yeasts to frogs to human beings."

1958 - Dr. Charles Drake perfects, documents and teaches surgical techniques on the repair of brain aneurysms for which he gained worldwide fame. (London, ON)

1961 - Dr. Ernest McCulloch and Dr. James Till discover the first stem cell while experimenting with bone marrow in laboratory mice. (Toronto)

1962 - Raymond Heimbecker conducts the first successful human heart valve transplant. (Toronto)

1966 - Canada's Medical Care Act provides free access to physician services. (Ottawa)

1967 - The first "Palm N Turn" childproof pill container is designed and adopted in Ontario (Windsor); the innovation spreads and the incidence of child poisonings drops dramatically.

1970 - The Canadian Aspirin Trial, headed by Dr. Henry Barnett, establishes for the first time that the antiplatelet drug could prevent stroke. (London, ON)

1972 - Dr. John Bienenstock pioneers the concept of the common mucosal system whereby surfaces within the gut, respiratory tract and reproductive system, share information to fight infection. (Hamilton, ON) His team demonstrates that vaccines taken by mouth induce immunity throughout the entire mucosal system.

1983 - Dr. Tak Mak discovers the T-cell receptor, a key component of acquired immunity. (Toronto)

1983 - Dr. Joel Cooper performs the world's first successful single-lung transplant. (Toronto)

"COLLABORATION COMES MORE EASILY IN CANADA."

DR. ANTOINE HAKIM, CEO AND SCIENTIFIC DIRECTOR OF THE CANADIAN STROKE NETWORK AND WINNER OF THE AMERICAN STROKE ASSOCIATION'S 2007 AWARD FOR OUTSTANDING LIFETIME ACHIEVEMENT.



California Governor Arnold Schwarzenegger greets Dr. Ernest McCulloch during a 2007 announcement at MaRS of a \$30 million Ontario-California cancer stem cell consortium centred at the Ontario Institute for Cancer Research.

WHAT IF COLLABORATION EQUALS DISCOVERY? IT DOES.

Q: So how did it happen that two guys working in a lab in Toronto found cells that people had been looking for 60 years without success?

Till: It was unusual for a person with a science background and a person with a medical background to get together on a collaborative project, because they never met. But a unique feature of the Ontario Cancer Institute when it was initiated was that disparate people, people with very different backgrounds, got together.

Q: So collaboration was intrinsic to what you did?

Till: Very important, crucial, particularly collaboration with our colleague Lou Siminovitch. He helped get us involved with some experiments that allowed us to develop a functional definition of stem cells. And we were able to attract extremely talented students and post docs, which was absolutely crucial for the development of our program.

Q: Interesting. There is an argument that says that collaboration is a Canadian characteristic.

Till: I come from Saskatchewan and in Saskatchewan in the early days, if you didn't cooperate, you froze. Individualism didn't work on the Prairies in the early days and that ethos has influenced me.

Q: What do you think of the larger efforts to turn stem cell research into a collaborative effort?

McCulloch: It's no longer a place for the kind of small, two people collaboration that Jim and I were able to do. Today it's always a big gang.

Till: Yes, and with all the organizational challenges, and leadership challenges that go with gangs. But I must say, in that regard, to have the Premier of the province step forward as a leader in that effort in terms of medical research, well, I think it's novel for Ontario. But it's also timely and appropriate.

Q: So why should companies come to partner and work with stem cell researchers in Ontario?

Till: Because there are so many people who you would be interested in talking to. There is a high critical mass here and if you're making a mistake you're likely to be told about it. And we have a track record of accomplishment. We're not just talk. You know the Western expression about being all hat and no cattle? Well, we've got cattle.

McCulloch: We have a tradition in Canada of quality work, partly out of necessity, being starved for funds. We make every research grant go as far as it can, and that sorts out the quality from the non-quality in a Darwinian kind of way.

1986 - Dr. John C. Polanyi receives the Nobel Prize for the development of reaction dynamics, a new field of research in chemistry that gives a detailed understanding of how chemical reactions take place. (Toronto)

1986 - Dr. Joel Cooper performs the first successful double-lung transplant. (Toronto)

1988 - Dr. David Grant of University Hospital at London Health Sciences Centre performs the world's first liver-small bowel transplant. (London, ON)

1989 - Dr. Lap-Chee Tsui discovers the single gene defect that leads to cystic fibrosis. (Toronto)

1994 - Dr. John Dick isolates the first cancer stem cell from acute myeloid leukemia patient - the first direct evidence for cancer stem cells. (Toronto)

2001 - Stem Cell Network is formed under Canada's Networks of Centres of Excellence program. (Ottawa)

2005 - Fathers of stem cell research, James Till and Ernest McCulloch are awarded the Lasker Prize for their groundbreaking work. (Toronto)

2006 - Dr. John Dick identifies that abnormal stem cells are the cause of cancer. (Toronto)

2007 - Researchers at SickKids (Toronto) and the University of British Columbia use skin-derived stem cells to repair spinal cord injuries in rats.

2008 - A Canadian team led by Dr. Stephen Scherer at SickKids (Toronto) — and part of the international Autism Genome Project — discovers gene abnormalities linked with susceptibility to autism spectrum disorder.

WHAT IF WE HAD THE TOP RESEARCHERS TO DRIVE STEM CELL EXCELLENCE? WE DO.

James Till and Ernest McCulloch's 50-year debate with one another about why it has taken so long for stem cell science to advance may have been resolved in November 2007. In that month, two groups, one in the United States and the other in Japan, published papers describing a simple way of reprogramming adult human cells so that they effectively become stem cells.

"It's a bit like learning how to turn lead into gold," enthused Robert Lanza, of Advanced Cell Technology about the sea change.

In one sweep it appears as if two of the major barriers to the wider application of stem cells in medicine have been resolved: the ethical and political concern over embryonic stem cell derivation may become moot, and any rejection issues would vanish if the cells came from a patient's own body in the first place.

For companies wishing to take quick advantage of the breakthrough, stem cell researchers in Ontario have a pointed message. "Everyone who visits Toronto or Ontario from outside says 'You guys are really poised to become the leaders in this area,'" notes Dr. Janet Rossant, Chief of Research at The Hospital for Sick Children, Toronto and one of the world's leading developmental biologists. Her work has contributed significantly to the understanding of how an embryo develops, how genes control normal and abnormal development and how embryonic and other stem cells arise.

"We have a very deep intellectual richness in understanding stem cells," adds Dr. Mick Bhatia, Scientific Director of the Cancer and Stem Cell Biology Research Institute at McMaster University in Hamilton. His team is currently investigating why it is that human stem cells often respond very differently from the stem cells found in mice and other animals, findings that will have important implications for preclinical drug testing. "The ways in which Canadians scientists approach the problem are very elegant because of that deep history. I think they're able to see through some of the fads of stem cell biology and really get to the nugget that's important to move the field forward."

Recent U.S. recruits — including Dr. Gordon Keller (see page 16) and Dr. Ben Neel, Director of the Ontario Cancer Institute — add to an already deep field of Ontario-based stem cell researchers, including Dr. John Dick (see picture at right) and Dr. John Hassell of McMaster University, whose research explores a set of genes overexpressed in breast cancer, which are thought to play key regulatory roles in the origin and progression of this disease.

"Canada is seen as a place where discoveries happen," says Dr. Michael Rudnicki, University of Ottawa-based director of the Canadian Stem Cell Network and the newly appointed first director of the International Regulome Consortium.

CANADA'S LEADING POSITION IN THE COMMERCIALIZATION OF STEM CELL RESEARCH:

Canada had the fastest rate of growth in external patent applications and industrial R&D investment among G7 nations.

Canada ranks third in its share of the 16 most influential stem cell patents, behind the U.S. and the U.K.

Alongside its deep research strength in stem cell biology, Ontario boasts a number of prominent researchers in tissue engineering and biomaterials; for example, six of the world's top 20 researchers in biomaterials are located in Toronto.

Source: Regenerative Medicine Industry Briefing: Commercial Opportunities and Strengths, MaRS Venture Group, 2008



The work of Dr. John Dick, Senior Scientist at University Health Network and head of the Cancer Stem Cell Program at the Ontario Institute for Cancer Research, has transformed the conventional view of the origin and nature of cancer.

In 2007, he confirmed the existence of uncommitted stem cells among the cells responsible for muscle growth. The finding holds out the possibility of harnessing stem cells' potential to counteract the wasting effects created by diseases such as muscular dystrophy, not to mention normal age-related deterioration of muscles in the body.

Rudnicki points out that his laboratory was the first to look at adult muscles through the prism of stem cell function. This is something that has allowed them to better understand congenital muscle weaknesses seen in test animals, providing an intellectual focus many stem cell biologists don't yet have. "I would say that a lot of stem cell biologists are still in the descriptive phase of their work, while we really like to drill down into mechanism and understand what makes the cells tick."

But Canada's advantage in this field lies not only in strong fundamental research and patent activity but also in a coordinated approach to commercial development: in 2005, the Canadian Stem Cell Network established Aggregate Therapeutics Inc. as its commercialization arm, allowing an exclusive first right to commercialize the unencumbered intellectual property from Network funded research conducted in 16 major universities and research hospitals across Canada. To date, Aggregate, which is based at the MaRS Centre, has screened more than 60 technologies and optioned/licensed seven for further development.

Dr. Freda Miller, a Senior Scientist at The Hospital for Sick Children who has found that skin could be a source of stem cells, has licensed her skin precursor cells to Aggregate Therapeutics. While initially interested in nerve damage repair, she also points to the military's need to heal the wounds of soldiers whose injuries are too severe for conventional treatments.

"I think the Stem Cell Network has been amazing," Miller says. "It brought together people who would never talk to each other because they live in different communities — and we're not only talking but we're working together."

ONTARIO WELL-POSITIONED TO LEAD THE REVOLUTION IN MEDICINE

In spring 2008, Ontario was selected to coordinate the International Regulome Consortium (IRC). This research effort is bringing together more than 60 investigators from 34 institutions in 12 countries to undertake the next crucial step in genomics research – understanding how gene function is regulated in mammalian cells during development. The IRC Secretariat is located at the Ottawa Health Research Institute (OHRI).

The OHRI, with 1,350 researchers and staff, is at the forefront of this brave new era, with a number of exciting projects now moving forward into clinical studies. Examples include viruses that selectively attack cancer cells while leaving normal cells intact, and a stem cell therapy that throws multiple sclerosis into reverse.

With the recent opening of new facilities for regenerative medicine, vision and kidney research, and the launch of several important initiatives to support clinical research, OHRI is exceptionally well-positioned to play a leading role in the coming revolution in medicine.

The Gairdner Foundation recognizes the world's leading medical research scientists through the Gairdner International Awards. Since 1957, when the late Toronto businessman James Gairdner founded the awards, 70 of 288 Gairdner winners have gone on to win the Nobel Prize in either Medicine or Chemistry.

The Wightman Award is given to a Canadian who has demonstrated outstanding leadership in medicine and medical science.

AMONG THE GAIRDNER WINNERS FROM ONTARIO:

Alan Bernstein*	2008
Allan R. Ronald*	2006
Endel Tulving	2005
Henry Friesen*	2001
Jack Hirsh	2000
Charles Hollenberg*	1999
Peter Macklem*	1999
Anthony Pawson	1994
Yoshio Masui	1992
John Evans*	1992
David MacLennan	1991
Lap-Chee Tsui	1990
Victor Ling	1990
Lloyd D. MacLean*	1989
Tak Mak	1989
Adolfo de Bold	1986
Geoffrey Flynn	1986
Harald Sonnenberg	1986
Aser Rothstein	1986
Douglas G. Cameron*	1984
Louis Siminovitch*	1981
Irving Fritz	1980
Claude Fortier*	1979
Keith Wightman*	1976
John Keith	1975
William Mustard	1975
Harold Johns	1973
Oleh Hornykiewicz	1972
Charles Best	1971
Robert Salter	1969
James Till	1969
Peter Moloney	1967
Fraser Mustard	1967
Gordon Murray	1964
Murray Barr	1963
Alan Burton	1961
Wilfred Bigelow	1959

*Wightman Award recipient

WHAT IF WE ATTRACTED THE BEST RESEARCHERS IN THE WORLD? WE DO.

When Dr. Gordon Keller moved back to Toronto from New York City in 2006, his arrival was greeted with the sort of collective whoopee generally reserved for all-star athletes signing on with the home team.

Part of the enthusiasm came from journalists recounting that Keller — Director of Toronto's McEwen Centre for Regenerative Medicine, the stem cell research arm of the University Health Network (UHN) — had been identified earlier that year by *New York* magazine as one of the six researchers New York City could ill afford to lose.

That sentiment seems well-justified two years later as a *Nature* paper published in April 2008, on which Keller was the lead author, made headlines around the world. The publication showed that Keller's laboratory could make three of the major cell types found in the human heart from embryonic stem cells. Keller reflects on his move from New York, what he has learned, and his views for the future in Canada:

Q: Why did you make the move to Toronto?

A: From a scientific point of view I came because of the excellence of stem cell biology and regenerative medicine, but as well I viewed the Toronto community as one of the richest areas in the world in which to do translational research. We have people here who understand the steps necessary to go from basic observations to more applied applications and we have a community of clinicians who are actively involved in research and enthusiastically embrace the collaborations we offer them.

Q: How has staffing gone for the new laboratory you set up here at the McEwen Centre?

A: I have found a vast resource of very well-trained people to hire into the lab. You know, even people who have completed say a PhD, or a post-doctorate want to remain in Toronto. Really I think the proportion of good applications I get here are higher than when I was at Mount Sinai in New York.

Q: Has the relative lack of Canadian biotech companies affected you?

A: As a researcher you want to have an opportunity to work with companies, and I don't think it matters so much if they started in Canada. That would be nice, but at this point let's get involved with whoever wants to come. Do that and the rest will follow. Well, that's my view at least.

Q: What have you seen that you would like to be better?

A: I think that we as Canadians continue to undersell ourselves and we should not be afraid to say we're the best at something. We're very reluctant to say that but I think that "the best" are the right words to apply when it comes to stem cell research in Toronto.



Dr. Gordon Keller views Toronto as one of the richest areas in the world in which to pursue translational research.

CANADA'S HEALTH RESEARCHERS OF THE YEAR

Ontario-based recipients of the CIHR Michael Smith Prizes in Health Research:

- Dr. Peter A. Singer** (2007)
University Health Network, Toronto
- Dr. Janet Rossant** (2005)
The Hospital for Sick Children, Toronto
- Dr. Sergio Grinstein** (2004)
The Hospital for Sick Children, Toronto
- Dr. Anthony Pawson** (2002)
Mount Sinai Hospital, Toronto
- Dr. Michael Tyers** (1999)
Mount Sinai Hospital, Toronto
- Dr. David Naylor** (1998)
Institute for Clinical and Evaluative Sciences, Toronto
- Dr. John Dick** (1997)
The Hospital for Sick Children, Toronto
- Dr. Peter St. George-Hyslop** (1996)
University of Toronto, Toronto

SAN FRANCISCO STEM CELL COMPANY FOLLOWS KELLER NORTH

The same massive expansion of facilities and technologies, infusion of scientific talent and government support that is allowing native Ontario biotech companies to bloom is also luring companies from outside the country into the province.

A prime example is VistaGen, a San Francisco-based firm that sees stem cells as “Clinical Trials In A Test Tube.”

VistaGen has been working with Gordon Keller, whose move to Toronto has meant that the collaboration has expanded to include an R & D alliance with the University Health Network, Canada’s leading research hospital, and its McEwen Centre for Regenerative Medicine. VistaGen has not only pledged to underwrite Keller’s basic research but the collaboration also supports what VistaGen is describing as “the next generation of its customized embryonic stem cell-based heart, liver, and pancreatic beta-islet cells differentiation systems for discovering new drugs to treat heart disease, liver disease and diabetes.”

Ralph Snodgrass, VistaGen President, says that researchers should be able to routinely screen for drug toxicity and potency on a variety of living — and sometimes beating — human heart cells. This testing has potentially huge economic ramifications as a 2004 U.S. Food and Drug Administration report suggests that increasing the efficiency of identifying drug toxicities by as little as 10 per cent would save the pharmaceutical industry \$100 million per drug being developed.

VistaGen is planning to set up a facility in Toronto to develop the commercial applications of stem cells.

“I think the issues which have the biggest selling point for opening a group in Canada is that there is a wealth of significant scientific leadership in the Toronto area, in multiple disciplines that are relevant to our technologies and drug discovery and the pharmaceutical industry. Not only from very strong biology, which includes stem cell biology, but also very important leadership in the structural function groups like the Structural Genomics Consortium. It’s very important to understand the structure of compounds and then use that understanding to design better drugs,” Snodgrass says.

ONTARIO'S RESEARCH STRENGTH STRETCHES ACROSS A NUMBER OF DISCIPLINES.

Top 3 Canadian Universities, 2000-04 Ranked by average citations per paper (in parentheses)

FIELD	1	2	3
Clinical Medicine	McMaster U. (10.26)	U. Ottawa (8.43)	U. Toronto (7.71)
Immunology	U. Western Ontario (16.03)	U. Toronto (13.48)	U. Ottawa (13.39)
Microbiology	U. Toronto (8.27)	U. Calgary (7.96)	U. Brit. Columbia (7.56)
Biology & Biochemistry	U. Toronto (9.57)	U. Brit. Columbia (9.12)	McGill U (8.37)
Molec. Bio./Genetics	U. Toronto (17.25)	McGill U. (16.11)	U. Montreal (11.63)
Neurosciences	U. Ottawa (9.33)	McGill U. (9.31)	U. Laval (9.06)
Pharmacology	U. Western Ontario (12.17)	U. Calgary (7.30)	U. Quebec (7.24)
Ecology/Environment	Trent U. (6.52)	U. Toronto (6.05)	McGill U. (4.68)
Plant & Animal Science	U. Waterloo (4.50)	U. Toronto (4.47)	McMaster U. (4.14)
Physics	Carleton U (22.33)	U. Brit. Columbia (10.02)	McGill U. (7.65)
Engineering	U. Toronto (2.42)	McGill U. (2.30)	U. Victoria (2.15)
Computer Science	U. Waterloo (1.98)	U. Toronto (1.97)	U. Brit. Columbia (1.92)

Source: Thomson Scientific University Science Indicators, Science Watch, September/October 2005

WHAT IF WE BUILT A ONE-STOP FACILITY FOR EMERGING PRECISION THERAPIES? WE DID.

When governments and industry leaders talk about the emerging age of “personalized medicine”, what they really mean is developing a range of precision therapies — particularly for complex diseases such as cancer — to replace a one-size-fits-all approach to treatment. Researchers at Toronto’s new STTARR facility are at the controls of a multi-modal suite of leading-edge tools designed to hone in on discoveries that will point the way toward such precision therapies. In so doing, their efforts also aim to unblock the current drug development pipeline, described by a landmark 2004 U.S. FDA analysis as “becoming increasingly challenging, inefficient, and costly.”

Opened in October 2007, the facility — STTARR stands for Spatio-Temporal Targeting and Amplification of Radiation Response — is, in Dr. Rob Bristow’s estimation, unique in the world. Bristow, a clinician-scientist and radiation oncologist at University Health Network’s world-renowned Princess Margaret Hospital and Senior Scientist at the Ontario Cancer Institute, together with his colleagues Drs. David Jaffray and Michael Milosevic, oversees STTARR’s more than \$23 million new cancer-oriented facility.

Funded by the Ontario government along with the Canada Foundation for Innovation, the uniqueness of STTARR is captured in the sweep of what it can do. “We envisioned setting up a sort of one-stop shopping centre for research in emerging areas of precision treatment,” says Bristow.

Specifically, STTARR researchers in the same facility are able to maximize the development of effective cancer treatment strategies, including radiation therapy, by integrating cellular, preclinical and human research. STTARR’s operations are administered within the Radiation Medicine Program at Princess Margaret Hospital and the facilities are located at the MaRS Centre just a half block away.

“STTARR is designed to track the efficacy of a drug or radiation during treatment so that we can develop a scan or biomarker which says either: ‘This is a great treatment’ or ‘This tumour is resistant and we need to add something to it’ or ‘We need to change the therapy altogether,’” says Bristow.

STTARR, with its plethora of imaging and tracking technologies, also explicitly set up preclinical trials to serve as a test bed for pharmaceutical companies seeking to unplug the jammed passageway created by hundreds of potential new cancer drugs.

“You can’t easily do 300 large clinical trials to determine the best cancer agent, so STTARR triages the therapies to select the best drugs to be used alone or in combination with current treatments,” says Bristow.



Dr. Rob Bristow oversees the new STTARR facility located at the MaRS Centre and run by University Health Network.

THE STTARR FACILITY IS DIVIDED INTO FOUR CORE FACILITIES:

CELL AND TISSUE IMAGING AND SUBCELLULAR RADIATION FACILITY, including Spinning Disc Confocal Microscope, a Leica Tissue Arrayer and Micro-environmental Chambers.

ANIMAL IMAGING AND PRECISION RADIATION FACILITY, including a GE Locus Ultra microCT unit Biospec 70/30 USR Ultra Shielded 7T MR; Vevo 770 High Frequency Ultrasound System; a UHN-developed Image-guided Radiation Therapy unit; a Siemens Focus 220 Micro PET and a Bioscan nanoSPECT/CT; Maestro In-vivo Hyperspectral Fluorescence system; Siemens Inveon microCT.

HUMAN IMAGING AND PRECISION RADIATION FACILITY, including a Multi-Slice CT simulator; PET-CT simulator; 1.5 Telsa MR Simulator.

COMPUTATIONAL CORE, including multi-organ biomechanical model based deformable registration for treatment planning, delivery and response assessment as well as image fusion. Image processing capabilities include respiratory sorting of temporal images. Analysis techniques include kinetic modeling, response assessment and quantitative evaluation of response imaging.

What STTARR will also do is try to prevent that financially stomach-turning moment when a clinical trial shows that the effect of a drug on normal cells is so destructive that it likely negates any of the cancer-fighting benefits. STTARR is rigorously testing both cancer cells and normal cells.

Not only is working with industry and other scientists a mandate for STTARR, but, says Bristow, “we would like to see ourselves as a sort of scientific hotel where someone from a company or other institution working on a specific project could come for six months, drive the project forward and then leave with definitive results. With this approach it is possible for STTARR partners to be truly collaborative with us.”

But the pipeline effectiveness of STTARR will not be limited to early stage “go/don’t go” recommendations around new drug candidates. Princess Margaret Hospital is currently home to 370 clinical trials and the STTARR group hopes that “we will get first crack at some of the new therapies coming down the pipeline, which have been shown to be a preclinically safe treatment in our MaRS facility across the street,” says Bristow. Not only would UHN be able to offer the drugs to patients in its clinical trials, but do so with a medical staff that have deep confidence in the process because STTARR researchers had already studied the drugs’ effects on both normal and cancerous cells.

And how will STTARR know in a decade if it has been successful?

“Great products and great partnerships,” says Bristow. “Examples of successful partnerships would be drugs that were developed along the entire length of the development pipeline within PMH. But successful examples would also occur where we did exquisite preclinical studies and a drug didn’t go on, as it is equally important that negative results are published as part of the medical literature to lead us to study the most promising pathways.”



INVESTMENT IN SCIENTIFIC INFRASTRUCTURE

The Government of Ontario has invested nearly \$900 million in scientific infrastructure over the past decade through the Ontario Innovation Trust and, more recently, the Ontario Research Fund’s Infrastructure Program. These programs have leveraged more than that amount again through the Canada Foundation for Innovation for a total infrastructure investment of more than \$2.4 billion since 1999. Among the highlights:

The Terrence Donnelly Centre for Cellular and Biomolecular Research, University of Toronto: \$30 million

Toronto Centre for Phenogenomics, Mount Sinai Hospital, The Hospital for Sick Children, University Health Network and St. Michael’s Hospital: \$26.8 million

London Regional Innovarium, The University of Western Ontario, London, ON: \$13.8 million

Institute for Animal-Human Health Links in Health Science Research, University of Guelph, ON: \$11 million

Functional Imaging Research Network, Baycrest, Toronto: \$10.7 million

Centre for the Integrative Biology of Polygenic and Monogenic Disease including Age and Degenerative Conditions, University of Toronto: \$10 million

McLaughlin Centre for Molecular and Cellular Response and Repair, University of Toronto: \$10 million

Centre on Molecular Epidemiology and Computational Biology of Polygenic Diseases, University of Toronto: \$10 million

Centre on Biomaterials and Tissue Engineering, University of Toronto: \$10 million

Centre on Gene Therapies, University of Toronto: \$10 million

Centre for Molecular Medicine and Health, McMaster University, Hamilton, ON: \$9.6 million

Queen’s University Cancer Research Institute Building, Kingston, ON: \$4.7 million

Centre for Stem Cell and Gene Therapy, University of Ottawa: \$4.4 million

WHAT IF WE TURN 'BLIND PROSPECTING' INTO RATIONAL DRUG DEVELOPMENT? WE ARE.

Separating winning drugs from losers — and doing it quickly before millions of R&D dollars drain away — is critical to success in the drug discovery challenge.

U.S. estimates are that it takes anywhere from \$800 million to \$1.7 billion to bring new drugs to market, and those entering Phase I clinical trials have only an eight per cent chance of making it through regulatory approvals to patient populations at large.

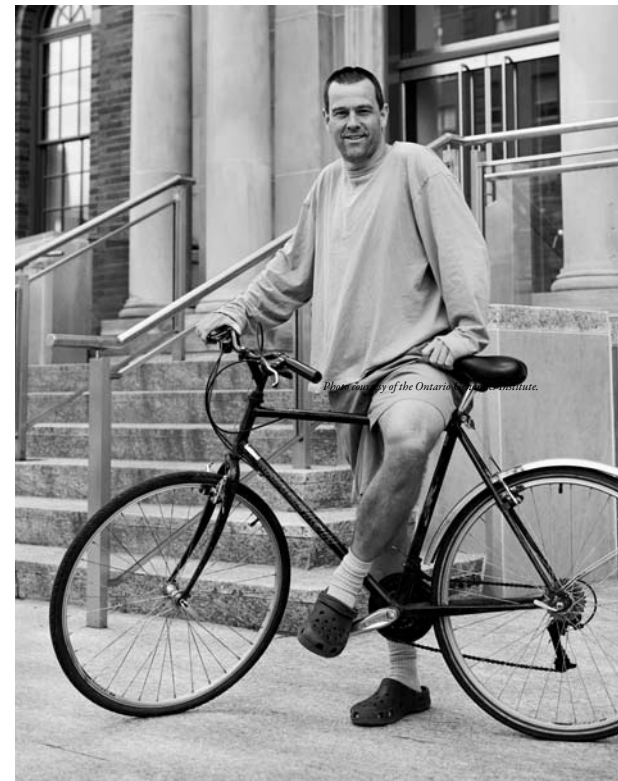
For Toronto-based Dr. Aled Edwards, Director and CEO of the Structural Genomics Consortium (SGC), the key to unblocking the inefficient drug development pipeline is unravelling the precise 3D structures of the proteins produced by our cells — and placing this information into the public domain immediately.

“This information is valuable because most medicines are designed to fit exactly into a protein’s grooves and channels and to stop it from working,” explains Edwards. “If you know the shape of the protein, you have a better understanding of how to design a drug to go in and block its function.”

Determining precise protein structures was something that companies recognized could transform drug discovery from blind prospecting into rational development, but after the sequencing of the human genome, many appreciated that a systematic search on such a scale was beyond any single company’s will or economic capacity. A collaboration between the University of Toronto, the University of Oxford and Sweden’s Karolinska Institute, the consortium was born, says Edwards, of drug companies’ understanding of the inefficiency of competition in the area.

“So in 1999 they said, why not pool the money, get one organization to generate the data and make the results free for all to use,” says Edwards.

With this as its intellectual template the Toronto-based consortium was set up in 2003 with \$95-million in funding from the Wellcome Trust in England, four Canadian funding agencies and GSK. Company participation was not only good, it was essential for government and Wellcome. “The public funders were clear: this is a private-public partnership. If there’s no private money here, they weren’t going to fund it,” says Edwards.



Dr. Aled Edwards, Director and CEO of the Structural Genomics Consortium at the MaRS Centre.

Photo courtesy of the Ontario Genomics Institute.

The results in the first three years were nothing short of astounding. From 2005 to the present the consortium has contributed over 25 per cent of the new human protein structures discovered worldwide — and at a cost of \$135,000 per protein. Edwards estimates this is one-third to one-eighth of industry and academic research laboratories' discovery costs.

The success of the initial original \$95-million effort has been rewarded by a renewal of funding through 2011, with a \$110-million investment, \$90-million of which is from the public sector. Furthermore, Novartis and Merck have joined GSK as industrial sponsors and now together contribute an additional \$20 million.

“THERE'S BEEN A SEA CHANGE IN CANADA WITHIN THE LAST FIVE YEARS IN TERMS OF FUNDING FOR RESEARCH AND THE OPENNESS AND WILLINGNESS TO REALLY INVEST IN THE BEST.”

DR. JANET ROSSANT, CHIEF OF RESEARCH AT THE HOSPITAL FOR SICK CHILDREN

But if the results are public, what value is there to a company?

“In many respects, access to the information without intellectual property strings is the greatest value. Companies also get to nominate targets (for structural investigation) and in some way influence direction. They can say: ‘We’d like you to work on these areas and we expect results to come out the end of this pipe,’” says Edwards.

But there are more specific benefits. Industrial partners are encouraged to send scientists into the consortium’s various laboratories to learn the most efficient way of finding proteins. “Our goal is to propagate not only the data but the technology so everyone gets better,” says Edwards.

One offshoot of that philosophy has been the formation of a spin-off company, Harbinger Biotechnology and Engineering. The company uses an approach first discovered by consortium scientists to create software that automatically collects, visually displays and analyzes protein data for scientific databases.

But with all his success, Edwards says that his mission in the next three years is to make more drug companies understand that funding collaborations like the Structural Genomics Consortium are in their and the world’s best interest.

“The way to make medicine cheaper is to stop failing all the time,” he counsels. “Ninety-per-cent of drugs fail not because scientists are dumb or they make mistakes; they fail because we have a very poor understanding of human physiology or pharmacology.”

SGC’s approach may not absolutely separate winning medications from losers, but, says Edwards, it should indicate where winning pathways lie.



WHAT IF WE APPROACHED CANCER RESEARCH IN NEW WAYS? WE DO.

In December 2005, the Government of Ontario announced that the province was going to approach cancer research in a fundamentally different way. The traditional model — with scientists in various locations doing often highly individualized research — was going to be enhanced by a research collective called the Ontario Institute for Cancer Research (OICR).

“Sometimes the big ideas with the great promise, ideas that required many teams to work together, didn’t always get the support they needed.” This was the view expressed by Ontario Premier Dalton McGuinty at the time and OICR was conceived as the solution.

The Government of Ontario committed approximately \$350 million over five years to OICR, attracting at least 50 of the world’s top researchers to work at the Institute, headquartered at the MaRS Centre in the heart of Toronto’s downtown hospital and biomedical research hub. Dr. Tom Hudson, formerly of McGill University, was appointed President and Scientific Director.

In 2007, a strategic plan was developed to focus on prevention, early detection, exploring the genomes of various cancers and discovering new therapies.

To accomplish these goals significant investments are being made in imaging technology and expertise, in bio-repositories and pathology, in medicinal chemistry, in genomics and high-throughput screening, and in informatics and bio-computing.

Perhaps most importantly, the Institute’s efforts fit into a framework that addresses the translation of discoveries into products and the speed with which these new medicines and techniques are applied in the clinic.

AS ANNOUNCED IN SPRING 2008, ONTARIO WAS CHOSEN TO COORDINATE A 10-COUNTRY INTERNATIONAL CANCER GENOME CONSORTIUM.

In its first two years, OICR has been moving forward on all fronts:

- Roughly one third of the new researchers and staff have been hired from global research powerhouses;
- Four promising early-stage discoveries have already received \$2 million in funding aimed at helping commercialize their efforts;
- A partnership has been forged with Boston’s Broad Institute, a research collaboration of Harvard, MIT and the Whitehead Institute;
- In Spring 2008, OICR announced it was becoming the global secretariat for the International Cancer Genome Consortium an effort launched by ten countries to explore the genetic mutations that underlie 50 different types of cancer that will accelerate efforts to develop new ways of preventing, diagnosing and treating cancer.



TWO YEARS INTO HIS WORK, DR. TOM HUDSON REFLECTS ON WHAT HAS BEEN ACCOMPLISHED SO FAR:

Q: What attracted a self-confessed DNA genome jock and MD with a specialty in immunology to heading a cancer research institute?

Dr. Tom Hudson: The ethos of it, first of all. There had been five years of work by people in Ontario working at two levels of government and I thought that they had a long-term vision to create something special. They had done their homework and identified where our research strengths were, where there was a potential for synergy and building clusters around common big themes. There was also a commitment not just to start up but to long-term funding.

Q: And what is that vision?

TH: One is to bridge the translation wall in things like prevention, detection and therapeutics. The truth is clinicians don't understand enough about the new sciences and the new scientists don't understand enough about clinical problems to actually be able to pass the baton to clinical trials.

Q: How will OICR bridge that gap?

TH: One way is to cross what we call "the IP Valley of Death." In order for there to be translation we want to add value to intellectual property we develop. So we are putting additional money into more business plans, into more validation experiments, looking at what might 'de-risk' an investment for an eventual partner.

Q: What's attracting the top-level people who are coming here?

TH: For one thing people from across the world are coming and doing site visits and saying, "Wow, they've got vision, equipment, funds, infrastructure, new buildings, they have operating funds." The rest of the world sees that Canada is doing something ambitious and is doing it in the right way.

Q: Is Toronto itself a draw?

TH: Yes. Every time I take someone to the corner office and say "this is where we work" they are impressed because they get to see the University of Toronto, and the Leslie Dan Pharmacy Building, the Terrence Donnelly Centre for Cellular and BioMolecular Research, Mount Sinai Hospital, The Hospital for Sick Children and Toronto General Hospital. They realize this is a big critical mass. It's not that you don't find that in that many places but I was amazed at the interactions that take place, and the number of colleagues you meet — not at meetings but at the cafeteria downstairs or on the street.

Q: So why should pharma link up with OICR?

TH: For one, we're very fresh. We only started a year and a half ago, but already we've got our niche areas and specialties — imaging, cancer stem cells, and genomics. And even though our strategic plan was only approved in 2007 we already have visibility... [through] the International Cancer Genome Consortium, whose secretariat is based at OICR. Our Cancer Stem Cell program under John Dick recently got four years of funding and our One Millimetre Cancer Challenge has received positive reviews from an international scientific review panel.

The other thing we have is clinical trials. OICR has doubled the number of patients in cancer trials. It has incorporated the Ontario Cancer Research Network's programs and put standard operating procedures, databases, personnel — 180 staff at 23 adult sites and five pediatric sites — in the province.

When I am trying to attract people I show them the big view from the top floor and then I show them Banting's desk, which is located downstairs on the first floor at MaRS, and remind them that insulin was discovered right here. They look at the desk and often say: "Wow, that's extraordinary." In a way insulin is our model: Discovery moving quickly to application, moving to a worldwide wow.

WHAT IF WE CREATED A CLINICAL TRIAL DESTINATION? WE HAVE.

One of the great founts of biomedical excellence in Ontario has been in clinical trials. All major teaching hospitals in affiliation with surrounding universities have become involved in groundbreaking trials on a local, national and international level.

Queen's University in Kingston, Ontario, is home of the The National Cancer Institute of Canada, Clinical Trials Group (NCIC CTG). This organization has completed an impressive 175 Phase III trials involving over 50,000 patients. Their tamoxifen and letrozole trials have dramatically changed the treatment regimen for breast cancer. Collectively, NCIC CTG researchers have initiated or completed 190 Phase I and Phase II trials in which they have enrolled 3,500 people in studies of 75 new anti-cancer drugs.

McMaster University's Population Health Research Institute, under Dr. Salim Yusuf's leadership, is the province's international clinical trial colossus. McMaster now has 225 people working with this research group, which is networked with 79 countries and 1,500 hospitals. Among its most well-known studies has been the HOPE trials with 10,000 participants, which showed that ACE inhibitors reduced the number of heart attacks, strokes, and deaths.

If, as expected, the Canadian Institutes of Health Research (CIHR) approves a McMaster University proposal for an internationally linked, cross-country network for clinical trials, it will join every teaching hospital in the country with 255 community hospitals and practices — and 1,500 hospitals around the world. The Canadian Network and Centre for Trials Internationally (CANNECTIN) project will leverage this expanded geographic reach and sample size to conduct trials on issues that have confounded previous efforts, including neglected diseases or conditions and understudied treatments and outcomes.

At The University of Western Ontario, in London, Ontario, the Robarts Clinical Trials Group is a world leader in trials related to inflammatory bowel diseases.

“Our medical system is conducive to multi-centre clinical trials because there's not the direct commercial competition for patients like that which exists in the U.S.,” says director Dr. Brian Feagan. “For example, if you go to a place like Houston you've got ten hospitals on the same street competing with each other.”

Canadian clinical trials also maximize a national instinct to operate collaboratively. “We're a relatively small country compared with some others, so we've got to have good ideas, and we've got to do high quality work that makes people want to collaborate with us,” says Ralph Meyer, who heads the NCIC CTG at Queen's.

The second reason: research excellence. “The academic health science centres have core expertise because they have access to methodological expertise at the universities, which facilitates conducting clinical trials,” Feagan says. Added to this institutional advantage is our experience designing trials that companies and hospitals find both objective and useful.

“We approach companies when we think there is a question that can be addressed by their drug that will move science forward,” Yusuf says.



“OUR MEDICAL SYSTEM IS CONDUCTIVE TO MULTI-CENTRE CLINICAL TRIALS BECAUSE THERE’S NOT THE DIRECT COMMERCIAL COMPETITION FOR PATIENTS LIKE THAT WHICH EXISTS IN THE U.S.”

DR. BRIAN FEAGAN, THE UNIVERSITY OF WESTERN ONTARIO



All of this, says Yusuf, sends a clear signal to drug and pharmaceutical companies, “Groups in Canada are well-organized, have done world class trials that have changed the way medicine is practiced, and have substantial expertise. Come.”

WHAT IF WE APPLIED SCIENTIFIC RIGOUR TO A NATURAL REMEDY? WE ARE.

Ginseng has long been used as a traditional Asian remedy to boost energy, immunity and sexual health. As with herbalism in general, ginseng’s medical efficacy remains unproven, although a new \$20 million Ontario natural drug research program is seeking to supplant legend and folklore.

Led by Edmund Lui, an associate professor in the department of physiology and pharmacology at The University of Western Ontario, the program involves researchers at six Ontario universities, industry and federal and provincial research establishments.

“The problem is that while there is considerable evidence for the use of these medicines based on cultural practices, in truth there is a lack of good clinical data to prove their effectiveness, safety, and perhaps most importantly their product quality,” Lui says. “This translates into a scientific reality where if you conduct some research which turns up some very exciting finding, generally it has turned out those results have not been reproducible.”

Researchers were never sure what went wrong: Did the ginseng differ among labs? Did a researcher’s perspective — a chemist versus a pharmacologist — make a difference? Lui knew clarity would only emerge when research questions were rigorously scrutinized across a spectrum of disciplines.

Through a global multi-disciplinary team of agricultural, biological and clinical scientists the program aims, among other objectives, to provide a uniform variety of seeds that contain particular constituents; conduct chemical analyses to better understand the activity levels of key substances within ginseng; and finally, screen for pharmacological activities as they relate to ginseng’s claim to myriad cures and treatments.

The goal is to build a model that can be applied to the entire natural products industry. “This collaborative multi-disciplinary way of doing thing is the way toward transforming all of natural medicine claims from anecdote to hard data. If successful, we will have created a Made-in-Canada model for how the world can turn natural products into truly clinically proven drugs.”

SOME OF THE SIGNIFICANT RECENT CLINICAL TRIALS CONDUCTED IN ONTARIO:

QUEEN’S UNIVERSITY, KINGSTON, ON Breast Cancer

A Randomized Trial of letrozole in Postmenopausal Women After Five Years of tamoxifen Therapy for Early-Stage Breast Cancer. *New England Journal of Medicine*, Volume 349:1793-802, November 6, 2003, No 19.

Lung Cancer

Erlotinib in Lung Cancer – Molecular and Clinical Predictors of Outcome.

New England Journal of Medicine, Volume 353:133-144, July 14, 2005, No. 2.

Colorectal Cancer

Cetuximab for the Treatment of Colorectal Cancer. *New England Journal of Medicine*, Volume 357:2040-2048, November 15, 2007, No. 20.

THE UNIVERSITY OF WESTERN ONTARIO, LONDON, ON Ulcerative Colitis

Treatment Of Ulcerative Colitis With A Humanized Antibody To The Alpha-4beta7 Integrin. *New England Journal of Medicine*, 2005 Jun 16;352(24):2499-507.

MCMASTER UNIVERSITY, HAMILTON, ON Cardiovascular Disease

Effects Of An Angiotensin-Converting-Enzyme Inhibitor, Ramipril, On Cardiovascular Events In High-Risk Patients. *New England Journal of Medicine* 2000 Jan 20;342(3):145-153.

Acute Coronary Syndrome

Effects of Pretreatment With Clopidogrel And Aspirin Followed By Long-Term Therapy In Patients Undergoing Percutaneous Coronary Intervention: The PCI-CURE Study. *Lancet* 2001, Aug 18;358(9281):527-33.

Cardiovascular Risk Factors

Effect Of Potentially Modifiable Risk Factors Associated With Myocardial Infarction In 52 Countries (The INTERHEART Study): case-control study. *Lancet* 2004 Sep 11-17;364(9438):937-52.

Sources: Dr. Brian Feagan, UWO; Dr. Ralph Meyer, Queen’s University; Dr. Salim Yusuf, McMaster University.

WHAT IF ONTARIO'S SCIENTISTS WERE ALSO ENTREPRENEURS? THEY ARE.

As a serial entrepreneur and CEO of Transition Therapeutics, Dr. Tony Cruz's responsibilities represent a dramatic change from his place in the world a little more than a decade ago when he was a successful senior scientist working at Toronto's Mount Sinai Hospital and author of 150 scientific papers.

What redirected him into business was a basic reconfiguration of Canada's research enterprise.

"In 1998 I was appointed the program director and CEO of a Network Centre of Excellence called the Canadian Arthritis Network. And one concept of the networks was to take technology from universities and start developing them," Cruz explains.

"I was a firm believer that, in order to do that properly, the first thing you've got to do was remove the technology from the institution. And so I started two or three little companies, all under the umbrella of the Network of Centres of Excellence, as an example to other academics who belonged to our network. The idea was to show that you could not only develop technologies that are commercially viable but that it was also feasible for academics to do."

For a couple of years the companies he founded operated almost as hobby enterprises financed with a little funding from Cruz and some friends. Then he happened upon a platform technology that inhibited inflammation, and it was so promising he was able to leverage \$5-million in private funding after Transition Therapeutics went public.

But, as often happens in the drug development business, it became obvious to Cruz that the anti-inflammation technology wasn't going to pan out. Instead of licking his wounds and closing shop, he went looking for another drug to shepherd through the often-perilous middle ground between discovery and clinical trials.

The business model is to look for "preclinical products that we can rapidly develop to pre-phase II so that they're well-positioned for a partnership with Big Pharma or Big Biotech," explains Cruz.

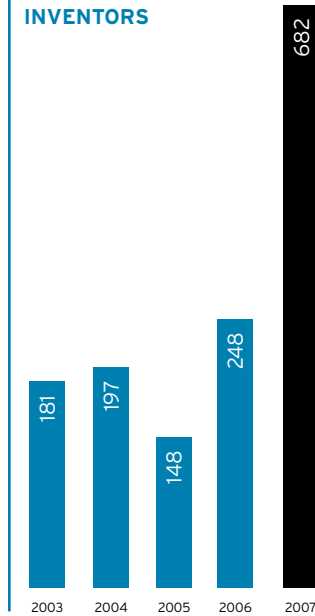
What he found was a company in Boston developing gastrin-based therapies to treat diabetes. Early experiments had indicated that gastrin has the ability to regenerate insulin-producing beta cells in the pancreas. So Cruz bought the U.S. company and transferred testing on gastrin to Toronto.

After bringing one of gastrin's compounds to early Phase II trials, Transition Therapeutics recently negotiated a deal with Eli Lilly and Company. Eli Lilly paid \$7 million for rights to develop gastrin and agreed to pay up to \$130 million more after certain development and sales milestones were hit.

DR. TONY CRUZ HAS BEEN INVOLVED WITH SEVEN BIOTECH COMPANIES:

Angiotech Pharmaceuticals, Inc.
(NASDAQ: ANPI, TSX: ANP)
Transition Therapeutics Inc.
(NASDAQ:TTHI, TSX:TTH)
NeuroMedix Inc.
HDM Diagnostics Inc.
OncoTherapeutics Inc.
AIM Therapeutics Inc.
Cascade Therapeutics Inc.

NUMBER OF U.S. PATENTS ASSIGNED TO ONTARIO-BASED INVENTORS



Source: Delphion.

Why not bring the gastrin-based therapy to clinical trials themselves? Cruz is candid: “Where are we going to get 400 million dollars to do a Phase III?”

On another front, the company’s Alzheimer’s treatment came out of research at the University of Toronto. To develop it, Transition partnered with Elan Pharmaceuticals and the drug is now in Phase II clinical trials.

Cruz also speaks frankly about the commercialization challenges that institution-led biotech has faced: insufficient venture capital and other funding, at the same time as universities have not yet fully mastered the balance between research and teaching on one side and the drivers and mechanics of commercialization on the other.

On top of that Cruz feels there is a need for government to accommodate the fact that certain drugs in development under their programs hit a dead end along the way. “Many biotech companies fail because they’re not vigilant enough killing things that aren’t going anywhere. And I think governments too have to do the same thing, because drug development exists within a culture where businesses dying off is the natural state of the industry.”

But governments also need to support those who are on the path to success. The Biopharmaceutical Investment Program, for example, aims to increase deal flow and stimulate public research collaborations for solid companies in Ontario’s growing biotechnology cluster. This will expand companies’ local footprints, increase the level of new R&D and advanced manufacturing in Ontario, and create a new generation of high value jobs for Ontarians.

For his part, Cruz is optimistic that the province’s growing strength in the biotech sector is going to lead to more serial entrepreneurs among Canadian scientists.

“I think it’s a phenomenal industry and I think Canada is well-positioned to benefit from it,” he says. “And, just as importantly, the U.S. has opened up to funding sound Canadian companies developing impact technologies.”



Dr. Tony Cruz, CEO, Transition Therapeutics, which is located at the MaRS Centre.

WHAT IF WE SPAN ANIMAL MEDICINE TO HUMAN THERAPEUTICS? WE DO.

At Bioniche Life Sciences Inc., in Belleville, Ontario, the traditional lines between agriculture-based research and human health research are converging.

Graeme McRae, an Australian who had worked for the animal health unit of Pfizer Inc, started Bioniche in 1979. He had identified a need to find non-antibiotic treatments for livestock illnesses given the prevalence of multi-drug resistant bacteria. Bioniche proceeded to develop veterinary products based on a non-pathogenic mycobacterium. Then McRae was approached by Alvaro Morales, currently Director of the Centre for Advanced Urological Research at Queen's University in Kingston, Ont., inquiring as to whether one of its animal products might have potential as a treatment for human bladder cancer, as the existing bladder cancer treatment and the Bioniche product were made (in different ways) from different strains of mycobacterium.

“That project has now taken on a life of its own,” says McRae, Bioniche President and CEO, noting Bioniche has spent more than \$100 million on research related to its mycobacterium cell wall technology. The company is now in the final stage of human clinical trials for a bladder cancer drug and the technology is so promising as an alternative to current therapies that the FDA has given the drug one of its coveted “fast track” designations.

Concurrent with this research, Bioniche also developed the world's first cattle vaccine against the *E. coli* O157:H7 bacterium. The bacterium, which was first identified as a foodborne pathogen in undercooked hamburger in the early 1980s, has since manifested itself in numerous food poisoning outbreaks around the world, many associated with vegetables contaminated via cow manure.

And it's a problem that is only getting bigger. While only about five per cent of North American cattle carried the bacterium in 2000 when Bioniche started working on a vaccine, “today you can't find a herd that tests negative,” says McRae.

Bioniche has responded to this situation by capitalizing on the research of Dr. Brett Finlay, a professor of cellular biology at the University of British Columbia, who first began investigating the 0157 strain in the 1990s. He demonstrated that the bacteria secrete certain proteins that allow them to attach to human intestinal walls and multiply.



Originally it was thought that blocking the attachment might be the basis for a human vaccine but when that proved impractical he teamed up with researchers in Saskatchewan and Alberta as well as those at Bioniche to develop an effective cattle vaccine that acts by preventing the attachment of the bacteria in the cattle intestines, thereby allowing it to pass through without reproducing in large quantities.

The vaccine won an Animal Pharm 2007 award for best new veterinary product for livestock, and Bioniche has been given provisional licences to sell the vaccine to vets in Canada and the U.S. And the vaccine's huge potential market — there are nearly 200 million cows in Europe and North America alone — has led to an infusion of \$25 million in federal and provincial money to support an expansion of Bioniche's Belleville vaccine manufacturing facility.

So what does this change from Bioniche, \$27 million-dollar vet medicine company, to Bioniche potential multi-billion dollar human and vet medicine company, signal to interested parties outside Ontario?

First, that the traditional model where Canadian universities do the research and companies based elsewhere do the development can be changed, at least in some instances.

“Our end game is not that we are going to sell our drugs to someone else to commercialize,” McRae says emphatically. “The point we have been making to government and others is that our manufacturing facilities — both human and veterinary — could generate hundreds of millions of dollars in exports of technologies which have limited competition.”

But this new emphasis on the D part of R&D also holds possibilities for foreign companies looking for a place to develop and grow.

“Today I would say to small U.S. companies: If you have a technology or a skill set capable of growing into commercial products, then Ontario is the place for you to come. Government is receptive in assisting to finance your facilities; highly skilled people are readily available; and companies like ours are happy to assist in creating successful ventures,” he says.

“...ONTARIO IS THE PLACE FOR YOU TO COME. GOVERNMENT IS RECEPTIVE IN ASSISTING TO FINANCE FACILITIES; HIGHLY SKILLED PEOPLE ARE READILY AVAILABLE; AND COMPANIES LIKE OURS ARE HAPPY TO ASSIST IN CREATING SUCCESSFUL VENTURES.”

GRAEME MCRAE, PRESIDENT AND CEO, BIONICHE LIFE SCIENCES INC.



WHAT IF CELLS COULD BE A DIAGNOSTIC TOOL? THEY ARE.

If there is a location on nature's genome that might be called Canada's place, it is mitochondrial DNA — that small string of genetic material found outside the cell's nucleus that governs cell energy distribution. In the last few years what Ontario-based researchers and companies have done is take mitochondrial DNA and spin off applications from it that are in the process of revolutionizing species identification and cancer detection.

CANADIAN BARCODE OF LIFE NETWORK, GUELPH, ONTARIO

In the late 1990s a light bulb went off for University of Guelph biologist Paul Hebert: Shouldn't it be possible to use DNA to identify species using techniques akin to the DNA fingerprinting approaches that were revolutionizing criminal investigations?

Few thought it would work in those early days but Hebert steamed ahead — initially using moths and butterflies he caught in his own backyard in Guelph. He chose to look for a species fingerprint in a mitochondrial gene because mitochondrial DNA changes more rapidly than nuclear DNA. What he found soon amazed the world. Not only could he link already identified species with a specific pattern in the DNA — Hebert called it a “species barcode” — but when you looked carefully it appeared that biologists had sometimes misclassified similar but genetically different species.

What followed was a rapid reconfiguration of how taxonomists identify species. Within four years of the first papers appearing on the subject, a \$30 million barcoding “factory” was built at Guelph, with the capacity for identifying 500,000 species a year at a cost of about \$10 per specimen. International programs were established to create a DNA species barcode for all the world's fishes, moths and butterflies, birds and Arctic creatures, among others. Many countries were shipping specimen DNA to Guelph to be identified.

Efforts to barcode plants, algae and microbes were moving forward.

“We couldn't have believed a few years ago that this would happen. I am shocked by how broadly the technique works,” Hebert has said.

While biologists are energized by the possibility of quickly identifying new species in a world where many seem perched on the brink of extinction, the Guelph group is also much taken with the practical applications of this work. For example, a 2004 study of fish found in eastern U.S. markets found that, according to the DNA species barcodes, 77 per cent of filets sold as red snapper had been mislabeled. Another study showed that you could tell the species of birds that had crashed into planes by analyzing DNA left behind. This is important for airport authorities in determining which bird species to implement controls for in their vicinity.

“We are convinced that bio-monitoring is going to be a very profitable business,” says Robert Hanner, Associate Director for the Canadian Barcode of Life Network in Guelph. Not only would that include determining whether cheap foodstuffs are being sold as higher priced items or endangered species are being illegally marketed, but this technique could also provide rapid identification of bugs or larvae found on imported produce or flowers.

The goal is to develop a quick and easy way of identifying a species on the spot. And this is what the Biodiversity Institute of Ontario in Guelph and Genesis Genomics are joining up to do. Their goal is to develop new ways of sequencing, which could lead to desktop machines that can run rapid species determination tests.

GENESIS GENOMICS, THUNDER BAY, ONTARIO



In the spring of 2000, a group of scientists associated with Lakehead University in Thunder Bay got together on Sundays to discuss the detection potential of mitochondrial DNA. They wondered if changes in mtDNA tiny packet of more than 16,000 base pairs might serve as an early warning signal for cancers — a telegraphing you couldn't easily see in nuclear DNA's often highly variable 3 billion base pairs.

Based on previous research — much rooted in studying changes in mitochondrial DNA seen in old bones — they decided not only was mtDNA cancer detection scientifically possible, it was potentially commercially valuable.

Fast forward to May 2008.

Genesis Genomics, the company the academics founded, begins to market a simple skin swab test — the sun-exposed nose is the ideal spot to gather skin — which uses mitochondrial DNA to tell people how much sun-related damage their skin has experienced and also categorizes a person by skin type to determine whether an individual possesses other variants that may increase their likelihood of developing skin cancer.

Partnering with Toronto-based VitalScience Corp., the Genesis Genomics product will be sold in more than 800 drug stores across Canada and distributed to Canadian dermatologists. Plans are for it to be sold internationally in 2009. On the horizon are early warning tests for difficult to detect prostate cancer.

Perhaps the most intriguing thing about the company is not that it has brought the world's first mitochondria-related IP product to market but rather how they did it.

Early on, the company learned about the research of Mark Birch-Machin, a professor of molecular dermatology at Newcastle University, England. “It was realized that the things he was researching with respect to mitochondrial DNA and the things our people were researching were effectively the same but for different diseases,” says company president Robert Poulter.

Genesis Genomics' response: Bring Birch-Machin in as a partner. Second, what might be seen an intrinsic disadvantage — establishing a biotechnology company in Northern Ontario — has so far worked in their favour. Lakehead University, which has a share in the company, sped up completion of necessary lab space. FedNor, the Canadian federal development agency and the provincial Northern Ontario Heritage Fund Corporation contributed nearly \$1.5 million to get the company off the ground.

“From a financing perspective I think it has actually been easier for us to be in Thunder Bay,” says Poulter, adding that the company has also drawn the support of more than 50 private local investors. And staffing hasn't been an issue with Lakehead's biology and biotechnology program graduates. “We have the pick of the crop. We get the brightest of the brightest.”

“BIO-MONITORING
IS GOING TO BE A
VERY PROFITABLE
BUSINESS.”

ROBERT HANNER, CANADIAN BARCODE
OF LIFE NETWORK, GUELPH, ONTARIO

WHAT IF ONTARIO'S DIVERSITY INSPIRED INNOVATION? IT DOES.

Why should knowledge-based industries come to Ontario or partner with people and institutions already established here?

Kevin Stolarick, Associate Director and Research Associate with the University of Toronto's Martin Prosperity Institute, has a ready and, to his mind, obvious answer: "It's either that you are going to recruit the people who are creating the innovations and doing the thinking, or you are going to decline," he proclaims and then adds, "and diversity breeds innovation. Period."

It is an assertion that Stolarick's boss and research collaborator, Richard Florida, has made a centerpiece of his now famous theories explaining why some places prosper in the modern world and others do not. First enunciated in his 2002 bestseller, *The Rise of The Creative Class*, Florida has argued that locales where a large number of knowledge creators choose to live — scientists, engineers, university professors, poets, novelists, artists, entertainers, actors, designers, architects, editors, cultural figures, think tank researchers, and analysts — have turned into the engines of the modern economy.

There have to be other elements — a strong high technology base and major research universities — but where the "creative class" truly wants to live is a kind of city that feels as open as their imagination.

Stolarick says that when he and Florida surveyed why creative class people were moving to other places, salary and job opportunities clearly played a part, but overriding this was their desire to find openness. "They kept telling us: 'What I want is a community that is open. Where anyone can be successful. Where I can move in and know that there will be other people like me. But also where I know there are going to be people who are different than me.'"

This makes the Greater Toronto Area, a place Florida has said has "arguably the most diverse population in the world", a magnet to the creative class. Florida himself made the journey, now calling Toronto home.

On one level it means that in a world where the movement of talent is almost as guaranteed a characteristic of modern life as the ebb and flow of tides, companies can know that not only will they find creative people here, but they can bring creative people in with little problem. "You can recruit internationally and have no trouble bringing in that absolutely fabulous oncologist you want to recruit from China," says Stolarick.



"Ultimately I decided to accept the offer in Toronto because I think Toronto really is the hottest place in Canada for research. Not only is the calibre of research as good as in any American University, but we have superstars like you might find at Harvard, Yale, Princeton, Oxford and Cambridge."

- Dr. John Rubinstein, a bio physicist who earned his PhD at the University of Cambridge, is now a principal investigator at the \$1.5 million cryo-electron microscopy facility recently opened at The Hospital for Sick Children.

“(TORONTO) ARGUABLY HAS THE MOST DIVERSE POPULATION IN THE WORLD, A MECCA TO THE CREATIVE CLASS.”

-RICHARD FLORIDA, DIRECTOR
MARTIN PROSPERITY INSTITUTE,
UNIVERSITY OF TORONTO



On another level creative people also like convenience, affordability, safety, theatres, clubs, and, good schools too. Here too, Toronto scores an A.

“Toronto is a significant economic centre with superb universities, leading arts, entertainment, design and culture industries,” Florida writes in his new book *Who’s Your City?: How The Creative Economy Is Making Where To Live The Most Important Decision Of Your Life?* “...Like London, but unlike most U.S. cities, Toronto offers schools that work, low crime and safe streets. Unlike London, New York, Los Angeles or San Francisco, it remains relatively affordable, which allows it to retain a wide mix of social and economic classes. Nearby Waterloo in Ontario houses Research in Motion, the BlackBerry Company.”

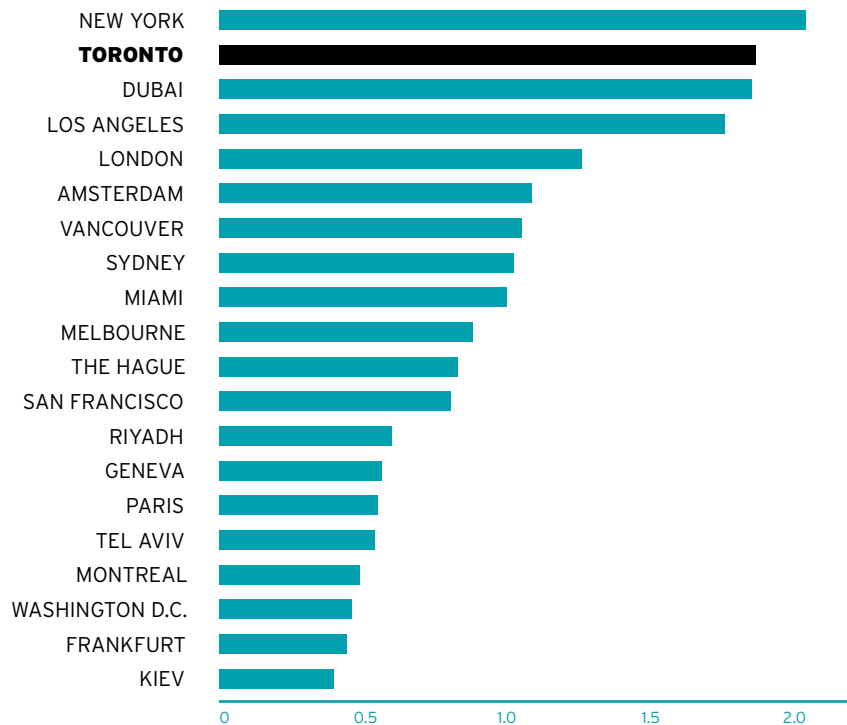
But are the notorious bad Canadian winters not a disincentive?

Hardly, says Stolarick. “Is it any worse than Boston, or London or Stockholm or Copenhagen — all cities which are doing phenomenally well economically.”

So is there a final message to anyone coming here?

“Toronto is the world and that is why the world wants to come to Toronto,” says Stolarick. “Not only can they come, but the dynamics of Toronto mean there is work for their spouse — there are programs in their own language for their children, and above all there is a sense Canadians and Torontonians love their city mosaic and everybody is welcome.”

THE MOSAIC INDEX INDICATES DESTINATIONS FOR IMMIGRANTS FROM AROUND THE WORLD.



Source: Lisa Benton-Short, Marie Price, and Samantha Friedman, “A Global Perspective on the Connections Between Immigrants and World Cities,” The George Washington Center for the Study of Globalization, 2004.

WHAT IF WE FOSTERED GLOBAL TALENT? WE DO.

Fang Liu, MD, PhD, Senior Scientist, Centre for Addiction and Mental Health, Toronto

The brain has always been on the brain of Ontario-based researchers, and in particular those parts of the brain that relate to mental illness and addiction. Seminal work in this field was done by Philip Seeman in 1974-75 when he found that the effectiveness of antipsychotic drugs is directly related to their ability to block the dopamine D2 receptor. This opened the way to a scientific explanation for drug reactions and continues today in the work of a number of Ontario labs and companies dedicated to neuromedicine.

A worthy successor to that legacy is Fang Liu, Senior Scientist and Section Head for the Molecular Neuroscience section in the Centre for Addiction and Mental Health's Neuroscience Research Department and an associate professor at the University of Toronto. Liu has won numbers of awards, including an award from the U.S. National Alliance for Research on Schizophrenia and Depression.

But her combination of personal and professional achievements goes beyond that. If Horatio Alger was reborn in the 21st century, he would have the face and drive of Fang Liu. Her story:

"I studied to become a pediatrician at Shanghai Medical College, one of the best medical schools in China, and then practiced for five years. I came to Canada in 1992 as a visitor with my husband, who had been accepted to do his M.A at York University, and quickly discovered the reality that I could not practise medicine as a foreign medical school graduate. This left me with a quandary of how to intellectually survive. And I decided that the most natural thing to do was move into medical research because as a clinician I had seen that doctors often used a drug without understanding its mechanism.

I was accepted into the U of T and the lab of Hyman Niznik, which initially was a financial struggle as I didn't have a green card and had to pay international student fees. But I threw myself into the work and became a kind of professional fast tracker. I finished my PhD in two-and-a-half years, had a second child, published a paper in *Nature*, and after a year's post doc got an Independent Scientist position.

What I became interested in was the role of dopamine receptors. Dopamine is the brain-stimulating substance, which is released in the brain by almost any addiction — nicotine, alcohol etc. As well, it is involved in virtually all psychiatric diseases, most notably schizophrenia. Part of what directed my efforts is that the University of Toronto is probably the world centre in dopamine research growing out of the pioneering work done by Phil Seeman.



As a foreign medical school graduate and newcomer to Canada, Fang Liu (centre with her family) is now a PhD neuroscientist exploring glutamate's role in schizophrenia.

“ BECAUSE OF THE CULTURAL EASE HERE, WE FOUND IT EASY TO FIT INTO THE CITY.”

FANG LIU, SENIOR SCIENTIST, CENTRE FOR ADDICTION AND MENTAL HEALTH, TORONTO

Research in my lab is focusing on protein-protein interaction, specifically neurotransmitter receptors in the brain. I am interested in what you might call the raincoat problem. What we would like to do is block the effect of a neurotransmitter that is linked to one negative condition — let’s say glutamate-induced brain cell death following stroke — but still allow for glutamate’s fundamental role in ensuring normal brain function. Total glutamate blockage effectively shuts down the brain. So what you would like to create would be the chemical equivalent of a farmer putting on a raincoat during a thunderstorm while the same rain is watering his fields.

We have found that the interaction of AMPA glutamate receptors with other proteins in the brain allows for this. And we have applied for a patent on a peptide that allows us to stop glutamate’s brain cell killing effect after a stroke, while at the same time permitting normal brain function to continue.

Similarly we are looking for protein-protein interactions that relate to controlling nicotine addiction and schizophrenia.

Part of what has allowed us to move forward has been a realization on the part of the Ontario government that one of the key things missing in the pathway of drug development has been the middle step where a scientist went from discovery to proof of principle. We have received a grant from the Ontario Research Commercialization Program (ORCP), which has allowed us to show in animal models that we can protect brain cells from glutamate’s killing effects while permitting brain functioning activities to continue.

What I hope for in ten or 15 years is that my two careers will have come together. I want people to be clinically helped and not just have scientific knowledge going forward. And I guess I should add, in that vein, that while I am grateful for the ORCP grant I understand that there is only very limited monies available for academics such as myself who need proof-of-principle funding to add value to our discoveries to make them attractive to industry.

I also have to say how comfortable it has been for me and my husband, who works in information technology for the Royal Bank, to be immigrants to Canada. Because of the cultural ease here, we found it easy to fit into the city. Part of that has been how easily I have been able to fit into my other, and I think most important role: Mom. Here in Toronto I am a hockey mom in winter and a soccer mom in summer.”

WHAT IF WE CREATED A CENTRE THAT IMPROVED BRAIN FITNESS? WE HAVE.

With a \$10 million funding injection from the Province of Ontario, Baycrest, one of the world's premier health sciences centres focused on aging, announced in April 2008, the creation of the Centre for Brain Fitness. A principal aim of the centre is to develop and commercialize a range of innovative products specifically designed to improve brain fitness in aging populations.

"There are few things as frightening as the prospect of declining brain fitness as we age and the loss of our mental faculties," says Dr. William E. Reichman, Baycrest President and CEO. "Baycrest's strengths in aging brain research, cognitive assessment and rehabilitation make it well-positioned to develop innovative, market-driven research products that will transform the way we age."

Baycrest, which is based in Toronto, will do this by partnering with the MaRS Venture Group team of business advisors. This group has been specifically constituted to link science and technology researchers and innovators with the networks and capital needed to create and grow successful Canadian enterprises.

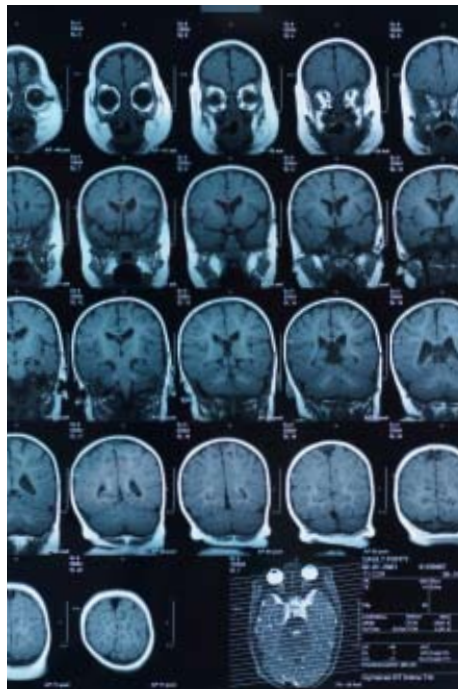
The province's \$10-million investment matches \$10 million from private donors. Products in development over the next 10 years will include:

CLINICAL ASSESSMENT SOFTWARE for use by doctors to assess memory, processing and reasoning in patients, from stroke survivors to those with Alzheimer's disease and other cognitive impairments. Baycrest is currently developing a prototype diagnostic tool (computer tablet) in collaboration with Sunnybrook Health Sciences Centre.

BRAIN FITNESS PRODUCTS to help healthy aging adults (ages 45-75) maintain their cognitive functions, plus an additional product suite for caregivers to provide cognitive rehabilitation to people with mild cognitive impairment and dementia who live in long-term care facilities and retirement homes.

EXECUTIVE TRAINING PROGRAM for corporations wishing to help their aging employees improve cognitive functions to remain productive.

WEB-BASED OUTREACH PROGRAM to support people caring for loved ones with mild to medium cognitive impairment.



DOPAMINE-RELATED DISCOVERIES AT UNIVERSITY OF TORONTO:

1974-75

Philip Seeman discovers that the effectiveness of antipsychotic drugs is directly related to their ability to block the dopamine D2 receptor. This opens the way to a scientific explanation for the drugs' reactions. His papers are among the most highly cited in the schizophrenia literature.

1988

Hubert Van Tol and his colleagues were the first to report the cloning of the dopamine D2 receptor.

2000

Fang Liu and others uncover a previously unknown method of signal transduction between two structurally different neurotransmitter receptor systems.

2000

Shitij Kapur and associates use brain imaging to explore how to treat schizophrenia with lower doses of medication and fewer side effects.

2002

Seeman and others find the first gene whose mutations put one at risk for schizophrenia.

2005

An international team led by Seeman finds that mutations to genes that have no relation to the brain's dopamine receptors can still cause those receptors to become highly sensitive to their own dopamine, a condition that often leads to psychosis.

2007

Susan George and Brian O'Dowd discover that the brain has a distinct dopamine signaling complex, a finding they believe opens the way to a new class of anti-schizophrenic drugs.

Source: University of Toronto and Science Daily

WHAT IF WE MADE INNOVATION A DESTINATION? WE HAVE.



MaRS AIMS TO
CREATE GLOBAL
COMPANIES
FROM CANADA'S
SCIENCE,
TECHNOLOGY
AND SOCIAL
INNOVATION.

When the concept of MaRS was being developed in 2000 no one was quite sure what exactly it would look like.

Academic and industry leaders knew that Ontario — the birthplace of insulin and stem cell biology, home to leading hospitals and universities — was rich with top-ranked research. They also recognized that the province had only a modest track record in harnessing the commercial potential of that research.

Yet the potential abounds. Toronto alone boasts the third largest cluster of biosciences expertise in North America, and the University of Toronto publishes more scientific papers than any other North American academic institution apart from Harvard.

That research prowess extends across the province thanks, in large part, to significant federal and provincial investments in the scientific enterprise since the early 1990s.

As an independent non-profit organization, MaRS was born from the idea that Ontario needs not only to better capture the relevant commercial potential of its research but it needs to directly connect the worlds of science, business and capital and stimulate a culture of innovation.

By 2000, a small group of influential Ontario business and community leaders had raised an initial \$11 million seed fund, which went on to leverage significant provincial and federal investments. Thus began a collective effort to turn a vision into MaRS — an agile, market-facing engine designed to drive commercial success and help create global companies from Ontario's science and technology.

Fast forward to 2008, three years after MaRS opened its doors on a newly developed 700,000 sq. ft. centre, and that innovation engine is humming — not only through an expansive physical presence but also a vibrant regional and online network, inventive programming and hands-on advisory services for entrepreneurs.

MaRS' physical footprint lies at the heart of Canada's most diverse and creative city — in an inspiring blend of heritage and modern lab and office space, backed by an impressive technical and conference infrastructure. The building itself is home to a mix of 70 tenants employing more than 2,000 people, from leading research groups to emerging tech and biotech companies, mature private-sector tenants and venture capitalists alongside policymakers, professional service providers and networking organizations.

And that footprint is growing with a 700,000 sq. ft. Phase II development — in partnership with Alexandria Real Estate Equities Inc. of Pasadena, California — expected to be complete in 2010 at one of the most visible and desirable locations in downtown Toronto.

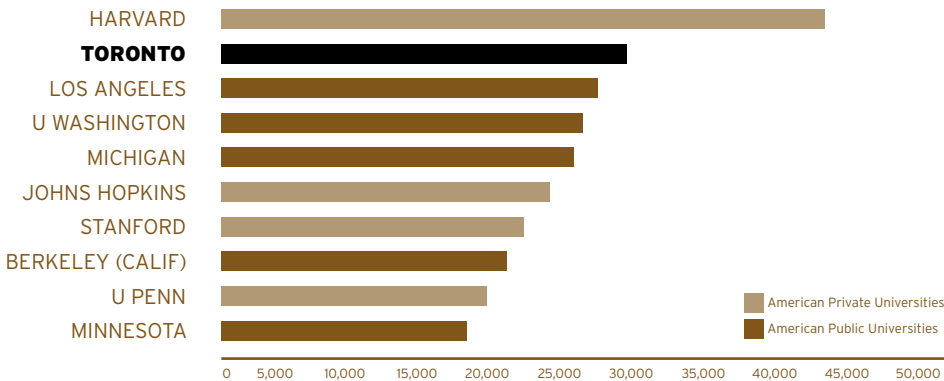
“Projects like this one are further evidence of the architectural renaissance that is taking place in Toronto,” Mayor David Miller said at the announcement of the Phase II project in summer 2007. “But more than that, it’s a display of the trust that companies have in our city as a place to invest and bring high quality knowledge-based jobs, which is what makes us North America’s third largest biotech centre.”

Adjacent to the financial district, cultural attractions and the provincial legislature, MaRS has quickly become a premier event venue, now attracting approximately 100,000 participants annually to workshops, meetings, conferences, exhibits and performances.

PUBLICATIONS AND CITATIONS

COUNTS BY INSTITUTION

Publications and citations are indexed by a number of organizations including Thomson ISI, whose data were used in the present analysis. The goal was to rank the University of Toronto against members of two leading research-intensive university groups: the Canadian G13 group and the American Association of Universities¹ (AAU). U of T is a member of both groups, as is McGill.



Sources of primary data: Thomson ISI U.S. and Canadian University Indicators - Deluxe Edition 2005.

¹Note that the University of California, San Francisco, has all its four faculties in the health sciences and is a recognized leader in these fields, but is not a member of AAU.



MaRS CEO, Dr. Ilse Treurnicht, joins founding Board Chair, Dr. John Evans (left), and incoming Board Chair, Gord Nixon, CEO of the Royal Bank of Canada.



“WHEN WE BRING INVESTORS HERE FROM THE U.S. – AND MORE AND MORE ARE COMING – THEY TAKE ONE LOOK AT MaRS AND IMMEDIATELY BELIEVE THAT THE GOVERNMENT NOW HAS A REAL COMMITMENT TO PHARMACEUTICAL DEVELOPMENT.”

MaRS TENANT DR. TONY CRUZ, CEO, TRANSITION THERAPEUTICS INC.

But the heart of MaRS’ mission lies in connecting entrepreneurs with the resources they need to succeed, not only in science and technology but also in the emerging field of social enterprise. In addition to providing market intelligence and extensive advisory and mentorship services, MaRS designs and delivers engaging hands-on entrepreneurship programs both with partners and through a MaRS-branded series, which includes peer-to-peer offerings, best practices and bio-entrepreneurship. These programs deliver real-world content to real-world innovators.

Achieving the mission also means overcoming traditional barriers to commercialization by developing a market-facing approach that is able to pool intellectual property for a global market.

Looking ahead, one of the most exciting developments is the creation of MaRS Innovation, a collaboration designed to aggregate the commercial output of 14 research institutions in the Toronto area. The goal, over the next five years, is to build a diversified portfolio of assets, and harness the economic potential of the best opportunities. The Founding Board Chair of MaRS Innovation is Mary Jo Haddad, President and CEO of The Hospital for Sick Children.

MaRS INNOVATION AGGREGATES THE DISCOVERY AND COMMERCIALIZATION ASSETS OF TORONTO INSTITUTIONS:

Baycrest
BioDiscovery Toronto
Bloorview Kids Rehab
Centre for Addiction and Mental Health
The Hospital for Sick Children
MaRS Discovery District
Mount Sinai Hospital
The New Women’s College Hospital
Ontario College of Art and Design
Ontario Institute for Cancer Research
Ryerson University
St. Michael’s Hospital
Sunnybrook Health Sciences Centre
Toronto Rehabilitation Institute
University Health Network
University of Toronto

It’s a growing and ambitious slate of activities for MaRS, a one-time start-up that is now a growth-phase enterprise — and one that has attracted attention from some key supporters in the private sector.

“I believe passionately in the mission as a means of creating prosperity and competitiveness for Canada,” said Gord Nixon, CEO of RBC, Canada’s leading bank, and incoming Chair of the MaRS Board of Directors. “It is essential that we continue to transform our economy and utilize our strength in science, technology and innovation to create successful businesses — and MaRS is well-positioned to play a leading role.”

AS MaRS ENTERS ITS THIRD YEAR, IT'S ACHIEVED THE FOLLOWING MILESTONES:

- 1,000 case studies for 300 early-stage start-up companies.
- More than half of those clients are located outside the Greater Toronto Area, including Artenga (Ottawa), Forte (Waterloo) and Medix Technologies (London); all are either pre-revenue or in the early stages of generating revenue (\$1M/year).
- The majority of MaRS business advisory services are provided in strategic and business planning, with the primary service being market research and competitive intelligence.
- Flagship program Entrepreneurship 101 drew more than 900 registrants in 07/08 up from 400 in its first year 05/06.

“IT'S MUCH QUICKER TO DO AN EXPERIMENT THROUGH COLLABORATION THAN TO LEARN OR IMPORT THE TECHNOLOGY, SO THAT'S ONE OF THE REASONS IT'S SO ADVANTAGEOUS TO BE IN THE MaRS CENTRE HERE AND WITHIN THIS UNIVERSITY OF TORONTO TEACHING HOSPITAL COMMUNITY. IF I CAN'T DO SOMETHING IN MY LAB, I CAN GO ACROSS THE STREET AND I HAVE EVERYTHING WITHIN A ONE-BLOCK RADIUS.”

DR. STEPHEN SCHERER, SENIOR SCIENTIST, THE HOSPITAL FOR SICK CHILDREN, AND WINNER 2008 PREMIER'S SUMMIT AWARD FOR MEDICAL RESEARCH.



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“TORONTO IS ESTABLISHING ITSELF
AS A REAL FORCE IN THE LIFE SCIENCE
AND TECH SECTORS – MaRS IS AT THE
EPICENTER OF THAT.”

JIM RICHARDSON, PRESIDENT, ALEXANDRIA REAL ESTATE EQUITIES INC.
PASADENA, CALIFORNIA, DEVELOPER, MaRS PHASE II

Acknowledgments

The Ministry of Research and Innovation and MaRS gratefully acknowledge the Ontario Genomics Institute, Ontario Innovation Trust, Ontario Institute for Cancer Research and the Toronto Region Research Alliance for their assistance with photos and data.

For more information, please visit the Ministry of Research and Innovation website at www.ontario.ca/innovation or call 1 800 819 8701. Or contact MaRS at 416 673 8104 or marsdiscoverydistrict@marsdd.com

“ OFFERING A CREATIVE ENVIRONMENT,
A DIVERSE CULTURE, A HIGHLY SKILLED
WORKFORCE AND A STRONG TRACK RECORD
OF RESEARCH AND COMMERCIAL SUCCESS,
ONTARIO, CANADA IS WELL POSITIONED TO
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ECONOMIES IN THE WORLD.”



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