

TORONTO REGION: A GLOBAL LEADER IN STEM CELLS AND REGENERATIVE MEDICINE



“Toronto has the critical mass and collaborative environment. All the different pieces needed to solve the stem cell puzzle are in place. We provide the bioengineering translation part, while others provide a development or genetic engineering perspective. You can go right from discovery to therapy all in the same place.”

- **Dr. Peter Zandstra**, Canada Research Chair in Stem Cell Bioengineering and Professor of Tissue Engineering at University of Toronto’s Institute of Biomaterials and Biomedical Engineering, and Department of Chemical Engineering and Applied Chemistry

STRATEGIC INVESTMENT IN STEM CELL RESEARCH IN THE TORONTO REGION

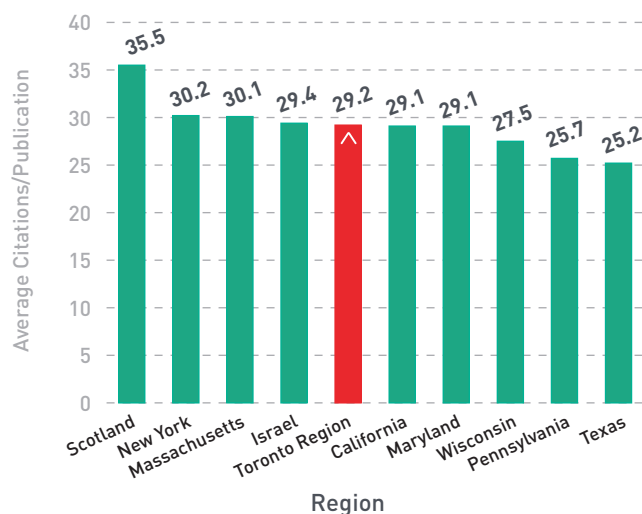
The Toronto Region is world-renowned for its leading research in stem cells. In the early 1960s, Dr. James Till and Dr. Ernest McCulloch first showed the existence of stem cells. Current researchers like Dr. Gordon Keller at the McEwen Centre for Regenerative Medicine, Dr. Janet Rossant at The Hospital for Sick Children, Dr. John Dick at the University Health Network, and Dr. Mick Bhatia at McMaster University in Hamilton continue the tradition of cutting-edge research in the Toronto Region, building upon the solid foundation established by Till and McCulloch four decades ago.

This extensive level of activity has led to a series of strategic initiatives to concentrate the different biomedical expertise. These initiatives are meant to address the most daunting challenges in stem cell biology research as discoveries move from the laboratories to the clinic. One of these initiatives is the **Toronto Stem Cell Initiative (TSCI)**, an inclusive collection of stem cell research laboratories at the University of Toronto and at hospital research institutes. The goal of this initiative is to conduct stem cell research at all stages and to represent the ‘national and international face’ of stem cell research for the entire University of Toronto community.

The **Cancer Stem Cell Consortium (CSCC)**, established in 2007, will allow the biomedical community to move quickly and effectively from discoveries to application in the clinic and to launch partnerships among organizations within Canada. In 2008, the CSCC announced its first international partnership with the **California Institute for Regenerative Medicine (CIRM)**. One of the first initiatives will be the Disease Team Research Awards. Proposals will be evaluated by an international team of experts who will focus on applications that have a chance of clinical impact within five years. The CSCC has committed up to \$40 million to support the Canadian component of this research.

TORONTO REGION STEM CELL RESEARCHERS HAVE GLOBAL IMPACT

Average Citations/Publication, 1998-2008



HIGH-IMPACT, HIGH-VALUE STEM CELL RESEARCH

The Toronto Region has a large concentration of research centres conducting high-impact, high-value research. Stem cell research activity in the region ranges from deriving new stem cell lines to translational research, and rivals the other North American stem cell centres such as Boston and California. More than 70 scientists and principal investigators focus on five broad areas: cancer stem cells, adult stem cells, embryonic stem cells, regenerative medicine, and bioengineering/tissue engineering.

MCEWEN CENTRE FOR REGENERATIVE MEDICINE (TORONTO)

The **McEwen Centre for Regenerative Medicine** is a collaborative entity, which brings together 15 clinicians and scientists across University of Toronto-affiliated hospitals that focus on regenerative medicine and biomedical research. The Centre focuses on three themes: repair and regeneration, origin and modeling diseases, and new tool discoveries. It has brought together the best stem cell biology scientists in the Toronto area and their disease-specific expertise.

The Centre focuses on the following disease research areas: heart disease, diabetes, spinal cord injury and neurodegenerative diseases, blood cell disorders, lung disease and musculoskeletal diseases. Cutting-edge stem cell technologies such as enhancing the regenerative capacity of the heart, cellular therapy and tissue engineering are used to investigate these diseases. For example, world-renowned scientist Dr. Gordon Keller has optimized differentiation of human embryonic stem (ES) cells into a homogenous layer of cardiomyocytes free from animal contaminants. By understanding the molecular requirements for heart precursors in the embryo, his laboratory is now able to use these cues to systematically differentiate uncommitted ES cells to fully differentiated cardiomyocytes fated for the different chambers of the heart.

ONTARIO INSTITUTE FOR CANCER RESEARCH (TORONTO)

The **Ontario Institute for Cancer Research** (OICR) is a not-for-profit corporation funded by the Province of Ontario. This institute is dedicated to the prevention, early detection, diagnosis and the treatment of cancer. As part of this endeavor, a division for cancer stem cell research was established.

Dr. John Dick, a Senior Scientist at the Ontario Cancer Institute, the research arm of the University Health Network's Princess Margaret Hospital, heads the OICR Cancer Stem Cell program. The program coordinates the work of 30 scientists at three sites across Ontario to identify ways to selectively target cancer stem cells to eradicate the disease, and to prevent metastases and recurrence. The Cancer Stem Cell group uses a variety of tools for stem cell identification, including: bio-repositories and pathology, genomics and high-throughput screening and mouse models.

OICR is one of the founding partners of the Cancer Stem Cell Consortium, along with Genome Canada, the Canadian Institutes of Health Research, the Canada Foundation for Innovation and the Stem Cell Network. The CSCC is backed by an initial \$100 million funding commitment from its Canadian partners.

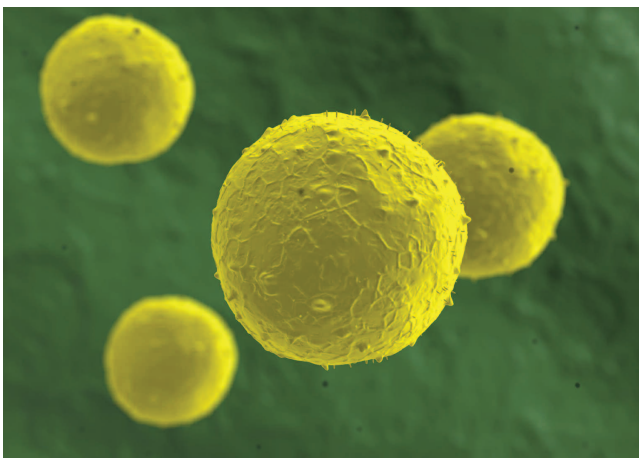
MCMASTER STEM CELL AND CANCER RESEARCH INSTITUTE (HAMILTON)

Founded in 2006, the **McMaster Stem Cell and Cancer Research Institute** receives funds from the OICR. Inaugural Scientific Director Mick Bhatia, leads a group of eager scientists who investigate the biology of human cancer stem cells, embryonic stem cells and adult stem cells.

The team of scientists is on the cutting-edge of human stem cell research and has already established themselves as experts in the field. They have integrated expertise in epigenetics, signaling pathways, neural cancer stem cells, human leukemia and pluripotent stem cells. This team of investigators for the first time – have demonstrated the difference between normal stem cells and cancer stem cells in humans.

“The culture of collaboration and cooperation is really quite special here. We can compete with the rest of the world but we try not to compete with each other. It makes us stronger but it also makes us attractive to other partners too.”

- **Dr. Janet Rossant**, Chief of Research at Toronto's Hospital for Sick Children and Senior Scientist in the Developmental and Stem Cell Biology program.



UNIVERSITY OF TORONTO – INSTITUTE OF BIOMATERIAL AND BIOMEDICAL ENGINEERING (TORONTO)

As part of the University of Toronto, the **Institute of Biomaterial and Biomedical Engineering (IBBE)** pursues research in four areas: neural, sensory systems and rehabilitation engineering; biomaterials, tissue engineering and regenerative medicine; molecular imaging and biomedical nanotechnology; medical devices and clinical technologies. The tissue engineering and regenerative medicine group study: orthopaedic, dental, cardiovascular and soft tissue biomaterials; stem cell bioengineering and functional genomics; cellular engineering; and hemodynamics, cellular and tissue biomechanics.

The IBBE houses the **Centre for Modeling Human Disease (CMHD)** gene trap resource headed by Dr. William Stanford as part of the **International Gene Trap Consortium**. This venture has developed a library of mutagenized mouse embryonic stem cells freely available to the scientific community.

THE HOSPITAL FOR SICK CHILDREN (TORONTO)

The Research Institute at **The Hospital for Sick Children (SickKids)** has a strong history in stem cell research with countless collaborations and key breakthrough

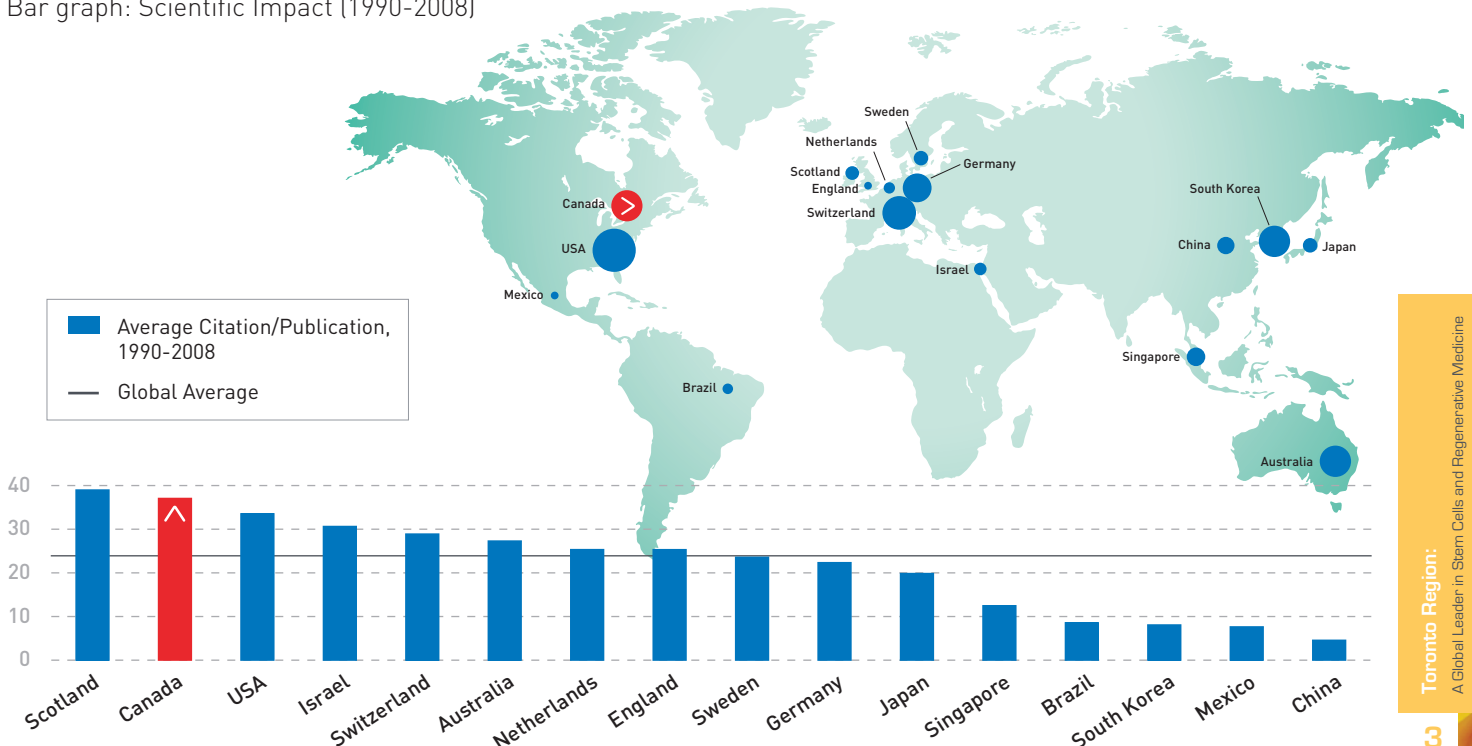
discoveries. Through the **Developmental & Stem Cell Biology** program, the Institute has an extensive stem cell research agenda and is supported by imaging (MiCe), genome centre (**The Center for Applied Genomics – sequenced chromosome 7**), and the **Ontario Induced Pluripotent Cell Facility (iPS)**.

The Institute incorporates basic stem cell research with translational research and focuses on children’s health issues. Current research activities include studying the mechanisms that determine the developmental potential of endogenous embryonic and adult stem cells as well as induced pluripotent stem cells, and how cells are transformed into cancer initiating cells. As well, teams are investigating how stem cells can be used in regenerative medicine and tissue engineering, e.g. spinal cord injury and bladder regeneration.

Scientists at SickKids have contributed greatly to the stem cell knowledge base and have collaborated in numerous important discoveries such as: producing early endoderm cells from human embryonic stem cells; the discovery of the SIRPalpha gene which has properties that allow for the successful engraftment of stem cells from human bone marrow into mice; advances in repairing spinal cord injuries through the use of skin-derived stem cells; and the isolation and characterization of a cancer stem cell from human brain tumours of different phenotypes that express neural stem cell markers and have stem cell-like behaviour in vitro and in vivo.

GLOBAL STEM CELL RESEARCH ACTIVITY: CANADA RANKS AMONG TOP 5 IN NUMBERS OF SCIENTISTS AND IN SCIENTIFIC IMPACT

Circle area: Number of Principal Investigators
Bar graph: Scientific Impact (1990-2008)



MOUNT SINAI HOSPITAL – THE SAMUEL LUNENFELD RESEARCH INSTITUTE (TORONTO)

Established in 1985, the **Samuel Lunenfeld Research Institute of Mount Sinai Hospital** is a leader in stem cell research internationally, and is one of the founding centres to have revolutionized the field of genome manipulation in mammalian embryonic stem cell research.

Former Lunenfeld researcher Dr. Alexandra Joyner developed technologies to 'trap' genes to follow gene expression and eliminate function at once which is now the basis of Knockout Mouse Project (KOMP). Subsequently, Lunenfeld Senior Investigator Dr. Andras Nagy generated mutant mice directly from the dish, and has since improved the process.

In 2005, Dr. Nagy established the first Canadian human embryonic stem cell lines. He and his colleagues across Canada have since used these lines to study their regenerative properties. More recently, a project spearheaded by Dr. Knut Woltjen, a postdoctoral fellow in the Nagy laboratory, achieved the derivation of stem cells from fibroblasts without the use of viruses, making regenerative medicine even more tangible for translation into the clinic.

Collaborations with the Toronto Centre for Phenogenomics (TCP) and access to leading-edge robotics facilities allow the Lunenfeld to continue to build on leading research breakthroughs.

QUICK FACTS ABOUT TORONTO REGION BIO LIFE SCIENCES

- One of North America's largest health sciences complex:
 - 60 hospitals including 12 research hospitals affiliated with medical schools at the **University of Toronto** and **McMaster University** (Hamilton)
 - 37 medical institutions
 - 8,200 physicians; and 54,000 health professionals
- The location of one of North America's largest biomedical sectors:
 - More than 1,200 life sciences firms
 - 140,000 employees
 - \$8 billion in pharma revenues in Ontario (ethical, generic and OTC)
- A global research centre with sophisticated resources such as:
 - **Structural Genomics Consortium**, a \$30 million partnership between the University of Toronto, Oxford University, Karolinska Institute, Merck, Novartis and GlaxoSmithKline
 - **Toronto Centre for Phenogenomics**: a \$69 million state-of-the-art research facility studying mouse models of human disease, is the most advanced of its kind in the world
 - **Terrence Donnelly Centre for Cellular & Biomolecular Research** at the University of Toronto: centre for integrative biology, disease modeling, and functional imaging
- Home to **MaRS Innovation**, a partnership of 14 Toronto-based academic research institutions to accelerate the commercialization of promising research from its members

“The human capital in the Toronto
Region creates a huge dynamic
that is hard to replicate anywhere.”

- **Dr John Dick**, Senior Scientist at the Toronto General Research Institute of the University Health Network (UHN) and Professor of Molecular and Medical Genetics at the University of Toronto

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