UNIVERSITY HEALTH NETWORK
Research Report 2007

Welcome to the UHN *Research Report 2007*:

Regenerating Knowledge

University Health Network is Canada's premier research hospital and an affiliate of the University of Toronto.

Our vision is to have global impact in biomedical and health care research.

UHN Research comprises three research institutes: Ontario Cancer Institute (including Advanced Medical Discovery Institute and The Campbell Family Institute for Breast Cancer Research), at Princess Margaret Hospital; Toronto General Research Institute, at Toronto General Hospital; and Krembil Research Institute, at Toronto Western Hospital.

This year our Research Report focuses on our successes in regenerative medicine. Regenerative medicine is a compelling field of research that promises new treatments for some of the most devastating human diseases. And UHN is leading the way.

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Message from the President

UHN Transforms Regenerative Medicine

UHN's purpose statement is, "We are a caring, creative and accountable academic hospital, transforming health care for our patients, our community and the world".

One type of transformative health care is regenerative medicine. It offers the promise of dramatically changing current medical practice and improving the lives of millions worldwide. UHN investigators, working with UHN clinicians, staff and trainees, are at the forefront of this new field.

Our regenerative medicine initiatives are one reason why UHN is a leader among research hospitals. Please read on to learn more.

Dr. Robert S. Bell
President and CEO
University Health Network

Dr. Robert S. Bell, President and CEO, UHN

Message from the VP

UHN Invests in New Ways of Healing

This past year has been a year of tremendous growth and development of the UHN research enterprise.

We've welcomed new OCI Director Dr. Ben Neel to our leadership team. We've received $49M in new infrastructure funding towards the creation of five new research centres across UHN. We've seen additional institutions join our new Shanghai-Toronto Institute for Health Research.

But a major focus this year has been the dramatic expansion of our regenerative medicine program.

Regenerative medicine seeks to utilize the body's own cells in developing treatments for disease. A field which is in early stages, it has the potential to transform the lives of millions afflicted by numerous diseases, such as stroke, diabetes, rheumatoid arthritis, spinal cord injury, and Parkinson's disease.

Regenerative medicine constitutes one of UHN's research priority platforms and has been the focus of substantial investment of resources.

2006/07 saw several developments that further signified UHN's commitment to this area.

The McEwen Centre for Regenerative Medicine, generously funded by donors Rob and Cheryl McEwen, was launched last October, becoming UHN's official hub for regenerative medicine discoveries. Director Gordon Keller has overseen the opening of the centre, providing strong intellectual leadership in the field and creating a diverse, multi-institutional research team.

Two large RM initiatives—a cancer stem cell centre and a

Dr. Christopher J. Paige, VP, Research, UHN

UHN Research—International Research Advisory Board

Philip Branton (Chair), PhD, FRSC / MSRC
Scientific Director
CIHR Institute of Cancer Research

regenerative medicine program spanning cell therapy, gene therapy and tissue engineering—won nearly $23 million in government funding.

Regenerative medicine offers the promise of transforming current medical practice, and in these new initiatives UHN researchers are working to bring this dream to fruition. Together—UHN researchers, support staff, our Foundations and our colleagues from the University of Toronto and other Toronto Academic Health Science Network institutions—we are generating the innovations that will make this dream a reality.

Dr. Christopher J. Paige
Vice-President, Research
University Health Network

Victor Dzau, MD
President & CEO, Duke University Health System
The Chancellor for Health Affairs
Duke University Medical Center

Ralph Steinman, MD
Henry G. Kunkel Professor and Senior Physician
Rockefeller University

Hans Wigzell, MD, PhD
Professor, Microbiology and Tumor Biology Center
Karolinska Institute

UNIVERSITY HEALTH NETWORK
Research Report 2007

2007 Statistics

Research Space	**737,000 sq ft**	**Senior Scientists**	151	**Fellows**	493
Publications	**1,442**	**Scientists**	48	**Graduate Students**	374
External Research Funding	**$223,799,000**	**Affiliate Scientists**	56	**Total Trainees**	**867**
		CRSC/CRU Members	219	**Technical/Support Staff**	**1,289**
		Total Researchers	**474**		

Our Scientists and Clinical Research Staff

OCI Scientists

Applied Molecular Oncology

Senior Scientists
Asa, Sylvia
Bristow, Robert
Ezzat, Shereen
Gallie, Brenda
Hedley, David
Hill, Richard
Kamel-Reid, Suzanne
Liu, Fei-Fei
Moore, Malcolm
Squire, Jeremy
Tannock, Ian
Tsao, Ming-Sound

Scientists
Done, Susan
Martin, Lisa
Trudel, Suzanne
Liu, Geoffrey

Biophysics & Bioimaging

Senior Scientists
Chakrabartty, Avijit
Hunt, John
Jaffray, David
Sherar, Michael
Vitkin, Alex
Wilson, Brian
Zheng, Gang

Scientists
Lilge, Lothar
Siewerdsen, Jeffrey

Cancer Genomics & Proteomics

Senior Scientists
Arrowsmith, Cheryl
Gariépy, Jean
Pai, Emil
Penn, Linda
Privé, Gilbert
Rose, David

Scientists
Kislinger, Thomas
Raught, Brian
Schimmer, Aaron
Tillier, Elisabeth

Affiliate Scientist
Bradley, Grace

Epidemiology, Statistics & Behaviour

Senior Scientists
Boyd, Norman
Cunningham, Alastair
Minkin, Salomon
Till, James
Tritchler, David

Affiliate Scientist
Ritvo, Paul

Psychosocial Oncology & Palliative Care

TGRI Scientists

Behavioural Sciences & Health

Senior Scientists
Flint, Alastair
Kaplan, Allan
Katz, Joel
Olmsted, Marion
Rodin, Gary
Stewart, Donna

Scientists
Carter, Jacqueline
Jones, Jennifer
Nolan, Robert
Regehr, Glenn

Affiliate Scientists
Abbey, Susan
Baker, Brian
Colton, Patricia
Davis, Caroline
Grace, Sherry
Hall, Peter
Heslegrave, Ron
Hodges, Brian
Irvine, Jane
McVey, Gail
Reid, Graham
Robinson, Gail
Woodside, Blake

Cellular & Molecular Biology

Senior Scientists
Backx, Peter
Berger, Stuart
Cardella, Carl
Cybulsky, Myron
Dick, John
Elsholtz, Harry
Fantus, George
Fish, Eleanor
Gorczynski, Reginald
Gotlieb, Avrum
Grant, David
Johnston, Wayne
Langille, Lowell
Levy, Gary
Liu, Mingyao
Phillips, James
Rubin, Barry
Zacksenhaus, Eldad
Zhang, Li

Scientists
Cattral, Mark
Husain, Mansoor
Irwin, David
Jin, Tianru
Kotra, Lakshmi
Lam, Tony
Volchuk, Allen
Waddell, Thomas

Affiliate Scientists
Belsham, Denise
Branch, Donald
Clark, David
Cole, Edward
Drucker, Daniel
Wen, Xiao-Yan

Clinical Decision-Making & Health Care

Senior Scientists
Bombardier, Claire
Jadad, Alex
Naglie, Gary

Krembil Scientists

Brain, Imaging & Behaviour —Systems Neuroscience

Senior Scientists
Brotchie, Jonathan
Chen, Robert
Davis, Karen
Lozano, Andres
Hutchison, William
McAndrews, Mary Pat
Mikulis, Dave
Sandor, Paul
Strafella, Antonio

Scientist
Kucharczyk, Walter

Affiliate Scientists
De Nil, Luc
Dostrovsky, Jonathan
Saint-Cyr, Jean

Fundamental Neurobiology

Senior Scientists
Broussard, Dianne
Carlen, Peter
Skinner, Frances
Tymianski, Michael
Wan, Qi

Scientist
Sugita, Shuzo

Affiliate Scientists
El-Beheiry, Hossam
Gaisano, Herbert
Zhang, Liang

Genetics & Development

Senior Scientists
Barr, Cathy
Bremner, Rod
Cardella, Carl
Eubanks, James
Fehlings, Michael
Inman, Robert
Jongstra, Jan
Mills, Linda
Schlichter, Lyanne
Stanley, Elise
Tsui, Florence
Wither, Joan
Tator, Charles

Scientist
Monnier, Philippe

Affiliate Scientist
Guha, Abhijit

Health Care & Outcomes Research

Senior Scientists
Devins, Gerald
Gagliese, Lucia
Rodin, Gary

Scientists
Edelstein, Kim
Howell, Doris
Zimmermann, Camilla

Affiliate Scientists
Esplen, Mary Jane
Stewart, Donna

Signaling Biology

Senior Scientists
Ikura, Mitsu
Khokha, Rama
Manoukian, Armen
Ohashi, Pamela

Scientists
Cheung, Peter
Hakem, Razqallah
Jurisica, Igor
Koch, Anne
Okada, Hitoshi
Stambolic, Vuk
Vaziri, Homayoun

Stem Cells & Developmental Biology

Senior Scientists
Barber, Dwayne
Iscove, Norman
Keller, Gordon
Mak, Tak
McCulloch, Ernest
Medin, Jeffrey
Messner, Hans
Minden, Mark
Neel, Benjamin
Paige, Christopher
Rottapel, Robert
Schuh, Andre

OCI Clinical Research Unit

Members

Bayley, Andrew
Bell, Bob
Bezjak, Andrea
Boerner, Scott
Brandwein, Joseph
Brierley, James
Brown, Dale
Catton, Charles
Catton, Pamela
Chang, Hong
Chapman, William
Chen, Christine
Chen, Xueyu
Chetty, Runjan
Cho, John
Chung, Peter
Crook, Juanita
Croul, Sidney
Crump, Michael
Cummings, Bernard
Darling, Gail
Dawson, Laura
de Perrot, Marc
Dodge, Jason
Easson, Alexandra
Elliott, Mary
Evans, Andrew
Feld, Ronald
Finelli, Antonio
Laperriere, Normand
Leighl, Natasha
Levin, Wildred
Lipa, Joan
Lipton, Jeffrey
Manchul, Lee
Mason, Warren
McCready, David
McLean, Linda
McLean, Michael
Menard, Cynthia
Mikhael, Joseph
Millar, Barbara-Ann
Miller, Naomi
Milosevic, Michael
Neligan, Peter
O'Sullivan, Brian
Oza, Amit
Paul, Narinder
Payne, David
Perez-Ordonez, Bayardo
Pierre, Andrew
Quirt, Ian
Reece, Donna
Ringash, Jolie
Rosen, Barry
Rotstein, Lorne
Shaw, Patricia
Shepherd, Daar, Abdallah
Eysenbach, Gunther
Singer, Peter

Scientists
Alibhai, Shabbir
Cheung, Angela
Krahn, Murray
Urbach, David
Wilson, Kumanan

Affiliate Scientists
Goel, Vivek
Lok, Charmaine
Tomlinson, George

CSRC Members
Daly, Paul
Jewett, Michael
Kapral, Moira
Singer, Lianne

Clinical Investigation & Human Physiology

Senior Scientists
Allard, Johane
Bradley, Douglas
Cattran, Daniel
Floras, John
Kucharczyk, Walter
Lewis, Gary
Miller, Judith
Olivieri, Nancy
Steiner, George
Walmsley, Sharon

Scientists
Perkins, Bruce
Wong, Florence

Affiliate Scientists
Detsky, Allan
Downar, Eugene
Easty, Anthony
Logan, Alexander
Raboud, Janet
Reilly, Raymond
Sawka, Anna
Zamel, Noe

CSRC Members
Bril, Vera
Cameron, Douglas
Chan, Charles
Chan, Christopher
Chauhan, Vijay
Cooper, Richard
Djaiani, George
Fedorko, Ludwik
Harris, Louise
Herridge, Margaret
Ing, Douglas
Jassal, Vanita
Johnston, Michael
Karkouti, Keyvan
Karski, Jacek
McCluskey, Stuart
McRae, Karen
Parker, John
Ross, Heather
Salit, Irving
Schwartz, Len
Seidelin, Peter
Sherman, Morris
Siu, Samuel
Slinger, Peter

Experimental Therapeutics

Senior Scientists
Keating, Armand
Kelvin, David
Keshavjee, Shaf
Li, Ren-Ke
Lindsay, Thomas
Liu, Peter
von Harsdorf, Rudiger
Weisel, Richard

Scientists
de Perrot, Marc
Nanthakumar, Kumar
Rao, Vivek
Yau, Terrence

Affiliate Scientists
Fremes, Stephen
Hwang, David
McCart, Andrea
McGilvray, Ian
Medin, Jeffrey

Genomic Medicine

Senior Scientists
Badley, Elizabeth
Carette, Simon
Cassidy, David
Davis, Aileen
Fortin, Paul
Gignac, Monique
Gladman, Dafna
Mahomed, Nizar
Mailis, Angela
Urowitz, Murray

Affiliate Scientists
Côté, Pierre
Cott, Cheryl
Lineker, Sydney
Martino, Rosemary

Patient Based Clinical Research

Senior Scientists
Diamant, Nicholas
Heathcote, Jenny
Lang, Anthony
Shapiro, Colin
Sharpe, James

Affiliate Scientist
Stephens, Robyn

Visual Science

Senior Scientists
Flanagan, John
Steinbach, Martin
Trope, Graham

Scientists
Hudson, Christopher
Wong, Agnes

Affiliate Scientists
Eizenman, Moshe
Ethier, Ross
Gallie, Brenda
Gonzalez, Esther
Irving, Elizabeth
Wilkinson, Frances

Krembil Clinical Studies Resource Centre (CRSC)

Members

Anastakis, Dimitri
Bernstein, Mark
Bookman, Arthur
Buys, Yvonne
Chan, Vincent
Chapman, Kenneth
Chung, Frances
Davey, Roderick
del Campo, Jose
Devenyi, Robert
Epstein, Trina
Escallon, Jaime
Etlin, David
Evans, Michael
Farb, Richard
Fung, Ken
Gentili, Fred
Graham, Brent
Hawa, Raed
Iwanochko, Mark
Lam, Wai-Ching
Lam, Robert
Manninen, Pirjo
Massicotte, Eric
McCartney, Colin
McGuire, Glenn
McIntyre, Roger
Melvin, Kenneth
Miyasaki, Janis
Montanera, Walter
Panisko, Daniel
Parikh, Sagar
Peng, Philip
Radomski, Sidney
Rampersaud, Yoga
Rootman, David
Rosen, Cheryl
Saltzman-Benaiah, Jennifer
Seyone, Chanth
Shannon, Patrick
Shaw, James
Silver, Frank
Simons, Martin
Singer, Shaun
Slomovic, Allan
St George-Hyslop, Peter
Stanbrook, Matthew
Stubbs, Barbara
Tarlo, Susan
Terbrugge, Karel
Tu, Karen
Tumber, Paul
von Schroeder, Herbert
Voon, Valerie
Wherrett, John
Willinsky, Robert

Fleshner, Neil
Fyles, Anthony
Gallinger, Steven
Geddie, William
Ghazarian, Danny
Gospodarowicz, Mary
Greig, Paul
Gryfe, Robert
Hodgson, David
Irish, Jonathan
Jewett, Michael
Johnston, Michael
Jones, Jennifer
Kane, Gabrielle
Keating, Armand
Keshavjee, Shaf
Kim, John
Knox, Jennifer
Krzyzanowska, Monika
Frances
Simpson, Rand
Siu, Lillian
Sturgeon, Jeremy
Sun, Alexander
Sutherland, Robert
Swallow, Carol
Sweet, Joan
Tkachuk, Douglas
Trachtenberg, John
Tsang, Richard
van der Kwast, Theodorus
Waddell, Thomas
Waldron, John
Warde, Padraig
Warr, David
Wei, Alice
Wells, Woodrow
Wong, Rebecca

Senior Scientists

Cole, David
Downey, Gregory
George, Susan
Hogg, David
Kain, Kevin
Liles, Conrad
MacDonald, Kelly
Pei, York
Siminovitch, Katherine
Sole, Michael

Scientist

Osborne, Lucy

Affiliate Scientists

Boright, Andrew
Denomme, Gregory

TGRI Clinical Studies Resource Centre (CSRC)

Members

Ali, Mohamed
Bargman, Joanne
Beattie, Scott
Brister, Stephanie
Colman, Jack
David, Tirone
Dzavik, Vladimir
Fenton, Stanley
Gardam, Michael
Girgrah, Nigel
Gold, Wayne
Goldszmidt, Eric
Granton, John
Grigoriadis, Sophie
Humar, Atul
Kachura, John
Kennedy, Sidney
Keystone, Edward
Lapinsky, Stephen
Lilly, Leslie
Loke, Julian
Manktelow, Ralph
Merchant, Naeem
Neary, Mary Ann
O'Malley, Martin
Rajan, Dheeraj
Rakowski, Harry
Ralph-Edwards, Anthony
Reznick, Richard
Richardson, Robert
Roberts, Heidi
Ross, John
Straus, Sharon
Sutton, David
Sweet, Joan
Wilson, Stephanie
Wolman, Stephen
Yeo, Erik
Moro, Elena
Nasmith, James
Oandasan, Ivy
Ogilvie, Richard
Ogilvie-Harris, Darrell
Wong, David
Wong, Jean
Yogendran, Suntheralingam
Yu, Eric

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Year In Review

New OCI Leadership Announced

June 2006: Dr. Benjamin Neel—world-renowned cell signaling researcher, Director of the Cancer Biology program at Boston's Beth Israel Deaconess Medical Centre and Professor of Medicine at Harvard Medical School—was recruited as new Director of OCI. Dr. Neel took up his position in January 2007.

New Regenerative Medicine Research Centre Opens Doors

October 2006: The opening of the new McEwen Centre for Regenerative Medicine was marked with a scientific symposium of internationally-recognized stem cell researchers. Singer/philanthropist Sir Bob Geldof and lead donors Rob and Cheryl McEwen led the celebrations.

Research Day a Success

November 2006: More than 400 UHN researchers took part in UHN's annual Research Day. The event showcased 20 talks and 130 poster presentations spanning the range of biomedical investigation at UHN.

Researchers Set $49M Funding Record

November 2006: Drs. Pamela Catton, John Dick, Igor Jurisica, Kathy Siminovitch and Richard Weisel won $28 million in funding from the Canada Foundation for Innovation (CFI), the highest amount ever awarded by the CFI to UHN in a single round. In April 2007, the Ontario Research Fund made additional awards, bringing the total to $49M for these projects.

UHN's International Research Advisory Board Visits

December 2006: UHN hosted our International Research Advisory Board members this month. During their visit, the group—Drs. Victor Dzau President & CEO, Duke University Health System), Ralph Steinman (Professor, Rockefeller University), Hans Wigzell (Professor, Karolinska Institute) and chair Philip Branton (Scientific Director, CIHR Institute of Cancer Research)—reviewed translational research initiatives at UHN and met with hospital and Foundation executives.

Dr. Benjamin Neel, recruited from Harvard, took up the OCI Directorship in January 2007.

Donor Robert McEwen (centre left) and Sir Bob Geldof (centre right) shared ribbon-cutting duties at the McEwen Centre for Regenerative Medicine's gala opening.

UHN researchers mingle at UHN Research Day.

A further $10M donation from lead donors Rob and Cheryl McEwen raises their total committment to their namesake centre to $20M.

Regenerative Medicine Supported at McEwen Centre with $10M Gift

April 2007: A new donation from Rob and Cheryl McEwen will support groundbreaking stem cell research through imaging facilities, an embryonic stem cell laboratory, post-doctoral fellowships and programs designed to accelerate the development of scientific discoveries.

Development Acceleration Awardees Announced

September 2007: Four UHN researchers—Drs. David Jaffray, Lothar Lilge, Li Zhang and Gang Zheng—were awarded Development Acceleration Awards, a joint initiative between Johnson & Johnson and UHN. The award provides funding for development of imaging technolgoies in the context of neoplastic, cardiovascular, autoimmune, infectious, and/or neurological disease.

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Ontario Cancer Institute

Leukemia: New Model Shows Human Disease Back to Its "Big Bang"

Cancer researchers led by OCI's Dr. John Dick have developed a method to convert normal human blood cells into "human" leukemia stem cells. The converted cells, when transplanted into special mice that permit the growth of human cells, can replicate the entire disease process from the very moment it begins.

Explains Dr. Dick: "Most human leukemia research involves studying a patient's diseased cells or a cell line grown from those cells. However, since cancer takes many months or years to develop, just studying the cells at the end of the process does not let you know what the series of changes were that caused the cells to become leukemic, and when they happened.

"With the method we developed, we have duplicated the natural process every step of the way. It opens the pathway generally to understanding the process of how cancer begins."

Science. 2007 Apr 27; 316(5824):600-4. [Abstract]

Cancer: Anti-Aging Molecule May Help in Cancer Fight

A UHN research team led by Dr. Tak Mak discovered that a molecule that helps extend the lifespan of flies and worms may also help protect against cancer.

FOXO3a, a member of a family of molecules that helps regulate anti-aging gene activity, was found to be capable of making cells self-destruct via a process that relies on the tumour suppressor molecule p53.

The researchers found that FOXO3a has a paradoxical role: If it is turned on in the cell's nucleus, it stops p53 from working; however, outside of the nucleus, it can do the opposite-actively inducing p53-dependent programmed cell death.

"Interestingly, FOXO3a could trigger programmed cell death even in situations where p53 has lost its ability to work directly with DNA," says Dr. Mak. "Pinpointing FOXO3a's involvement in programmed cell death gives researchers a new target for future anticancer therapies."

PNAS. 2006 Jun 13; 103(24):9051-6. Epub 2006 Jun 6. [Abstract]

Pancreatic Cancer: Combination Therapy Offers Promises

A new combination therapy has been demonstrated to prolong survival time in people with advanced pancreatic cancer, according to UHN researchers Dr. Malcolm Moore and Steven Gallinger. The new approach uses the compound erlotinib to target specific pathways overproduced in pancreatic cancer.

The two-year UHN-led National Cancer Institute of Canada Clinical Trials Group study followed 569 patients treated with either gemcitabine—the current treatment standard—alone or in combination with erlotinib. Patients who received the combination

The Ontario Cancer Institute is the research arm of the Princess Margaret Hospital.

OCI at a Glance

Research Space	**389,000 sq ft**
Publications	**553**
Total External Funding	**$102,854,000**
Senior Scientists	49
Scientists	20
Affiliate Scientists	4
CSRC/CRU Members	95
Total Researchers	**168**
Fellows	201
Graduate Students	169
Total Trainees	**370**
Technical and Support Staff	**461**

OCI Council | Scientists | Clinical Research Unit | Full OCI Staff Listing

Research Council in Oncology

Director
Benjamin Neel

Division Heads
Applied Molecular Oncology
Fei-Fei Liu
Biophysics & Bioimaging
Brian Wilson
Cancer Genomics & Proteomics
Linda Penn
Psychosocial Oncology & Palliative Care
Gary Rodin

treatment experienced a significantly prolonged survival time and stabilization of disease.

"This combination therapy of gemcitabine plus erlotinib is the first advance in the treatment of pancreatic cancer in the past decade" says Dr. Moore. Erlotinib has been approved by the FDA and the European Medicines Evaluation Agency for the treatment of pancreatic cancer on the basis of this study and is under review by Health Canada.

J Clin Oncol. 2007 May 20;25(15):1960-6. Epub 2007 Apr 23. [Abstract]

Leukemia: Fusion Protein Structure Reveals Potential Target

Dr. Mitsu Ikura and postdoctoral fellow Dr. Michael Plevin have revealed the three-dimensional solution structure of the TAFH domain-a domain critical for E protein interactions-of the AML1-ETO fusion protein using NMR spectroscopy.

AML1-ETO is generated by a translocation between chromosomes 8 and 21, an event that occurs in up to 15% of acute myeloid leukemias (AML). AML1-ETO can silence E protein activation of transcription factors that are involved in regulating cell growth, differentiation and apoptosis. By mutating AML1-ETO, this activity is reduced.

"Resolving the structure of protein domains and doing mutational analysis is key to understanding protein function," says Dr. Ikura. "This domain of AML1-ETO showed a surprising similarity to another cancer gene regulator Sin3. Our findings help us to obtain deeper insights into leukemia and to design chemical inhibitors based on similarities and differences in their protein structures."

Proc. Natl. Acad. Sci. 2006. Jul 5; 103(27):10242-7. [Abstract]

Acute Myeloid Leukemia: Understanding Fatigue

A UHN study by researchers Drs. Shabbir Alibhai, George Tomlinson, Joseph Brandwein, Mark Minden and Matthew Kowgier and Mr. Marc Leach is the first to investigate fatigue associated with acute myeloid leukemia (AML) in detail. AML—a cancer of the blood—is more common in adults 60 years and older and has a significant effect on a patient's quality of life.

Patients were studied to characterize the prevalence and severity of fatigue. Study authors show that fatigue was universal for all patients throughout the study regardless of treatment therapy with 98% having reported fatigue.

"Fatigue has a significant effect on a patient's quality of life, so getting to the bottom is key," says Dr. Alibhai. "Our next steps are to dig deeper into causes of fatigue, and whether chemotherapy or improved disease control impact on fatigue and design interventions to alleviate fatigue."

Leukemia. 2007. Apr; 21(4):845-8. [Abstract]

Signaling Biology
Mitsu Ikura
Stem Cells & Developmental Biology
Robert Rottapel
Clinical Research Unit
Padraig Warde (Medical Site Director)

Clinical Representatives
Sylvia Asa
Mary Gospodarowicz
Jonathan Irish
Malcolm Moore

Centre for Research Education and Training
David Rose

Vice President, Research
Christopher Paige

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Toronto General Research Institute

Acute Respiratory Distress Syndrome: Study Shows Long-Term Outcomes for Survivors

A recent study by UHN researchers Drs. Angela Cheung , Margaret Herridge and George Tomlinson established that most survivors of acute respiratory distress syndrome (ARDS) have a reduced health-related quality of life two years after being discharged from an intensive care facility. ARDS is a serious illness where fluid accumulates in the lungs, which causes oxygen levels in the blood to drop to dangerously low levels.

The researchers followed 109 ARDS survivors for two years to examine changes in the quality of life and associated healthcare costs. They found that all health-related quality of life domains, other than emotional and mental health, were diminished compared to those of the general population. However, most ARDS survivors adapted to their situation and could live independently and return to work.

"Our findings suggest that future research efforts should concentrate on early intensive rehabilitation programs for ARDS," says Dr. Cheung. "These types of programs could help improve the long term outcomes for ARDS survivors."

Am J Respir Crit Care Med. 2006 Sep 1; 174(5):538-44. Epub 2006 Jun 6. [Abstract]

Heart Attack: Bone Marrow Molecule Signals Repair "Troops"

UHN regenerative medicine researchers Drs. Shafie Fazel, Massimo Cimini, Liwen Chen, Shuhong Li, Denis Angoulvant, Paul Fedak, Richard Weisel, Armand Keating and Ren-Ke Li have identified the SOS distress signal that mobilizes specific repair cells to the heart after a heart attack.

C-kit, a molecule located on the surface of a subset of bone marrow cells, is turned on by the SOS signals sent by the damaged heart. C-kit binds to another molecule, activating c-kit to signal bone marrow cells to home in on the heart to help stimulate new blood vessel growth.

"Each year, 70,000 Canadians suffer from a heart attack and many of them are left with crushing disabilities, mainly because the heart muscle is not able to regenerate after a heart attack," says Dr. Li. "This study identifies how the body naturally repairs the heart and provides new potential therapies to stimulate cardiac regeneration and prevent heart failure in these patients."

J. Clin. Invest. 2006 Jul;116(7):1865-77. [Abstract]

Digestive System Diseases: Defining Treatment Criteria for Swallowing Disorder

Patients with the rare swallowing disorder achalasia are unable to relax the muscular ring that links the esophagus to the stomach. They experience difficulty swallowing and moving food from their

The Toronto General Research Institute is the research arm of the Toronto General Hospital.

TGRI at a Glance

Research Space	**243,000 sq ft**
Publications	**654**
Total External Funding	**$48,390,000**
Senior Scientists	59
Scientists	24
Affiliate Scientists	37
CSRC/CRU Members	67
Total Researchers	**187**
Fellows	177
Graduate Students	111
Total Trainees	**288**
Technical and Support Staff	**442**

TGRI Council | Scientists | Clinical Studies Resource Centre (CSRC) | Full TGRI Staff Listing

Research Council

Director
Richard Weisel

Division Heads
Behavioral Sciences & Health
Gary Rodin
Cell & Molecular Biology
Eleanor Fish
Clinical Decision-Making & Health Care
Claire Bombardier
Clinical Investigation & Human Physiology
Richard Weisel (interim head)

mouth to their stomach through their esophagus-sometimes leading to pain, regurgitation and dangerous weight loss.

There are two common surgical treatments for achalasia; however, it is not clear which treatment is less likely to result in the need for subsequent interventions. To address the controversy, UHN health services researcher Dr. David Urbach performed a retrospective study using data records from 1461 achalasia patients in Ontario.

"Our study shows that although both methods commonly result in the need for subsequent intervention, less than 40% of patients treated with surgical dissection of the muscle had to be treated again compared to more than 60% of patients treated by enlarging the contracted opening using an air-filled balloon," says Dr. Urbach.

"Knowing that surgical dissection is slightly more efficient overall, we suggest that doctors consider the patient's attitude toward surgical procedures and the desire to avoid further treatments when making recommendations."

JAMA. 2006 Nov 8;296(18):2227-33. [Abstract]

Heart Failure: Knowing the Signs

A recent UHN-led study provides insight into the series of events involved in f heart failure, the fastest growing epidemic in cardiovascular disease, the number one killer of Canadians. Drs. Peter Liu , Thomas Parker and Rama Khokha have determined the importance of tumour necrosis factor alpha (TNFa)—usually involved in many cell processes such as growth and survival—in regulating cardiac repair and remodeling.

Using a mouse model, researchers compared the effects of pressure load on the left ventricle of the heart in the presence and absence of TNFa. In the presence of TNFa, pressure-overloaded cardiac cells are riddled with high levels of inflammatory proteins, leading to heart dilation, and the cells eventually succumb to TNF effects, contributing to cardiac dysfunction.

When TNFa was removed, adverse heart effects were reduced. "Based on this effect, TNFa could be used to alert physicians when heart repair processes threaten to deteriorate into heart failure," says Dr. Liu. "Even more exciting is its potential as a therapeutic tool in the treatment of patients. We stumbled upon this finding quite unexpectedly, and were surprised at its absolutely potent effect."

Circulation. 2007 Mar 20;115(11):1398-407. Epub 2007 Mar 12. [Abstract]

Liver Transplant: Showing the Benefits of Live Donation

TGH has been a world leader in liver transplants involving living donors, and a recent study has proven the beneficial effects of this treatment strategy. Living donation allows suitable recipients to avoid the long organ waiting list but may represent unknown immediate and long-term health risks given that recipients receive only part of a liver.

To compare the risks of being on the list to those of receiving a living donation, UHN researchers Drs. David Grant, Gary Levy, Paul Greig, Ian McGilvray, Leslie Lilly, Nigel Girgrah and Mark Cattral reviewed survival rates and mortality of patients in the liver transplant program.

They found that patients who received a right-lobe of a liver from a living donor had a higher survival rate post-transplant and reduced mortality on the waiting list than those who received a transplant from a deceased donor.

Says study leader Dr. Grant: "Live donor transplants significantly shorten wait times and reduce the chance of death for those patients who are on waiting lists. We have shown that we are able to help

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Li Zhang
Microscopy Facility
Lowell Langille
Diabetes Program and the Human Physiology Division
George Fantus

patients quicker and more effectively with live donation. Future studies will have longer follow-up times to more clearly understand the advantages and disadvantages of living donors."

Am. J. Transplant. 2007 Apr; 7: 998-1002. [Abstract]

UNIVERSITY HEALTH NETWORK
Research Report 2007

Krembil Research Institute

Arthritis: Predicting Probability of Joint Replacement Surgery

The need for improved patient education of people with arthritis is highlighted in new work by UHN researcher Dr. Elizabeth Badley, Dr. Gillian Hawker (Women's College Hospital) and other Toronto-based researchers who looked at factors underlying a patient's decision to undergo joint replacement surgery.

In a prospective study, the researchers recorded information about 3,307 seniors who were experiencing symptoms of arthritis in 1995-1997. In 1999, the researchers followed up with 2,103 respondents and found that—out of factors including education level, height, weight, socioeconomic factors, employment and living arrangements—the most important determining factor was willingness to have the surgery.

"Joint replacement surgery is a cost-effective treatment for debilitating arthritis of the hip and knee, and disparities in rates of surgery are troubling. Willingness to consider surgery as a treatment option results from improved patient understanding. This underlines the fact that we need to continue to develop and implement strategies to educate the community about arthritis and replacement surgery outcomes," says Dr. Badley.

Arthritis Rheum. 2006 Oct;54(10):3212-20. [Abstract]

Brain Injury: Research at the Forefront of New Therapies

A new UHN finding is the first step towards developing new multi-pronged strategies for traumatic brain injury (TBI).

Damage to a brain cell sets off a cascade of internal and external events that combine to create a toxic environment, killing neighbouring cells over a large area. While neuroscientists are starting to understand this complex mechanism, treatments which address a single component of the cascade have proven unsuccessful in clinical trials. Thus researchers are moving to a multi-pronged paradigm to address two or more components simultaneously.

A pioneering study led by Dr. Michael Tymianski and graduate student Anthony Lau has shown that due to the effects of a lethal by-product of cell damage called peroxynitrate, TBI therapy should include both anti-oxidant and anti-apoptotic compounds.

"If we can use molecular approaches to prevent the oxidizing process, which forms hazardous reactive oxygen molecules in the brain, and the apoptosis process, which leads to programmed cell death, we may be able to reduce cell death in these injuries," explains Dr. Tymianski.

J Neurosci. 2006 Nov 8;26(45):11540-53. [Abstract]

Degenerative Disc Disease: Notochord Cells Help to Regenerate Disc Cartilage

Drs. Mark Erwin and Robert Inman have discovered that notochord

The Krembil Research Institute is the research arm of the Toronto Western Hospital.

Krembil at a Glance

Research Space	**105,000 sq ft**
Publications	**395**
Total External Funding	**$26,924,000**
Senior Scientists	45
Scientists	5
Affiliate Scientists	18
CSRC/CRU Members	65
Total Researchers	**133**
Fellows	78
Graduate Students	73
Total Trainees	**151**
Technical and Support Staff	**217**

Krembil Council | Scientists | Clinical Studies Resource Centre (CRSC) | Full Krembil Staff Listing

Research Council

Director
Peter St George-Hyslop

Division Heads
Genetics & Development
Rod Bremner
Fundamental Neurobiology
Peter Carlen
Brain, Imaging & Behaviour - Systems Neuroscience
Karen Davis
Visual Science

cells-which are primitive organizing cells of the developing embryo-release a factor called connective tissue growth factor (CTGF) that may be responsible for providing certain strains of dogs with their remarkable resistance to degenerative disc disease.

Degenerative disc disease is one of today's most common and costly medical conditions, marked by a progressive loss of disc height, mechanical properties and tissue degradation. However, in resistant dog strains it does not occur or occurs much later in life.

To find out why resistant dogs are protected, the UHN team obtained notochord cells from the discs of the dogs and determined the identity of some of the proteins secreted by these cells. They then used the proteins secreted by these cells to determine what disc cell genes are turned on by these notochord cells.

"Our results suggest that certain breeds of dogs are protected against this disease because their discs contain an abundance of notochord cells that are releasing CTGF," says Dr. Inman. "This research will likely provide the groundwork to regenerate disc cartilage for patient treatment in the future."

Arthritis Rheum. 2006 Dec;54(12):3859-67. [Abstract]

Spinal Cord Injury: Rebuilding from the Ground Up

A team led by Krembil researcher Dr. Michael Fehlings has demonstrated a new way to reconstruct an essential element in nerve function in the spinal cord in a paper jointly co-first authored by Drs. Eftekhar Eftekharpour and Soheila Karimi.

A tissue called myelin functions as an insulating casing around nerve fibers and takes part in conducting signals from the brain to the rest of the body. After transplanting specific neural precursor cells (aNPCs) from the brain of adult transgenic mice into the spinal cords of mice which lack myelin, investigators were able to generate oligodendrocytes—the building blocks of myelin—which traveled down the spinal cord and formed mature myelin.

"This is a major step forward in spinal cord injury research," says Dr. Fehlings. "The ability to restore the myelin insulation is a key component of a therapeutic strategy, and our study is the first to show this exciting result. Our future work will focus on generating neural precursor cells from alternative sources including embryonic stem cells and in applying this technology is concert with tissue engineering approaches to repair chronic spinal cord injury."

J Neurosci. Mar 28, 27(13): 3416-28. [Abstract]

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Patient Based Clinical Research
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Honour Roll

In 2006/07, UHN researchers were recognized by peers around the world for their achievements:

Dr. Frances Shepherd
O. Harold Warwick Prize for significantly impacting cancer control in Canada, awarded by the National Cancer Institute of Canada

Dr. Pamela Ohashi
Elected to the Royal Society of Canada

Dr. Robert Inman
Jonas Salk Award for making a new and outstanding contribution to prevent, alleviate or eliminate a physical disability, awarded by the Ontario March of Dimes

Drs. Vivek Rao and Aaron Schimmer
Canada 's "Top 40 Under 40"

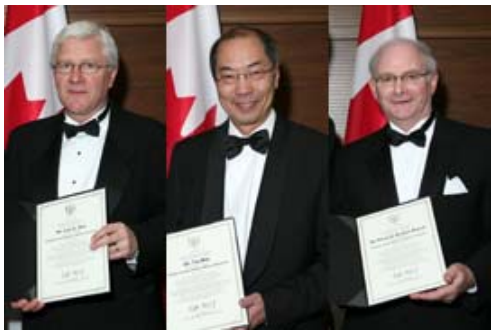
Drs. Conrad Liles, Gordon Keller, Benjamin Neel, Eleanor Fish and Linda Penn
Canada Research Chairs, Tier I

Drs. Igor Jurisica, Thomas Kislinger, Shuzo Sugita and Elisabeth Tillier
Canada Research Chairs, Tier II

Dr. Brian Wilson
Lifetime Achievement Award, Optical Imaging Workshop, National Institutes of Health (U.S.)

Dr. George Steiner
Named a Distinguished Fellow of the International Atherosclerosis Society

Dr. Peter St George-Hyslop
Howard Hughes Medical Institute International Research Scholar Award



Drs. John Dick, Tak Mak and Peter St George-Hyslop
UHN researchers swept three of the four inaugural Premier's Summit Awards awarded at a gala ceremony in April 2007. Drs. John Dick, Tak Mak and Peter St George-Hyslop will each receive $2,500,000 towards new research projects

Drs. Brenda Gallie, Ernest McCulloch and James Till
Three UHN researchers were invested into the Order of Ontario in 2006. Drs. Brenda Gallie, Ernest McCulloch and James Till received the province's highest offical honour for excellence and outstanding contribution to society in Ontario and around the world.

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CFI Grants Boost Funding

Support for Groundbreaking Research across UHN's Programs

2006/07 marked a record year for UHN in CFI grant funding earned. A round earned five UHN research teams a collective total of $21.4M in new infrastructure funding and $6.4M in operating funding—a UHN record. Later this year, projects were awarded an additional $21.4M through the Ontario Research Infrastructure program, resulting in a funding total of over $49M for these five projects.

The awards fund a variety of projects across UHN's priority research areas.

Regenerative Medicine Scores Twin Wins

Regenerative medicine is one of UHN's research priority platforms, and one of its flagship programs is the new *Regenerative Medicine* (REMEDI) *Project*, recently funded by CFI, which provided $7.2M in funding. This new centre will comprise cutting-edge multi-imaging infrastructure with multi-dimensional visualization. Led by Dr. Richard Weisel, this project drives regenerative medicine research to clinical applications for a variety of diseases.

"REMEDI is an innovative approach to regenerative medicine," Dr. Weisel explains. "It is a multidisciplinary initiative, which will enable innovative and customized research technologies to facilitate investigations intended to provide new regenerative therapies including: labeling, imaging, visualization and guided delivery. The project will unite experts from numerous fields: engineers, computer scientists, molecular biologists and clinicians to find unique new treatments to restore function to diseased organs. Ultimately, the vision of regenerative medicine research will be to provide cutting-edge therapeutic tools to improve the health of Canadians."

Another project within the regenerative medicine platform is Dr. John Dick's new *Cancer Stem Cell Centre*. This project, which secured over $4M in CFI funding, focuses on developing cancer stem cell therapies. It consists of several core activities including live cell banking, xenotransplanting, flow cytometry, high throughput screening and imaging. As a result, it will enable cancer stem cell scientists to develop improved predictive diagnostic and prognostic tests, as well as pursue new cancer therapies.

Genomics, Systems Biology and Survivorship Research Also Winners

Also receiving CFI funding this year was Dr. Katherine Siminovitch's *Disease Genomics: Reduction to Practice*. This $4.8M proposal, aligned with UHN research's priority platform in Genes, Proteins and People, builds on UHN's Clinical Genomics Centre, a state-of-the-art genomics and proteomics technology platform. The development of profiling tools and new medications are among the outcomes that ultimately lead to improved patient management.

Dr. Richard Weisel, head of the REMEDI Project, demonstrates the computer visualization lab.

CFI Grants Awarded at UHN, 2007

Regenerative Medicine (REMEDI) Project Dr. Richard Weisel	**$7.2M**
Disease Genomics: Reduction to Practice Dr. Katherine Siminovitch	**$4.8M**
Cancer Stem Cell Centre Dr. John Dick	**$4.3M**
Comprehensive Systems Biology Approach to Profiling and Modeling of Cancer Dr. Igor Jurisica	**$4.0M**
Electronic Living Laboratory for Interdisciplinary Cancer Survivorship Research Dr. Pamela Catton	**$1.2M**
Total Funding	**$21.5M**

Dr. Igor Jurisica's *Comprehensive Systems Biology Approach to Profiling and Modeling of Cancer* received over $4M from CFI. This project, which enables the interdisciplinary, integrated and collaborative profiling and modeling of cancer, is aligned with two of UHN research's priority platforms—Genes, Proteins and People, and Health Informatics. Through this endeavour, researchers aim to understand cancer at a molecular level, which can lead to a number of benefits: improvement in the quality and cost of cancer diagnosis and treatment via intelligent molecular medicine, the identification of novel and more specifically targeted drugs, as well as increased efficiency of current therapies.

The Electronic Living Laboratory for Interdisciplinary Cancer Survivorship Research, an innovative new approach to research in cancer, was awarded $1.2M in CFI funding. Headed by Dr. Pamela Catton, this initiative leverages the intellectual capital of cancer survivors to examine new approaches to predict, prevent and manage long-term adverse effects of cancer and its treatment. Through examining social networks and competency building, distributed models of care, health knowledge transfer and sustainability, innovative research into chronic disease health care delivery—using cancer survivorship as a model—will be performed.

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McEwen Centre Launches

Leading the Way in Regenerative Medicine

Last year, stem cell research took a large step forward with the opening of the McEwen Centre for Regenerative Medicine at UHN.

UHN Celebrates with Scientific Symposium

More than 300 members of the scientific community attended the scientific symposium which launched the festivities. Centre Director Dr. Gordon Keller, an internationally acclaimed embryonic stem cell scientist and co-chair of the symposium, was also officially introduced to the Toronto research community.

World-renowned researchers—including Drs. John Dick , Rudiger von Harsdorf, Thomas Waddell, Michael Fehlings, Janet Rossant, Derek van der Kooy, and keynote speaker Dr. George Daley—described stem cells and their significance to various biomedical fields, showcasing their unique ability to change the face of medicine and health on numerous fronts.

Following the symposium, a tour of the facilities—with musician Sir Bob Geldof among the attendees—continued the celebration. The event ended with a gala reception and dinner hosted by philanthropists and lead donors Robert and Cheryl McEwen.

Centre Focuses on Research & Commercialization

As a key component of UHN's regenerative medicine research priority platform, the Centre focuses on three specific areas: repair and regeneration, origins and models of disease and new tools for discovery. Heart disease, diabetes, blood cell disorders and spinal cord and neurodegenerative diseases are the core fields of investigation, while research in other diseases, including those of the lungs, as well as muscular/skeletal and gastro/intestinal conditions, will also be pursued.

In addition to establishing the Centre, which is located on the 8th floor of the Toronto Medical Discovery Tower , funding will allow regenerative medicine researchers from across UHN and across Toronto to attract new trainees through new postdoctoral fellowships as well as to pursue new modes of commercialization via enhanced support for this program.

"This is truly an exciting opportunity," says Dr. Keller. "There is an enormous pool of talented regenerative medicine researchers in Toronto. My goal as the Director of the McEwen Centre for Regenerative Medicine is to create an environment that will foster cross-disciplinary interactions and encourage investigators to work synergistically towards the development of innovative regenerative medicine approaches."

New Centre Director Dr. Gordon Keller was recruited to UHN from Mt. Sinai Hospital, New York.

Keynote speaker Dr. George Daley (left) was introduced by McEwen member Dr. John Dick.

Dignitaries and McEwen members celebrated the opening on-stage.

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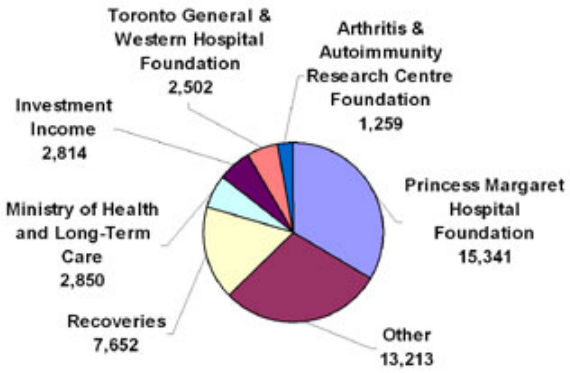
Research Funding Revenues

UHN Core Research Funding
(in thousands of dollars)

Princess Margaret Hospital Foundation	15,341
Toronto General & Western Hospital Foundation	2,502
Arthritis & Autoimmunity Research Centre Foundation	1,259
Ministry of Health & Long Term Care	2,850
Recoveries	7,652
Investment income	2,814
Other	13,213
TOTAL	**45,631**



UHN External Research Funding
(in thousands of dollars)

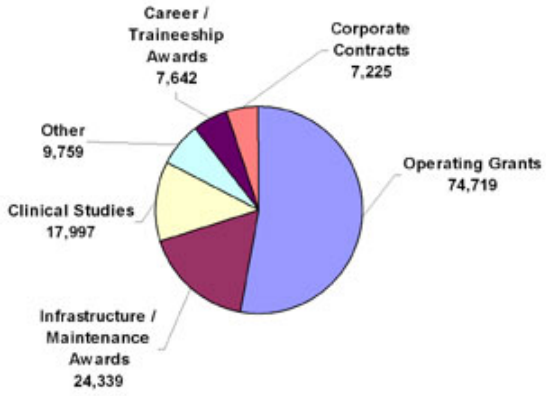
Operating Grants	74,719
Infrastructure / Maintenance Awards	24,339
Clinical Studies	17,997
Other	9,759
Career / Traineeship Awards	7,642
Corporate Contracts	7,225
TOTAL	**141,681**

External Agencies Funding UHN Research

A-C D-L M-O P-Z

Full Listing

Abbott Laboratories
Advanced Cardiovascular Systems
Advanced Neuromodulation Systems
Aegera Therapeutics
Agouron Pharma
Albert Einstein College of Medicine of Yeshiva University
Alberta Heritage Foundation for Medical Research
Alexion Pharmaceuticals
Allergan
American Association for Thoracic Surgery
American Association of Neurological Surgeons
American Cytoscope Makers
American Heart Association
American Society of Plastic Surgeons' Plastic Surgery Educational Foundation
American Society of Regional Anesthesia and Pain Medicine
Amgen
Amorfix Life Sciences
Amyotrophic Lateral Sclerosis Society of Canada
AOSpine North America
ArgiNOx Pharmaceuticals
Argonne National Laboratory
Argos Therapeutics
Arius Research
Arthritis Community Research & Evaluation Unit
Arthritis Society
Aspreva
Astellas Pharma Canada
Astra Pharma
AstraZeneca Canada
AtheroGenics
Atuka
Aventis Pasteur
Banting and Best Diabetes Centre
Bausch and Lomb
Baxter Healthcare
Baycrest
Bayer
Beckman Coulter
Bell Canada
BioAxone Therapeutic
BioChem Therapeutic
BioMimetic Therapeutics
Boehringer Ingelheim



Major Sources of External Funding
(in thousands of dollars)

Canadian Institutes of Health Research	24,653
Canada Foundation for Innovation/OIT	22,318
National Cancer Institute of Canada	7,275
National Institutes of Health (US)	6,843
Ontario Institute for Cancer Research	4,581
Heart and Stroke Foundations	3,973
Ontario Genomics Institute	2,726
Canada Research Chairs Program	2,556

All figures represent fiscal year 2006/07 and include Ontario Cancer Institute (Princess Margaret Hospital); Toronto General Research Institute (Toronto General Hospital); and Krembil Research Institute (Toronto Western Hospital).

These figures have been provided by UHN Research Financial Services and Research Grant and Contract Services. These figures have not been audited. However, they have been included in the overall UHN statements and, as a result, have been subjected to audit procedures deemed appropriate by auditors in order to determine their overall reasonableness.

Boston Scientific
Bristol-Myers Squibb
Burroughs Wellcome Fund
CAD Sciences
Calouste Gulbenkian Foundation
Canada Foundation for Innovation
Canada Research Chairs Program
Canadian Arthritis Network
Canadian Association of Gastroenterology
Canadian Breast Cancer Foundation
Canadian Breast Cancer Research Alliance
Canadian Breast Cancer Research Initiative
Canadian Coordinating Office for Health Technology Assessment
Canadian Cystic Fibrosis Foundation
Canadian Diabetes Association
Canadian Health Services Research Foundation
Canadian Institutes of Health Research
Canadian Liver Foundation
Canadian Neuromodulation Society
Canadian Patient Safety Institute
Canadian Urologic Oncology Group
Cancer Care Ontario
Cancer Research Institute
Cancer Research Society
Caprion Proteomics
Celgene
Cell Genesys
Centocor
Centre for Addiction and Mental Health
Centrum Foundation
CeraPedics
ChemBridge Research Laboratories
Chiron
Christopher Reeve Paralysis Foundation
Cleveland Clinic Lerner College of Medicine of Case Western Reserve University
Craig H. Neilsen Foundation
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Cyanamid
Cyclacel Pharmaceuticals

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