2004

RESEARCH REPORT

Toronto General Hospital

Toronto Western Hospital

Princess Margaret Hospital

University Health Network

2004

Contents

ABOUT RESEARCH AT UNIVERSITY HEALTH NETWORK

Total Number of Researchers	**468**
Senior Scientists	160
Scientists	54
Affiliate Scientists	47
CSRC Members	207
Total Number of Trainees	**770**
Fellows	397
PhD Students	81
Other Graduate Students	292
Staff	996
Research Space	**480,000 sq ft**
Publications	**1293**
Total Research Funding	**$155,976,000**

Tom Closson

Investing in Future Health

University Health Network in 2004 is an amazing place to be, and UHN Research is one of the things that makes it so.

Patient care, education, and research are all highly interconnected. UHN attracts some of the best clinicians—because it offers the opportunity to combine clinical practice with research. UHN attracts many patients from across Ontario due to high standards of care and the opportunity to participate in groundbreaking clinical research—all because of the thriving research community here.

The UHN strategic plan, *Strategic Directions 2011*, outlines ambitious targets for all of us at UHN. As this *Research Report* documents, Research is making great strides towards these targets. This year saw new buildings, new institutes, new initiatives and new partnership ventures in Research.

None of this would be possible without the hard work and commitment of our researchers and research staff and their partners in the government, community and private sector. From the research funding flowing from federal, provincial and international agencies, to the community volunteers who sit on our boards and committees, to the enormously dedicated work of the three UHN Foundations—the Arthritis & Autoimmunity Research Centre Foundation, the Princess Margaret Hospital Foundation and the Toronto General & Western Hospital Foundation—we owe an enormous debt of thanks to many groups for their ongoing support.

An investment in biomedical research is an investment in future health. UHN has much to be proud of in this area. Please read on to learn more.

Tom Closson

President and Chief Executive Officer

University Health Network

Christopher J. Paige, PhD

Strong Funding Based on Strong Science

Research has had an amazing year in 2003/04. This year for the first time our research budget topped $150M, with strong support from provincial and national agencies including an all-time high of $20.5M from the national Canadian Institutes of Health Research, nearly $10M from the National Cancer Institute of Canada and $6M from the new Ontario Cancer Research Network. These figures demonstrate yet again the scientific excellence of our scientists and the members of their research programs. They also show how reliant we are on a strong research funding environment to fuel research at UHN and how this support is key in realizing the research achievements that generate advances in patient care at Canada's largest hospital.

Topping off the year came the announcement in March that our researchers won $36.4M in infrastructure funding from federal and provincial sources to launch three new centres—the Advanced Medical Discovery Institute, the Centre for Research in Immune Tolerance in Transplantation, and the STTARR Centre in radiation medicine. We are tremendously proud of this achievement and it will prove critical in developing our research capacity in key areas in the next few years.

In 2003/04 UHN's list of scientific accomplishments was impressive. As a hospital-based research institute, our programs of inquiry span the spectrum from fundamental understanding of molecules and cells to mission-oriented, disease-specific clinical research. Our discoveries reflect this diversity: the first approved treatment for SARS; a multi-drug protocol that extends the lives of lung cancer patients; identification of a leukemia stem cell; discovery of a new mechanism that controls brain cell death during stroke; and a novel molecular switch that controls the process of inflammation. Breakthroughs like these hold the promise of improving the lives of our patients today or in the not too distant future.

This year for the first time our research budget topped $150M

UHN's achievements rest on the achievements of our individual investigators. UHN researchers have received many individual honours this year, achieving global and national renown. Some of these include:

- *The Paul Ehrlich and Ludwig Darmstaedter Prize, the highest prize awarded in Germany in the field of medicine, awarded to Dr. Tak Mak*
- *The appointments of Dr. Peter St George-Hyslop as Fellow*

of the Royal Society and Dr. John Dick as a Fellow of the Royal Society of Canada

- *The naming of Drs. Jim Woodgett and Peter St George-Hyslop as International Research Scholars by the Howard Hughes Medical Institute*
- *The appointments of Drs. Cheryl Arrowsmith, Dan Drucker and Mitsu Ikura as Tier I Canada Research Chairs and Dr. Peter Cheung as a Tier II Canada Research Chair*
- *The Society for Thoracic Surgeons' Earl Bakken award for lifetime scientific achievement, awarded to Dr. Richard Weisel*
- *Honorary degrees from the University of Toronto awarded to Drs. Jim Till and Ernest McCulloch, who were also this year elected to the Canadian Medical Hall of Fame*
- *Dr. Tony Lang, who received the American Academy of Neurology's Movement Disorders Research Award*

Finally, this year saw progress in three significant new ventures. The Toronto Medical Discovery Tower, critical for increasing research space capacity, neared completion this year and we are currently awaiting handover of the shell space for UHN's interior fit-out and occupancy in 2005. UHN Global Ventures was launched this year under the leadership of Dr. Brian Barber. This R&D interface will capitalize on UHN's strengths in basic, translational and clinical research to accelerate innovations further down the development pipeline and capture more value for UHN's research investment. A third new venture owes a great deal to the Princess Margaret Hospital Foundation, which was a driving force behind its development. The Institute for Breast Cancer Research, opened this year under the leadership of Dr. Tak Mak, is an exciting development in the field and will no doubt be the focus of many future pieces in this report.

UHN Global Ventures is a new R&D interface that will capitalize on UHN's strengths

All told, the year 2003/04 was an important year in the growth of UHN's research enterprise. And, as in previous years, I'd like to close by offering my thanks and congratulations to all who contributed to UHN Research's success in 2003/04: our scientists and clinician-scientists, our technical and support staff, our students and fellows, our colleagues in the Toronto Academic Health Sciences Network, and, most especially, our Foundations.

Christopher J. Paige, PhD
Vice President, Research
University Health Network

The Year in Review

NOVEMBER 2003

The second annual UHN Research Day held at a Toronto hotel provides a chance for researchers to mingle and learn about projects and findings from UHN colleagues. Keynote speaker was Dr. Catherine Verfaille, Director of the Stem Cell Institute at the University of Minnesota. Also announced at the event was the recipient of the inaugural UHN Inventor of the Year award: Dr. Kevin Kain, honoured for his work in new malaria treatments.

DECEMBER 2003

The second meeting of the UHN International Research Advisory Board brings together four internationally-recognized scientists in high-impact areas to meet with various UHN constituencies including researchers, platform leaders, medical program leaders, foundations and hospital and research leadership.

JANUARY 2004

The UHN Platform planning process, Phase II of *The Future Project*, launches. Led by Platform Chairs, the nine-month process aims to define visions and new tactical plans for the four UHN Platforms: *Genes, Proteins & People, Health Informatics, Medical Technology Innovation,* and *Regenerative Medicine.*

MARCH 2004

The Research strategic plan entitled *The Future Project* is approved by the UHN Board of Trustees.

Three teams of UHN researchers celebrate the announcement of awards totaling nearly $18.2M from the Canada Foundation

for Innovation to build new infrastructure to study the mechanisms of cancer, radiation medicine and immune tolerance. These awards were later matched by the Ontario government (Ministry of Economic Development and Trade/Ontario Innovation Trust), bringing funding to a total of $36.4M.

APRIL 2004

Dr. Peter St George-Hyslop becomes Director of the Toronto Western Research Institute. His research in determining the genetic and molecular processes underlying neurodegenerative diseases, particularly Alzheimer's disease, has had a major impact in the field and has been recognized by many national and international awards.

JUNE 2004

Integrating basic, translational and clinical research, the new $125M Institute for Breast Cancer Research launches on June 2, 2004. Director Dr. Tak Mak begins assembling Canada's first scientific team to develop new improved drugs and therapies to conquer breast cancer.

MAY 2004

◀ Dr. Brian Barber is recruited to helm UHN Global Ventures, a new initative promoting commercialization and partnership with UHN Research on an international level.

A significant milestone is reached as the new Toronto Medical Discovery Tower is topped off in a short ceremony held 15 floors above ground. UHN is eagerly anticipating the hand-over of the building for fit-out starting October 2004.

Ontario Cancer Institute
Princess Margaret Hospital

Research Space	**222,000 sq ft**
Publications	**370**
Total External Funding	**$55,000,000**

OCI includes the Advanced Medical Discovery Institute and the Institute for Breast Cancer Research

STAFF AND STUDENTS

Total Number of Researchers	**137**
Senior Scientists	48
Scientists	17
Affiliate Scientists	4
CSRC Members	69
Total Number of Trainees	**350**
Fellows	164
PhD Students	45
Other Graduate Students	141
Staff	397

Cancer Informatics

SENIOR SCIENTISTS
Asa, Sylvia
Gallie, Brenda

SCIENTIST
Jurisica, Igor

Cell & Molecular Biology

SENIOR SCIENTISTS
Barber, Dwayne
Benchimol, Sam
Iscove, Norman
Lepock, James
Mak, Tak
Manoukian, Armen
McCulloch, Ernest
Messner, Hans
Miller, Richard
Minden, Mark
Ohashi, Pam
Paige, Christopher
Penn, Linda
Squire, Jeremy
Tsao, Ming

SCIENTISTS
Hakem, Razq
Harrington, Lea
Schimmer, Aaron
Vaziri, Homayoun
Wells, Richard
Yeh, Wen-Chen

AFFILIATE SCIENTISTS
Bradley, Grace
Kamel-Reid, Suzanne

Epidemiology, Statistics & Behaviour

SENIOR SCIENTISTS
Boyd, Norman
Cunningham, Alastair
Minkin, Salomon
Till, James
Tritchler, David

AFFILIATE SCIENTIST
Ritvo, Paul

Experimental Therapeutics

SENIOR SCIENTISTS
Hedley, David
Hill, Richard
Hunt, John
Khokha, Rama
Liu, Fei-Fei
Moore, Malcolm
Rauth, Michael
Rottapel, Robert
Stewart, Keith
Tannock, Ian
Whitmore, Gordon
Woodgett, Jim

SCIENTISTS
Bristow, Robert
Cheung, Peter
Done, Susan
Koch, Anne
Medin, Jeffrey
Stambolic, Vuk
Tillier, Elisabeth
Vallis, Katherine

AFFILIATE SCIENTIST
Leong, Weh-Liang

Medical Physics

SENIOR SCIENTISTS
Jaffray, David
Sherar, Michael
Vitkin, Alex
Wilson, Brian

SCIENTISTS
Lilge, Lothar
Siewerdsen, Jeff

Molecular & Structural Biology

SENIOR SCIENTISTS

Arrowsmith, Cheryl
Chakrabartty, Avi
Edwards, Aled
Gariépy, Jean
Ikura, Mitsu
Ottensmeyer, Peter
Pai, Emil
Privé, Gilbert
Richardson, Christopher
Rose, David

Clinical Studies Resource Centre

MEMBERS

Bayley, Andrew
Bell, Robert
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Brandwein, Joseph
Brierley, James
Brown, Dale
Catton, Charles
Catton, Pam
Chen, Christine
Chen, Eric
Chetty, Runjan
Crook, Juanita
Crump, Michael
Cummings, Bernard
Darling, Gail
Dawson, Laura
Easson, Alexandra
Elliott, Mary
Evans, Andrew
Feld, Ronald
Fleshner, Neil
Fyles, Anthony
Gallinger, Steve
Gospodarowicz, Mary
Greig, Paul
Gryfe, Robert
Hodgson, David
Howell, Doris
Irish, Jonathan
Kane, Gabrielle
Kim, John
Knox, Jennifer
Krzyzanowska, Monika
Laperriere, Norm
Leighl, Natasha
Levin, Wildred
Lipa, Joan
Lipton, Jefferey
Manchul, Lee
Mason, Warren
McCready, David
McLean, Michael
Mikhael, Joseph
Milosevic, Michael
Neligan, Peter
O'Sullivan, Brian
Oza, Amit
Paul, Narinder
Payne, David
Pierre, Andrew
Quirt, Ian
Reece, Donna
Ringash, Jolie
Rosen, Barry
Rotstein, Lorne
Shaw, Patricia
Shepherd, Frances
Simpson, Rand
Siu, Lillian
Sturgeon, Jeremy
Sun, Alexander
Swallow, Carol
Tkachuk, Doug
Trachtenberg, John
Trudel, Suzanne
Tsang, Richard
Waldron, John
Warde, Padraig
Warr, David
Wells, Woodrow
Wong, Rebecca
Zimmermann, Camilla

NB-where members have more than one affiliation, only one affiliation is indicated

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MEDICAL PHYSICS
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Jonathan Irish

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Robert Bell

CLINICAL STUDIES RESOURCE CENTRE
Robert Bell

Toronto General Research Institute

Toronto General Hospital

Research Space	**153,000 sq ft**
Publications	**596**
Total External Funding	**$45,700,000**

STAFF AND STUDENTS

Total Number of Researchers	**198**
Senior Scientists	70
Scientists	25
Affiliate Scientists	29
CSRC Members	75
Total Number of Trainees	**291**
Fellows	159
PhD Students	25
Other Graduate Students	107
Staff	422

Behavioural Sciences & Health

SENIOR SCIENTISTS

Devins, Gerald
Flint, Alastair
Kaplan, Allan
Katz, Joel
Olmsted, Marion
Rodin, Gary
Stewart, Donna

SCIENTISTS

Carter, Jacqueline
Esplen, Mary Jane
Jones, Jennifer
Nolan, Robert
Regehr, Glenn

AFFILIATE SCIENTISTS

Abbey, Susan
Baker, Brian
Davis, Caroline
de Groot, Janet
Gagliese, Lucia
Grace, Sherry
Hamstra, Stanley
Heslegrave, Ron
Hodges, Brian
Irvine, Jane
Katz, Mark
McVey, Gail
Reid, Graham
Ritvo, Paul
Robinson, Gail
Styra, Rima
Woodside, Blake

Cell & Molecular Biology

SENIOR SCIENTISTS

Backx, Peter
Berger, Stuart
Cybulsky, Myron
Dick, John
Drucker, Daniel
Elsholtz, Harry
Fantus, George
Fish, Eleanor
Gorczynski, Reginald
Gotlieb, Avrum
Grant, David
Johnston, Wayne
Langille, Lowell
Levy, Gary
Liu, Mingyao
Phillips, James
Rotstein, Ori
Rubin, Barry
Schuh, Andre
Whiteside, Catherine
Zacksenhaus, Eldad
Zhang, Li

SCIENTISTS

Belsham, Denise
Cattral, Mark
Husain, Mansoor
Irwin, David
Jin, Tianru
Kapus, Andras
Trinh, Denny
Waddell, Thomas

AFFILIATE SCIENTISTS

Branch, Donald
Clark, David
Cole, Edward
Ojha, Matadial
Wilson, Gregory

Clinical Decision-Making & Health Care

SENIOR SCIENTISTS

Bombardier, Claire
Eysenbach, Gunther
Jadad, Alex
Naglie, Gary

SCIENTISTS

Alibhai, Shabbir
Krahn, Murray
Maetzel, Andreas
Urbach, David
Wilson, Kumanan

AFFILIATE SCIENTISTS
Goel, Vivek
Lok, Charmaine
Tomlinson, George

Clinical Investigation & Human Physiology

SENIOR SCIENTISTS
Allard, Johane
Bradley, Douglas
Cattran, Daniel
Detsky, Allan
Downar, Eugene
Floras, John
Goss, Paul
Kucharczyk, Walter
Lewis, Gary
Logan, Alexander
Marshall, John
Miller, Judith
Olivieri, Nancy
Phillipson, Eliot
Steiner, George
Walmsley, Sharon
Waxman, Menashe
Webb, Gary
Zamel, Noe

SCIENTISTS
Cheung, Angela
Reilly, Raymond
Wong, Florence

Experimental Therapeutics

SENIOR SCIENTISTS
Keating, Armand
Kelvin, David
Keshavjee, Shaf
Li, Ren-Ke
Lindsay, Thomas
Liu, Peter
Mickle, Donald
Stewart, Keith
Weisel, Richard

SCIENTISTS
Rao, Vivek
Volchuk, Allen
Yau, Terrence

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McCart, Andrea
McGilvray, Ian
Medin, Jeffrey

Genomic Medicine

SENIOR SCIENTISTS
Cole, David
Downey, Gregory
George, Susan
Hogg, David
Kain, Kevin
MacDonald, Kelly
Pei, York
Siminovitch, Kathy
Sole, Michael

SCIENTISTS
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Denomme, Greg

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Cardella, Carl
Chan, Charles
Chan, Christopher
Chauhan, Vijay
Colman, Jack
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Djaiani, George
Dzavik, Vladimir
Fedorko, Ludwik
Fenton, Stanley
Fisher, Joseph
Gallinger, Steve
Gardam, Michael
Girgrah, Nigel
Gold, Wayne
Goldszmidt, Eric
Granton, John
Greig, Paul
Grigoriadis, Sophie
Harris, Louise
Herridge, Margaret
Humar, Atal
Ing, Douglas
Jassal, Vanita
Jewett, Michael
Johnston, Michael
Kachura, John
Kapral, Moira
Karkouti, Keyvan
Karski, Jacek
Kennedy, Sidney
Keystone, Edward
Lapinsky, Stephen
Lilly, Leslie
Lipa, Joan
Loke, Julian
Manktelow, Ralph
McCluskey, Stuart
McLaughlin, Peter
McRae, Karen
Merchant, Naeem
Neligan, Peter
O'Malley, Martin
Parker, John
Rajan, Dheeraj
Rakowski, Harry
Ralph-Edwards, Anthony
Reznick, Richard
Richardson, Robert
Roberts, Heidi
Ross, John
Ross, Heather
Salit, Irving
Schwartz, Len
Seidelin, Peter
Sherman, Morris
Singer, Lianne
Siu, Samuel
Slinger, Peter
St George-Hyslop, Peter
Sternbach, Yaron
Strauss, Sharon
Sutton, David
Sweet, Joan
Wilson, Stephanie
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Yeo, Erik

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Christopher J. Paige

Toronto Western Research Institute

Toronto Western Hospital

Research Space	**105,000 sq ft**
Publications	**394**
Total External Funding	**$14,900,000**

STAFF AND STUDENTS

Total Number of Researchers	**134**
Senior Scientists	43
Scientists	12
Affiliate Scientists	15
CSRC Members	64
Total Number of Trainees	**129**
Fellows	74
PhD Students	11
Other Graduate Students	44
Staff	177

Applied & Interventional Research

SENIOR SCIENTISTS
Brotchie, Jonathan
Davis, Karen
De Nil, Luc
Diamant, Nicholas
Feindel, Christopher
Flanagan, John
Hassouna, Magdy
Lang, Anthony
Lozano, Andres
Mailis, Angela
McAndrews, Mary Pat
Mikulis, David
Saint-Cyr, Jean
Sandor, Paul
Shapiro, Colin
Sharpe, James
Steinbach, Martin
Trope, Graham
Wallace, Christopher

SCIENTISTS
Hutchison, William
Chen, Robert
Hudson, Christopher
Kucharczyk, Walter
Roberts, Timothy
Wong, Agnes

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Dostrovsky, Jonathan
Eizenman, Moshe
Ethier, Ross
Guha, Abhijit
Halliday, William
Hamstra, Stanley
Harvey, Patricia
Irving, Elizabeth
Kayumov, Leonid
Stephens, Robyn
Wilkinson, Frances

Cell & Molecular Biology

SENIOR SCIENTISTS
Barr, Cathy
Bremner, Roderick
Broussard, Dianne
Cardella, Carl
Carlen, Peter
Eubanks, James
Fehlings, Michael
Inman, Robert
Jongstra, Jan
Mills, Linda
Nag, Sukriti
Schlichter, Lyanne
Skinner, Frances
Stanley, Elise
Tator, Charles
Tsui, Florence
Tymianski, Michael
Wither, Joan

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Jongstra-Bilen, Jenny
Monnier, Philippe
Sugita, Shuzo
Wan, Qi
Zhang, Liang

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Badley, Elizabeth
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Lam, Wai-Ching
Manninen, Pirjo
Massicotte, Eric
McCartney, Colin
McGuire, Glenn
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Melvin, Kenneth
Miyasaki, Janis
Montanera, Walter
Moro, Elena
Nasmith, James
Oandasan, Ivy
Ogilvie, Richard
Ogilvie-Harris, Darrell
Panisko, Daniel
Parikh, Sagar
Peng, Philip
Radomski, Sidney
Rampersaud, Yoga Raja
Rootman, David
Rosen, Cheryl
Seyone, Chanth
Shannon, Patrick
Shaw, James
Silver, Frank
Simons, Martin
Singer, Shaun
Slomovic, Allan
St George-Hyslop, Peter
Stanbrook, Matthew
Tarlo, Susan
Terbrugge, Karel
Tu, Karen
Tumber, Paul
von Schroeder, Herbert
Voon, Valerie
Wherrett, John
Willinsky, Robert
Wong, David
Wong, Jean
Yogendran, Suntheralingam
Yu, Eric Ho Cheung

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Peter St George-Hyslop

APPLIED & INTERVENTIONAL RESEARCH
Andres Lozano

CELL & MOLECULAR BIOLOGY
Elise Stanley

OUTCOMES & POPULATION HEALTH
Elizabeth Badley

CLINICAL STUDIES RESOURCE CENTRE
Jenny Heathcote

CLINICAL REPRESENTATION
Michael Fehlings
Nizar Mahomed
Martin Steinbach

SITE REPRESENTATION
Catherine Zahn

VP RESEARCH
Christopher J. Paige

Toronto Medical Discovery Tower at MaRS

This year the new Toronto Medical Discovery Tower continued to take shape at the corner of College and Elizabeth Streets

The new Toronto Medical Discovery Tower, first phase of the Medical and Related Sciences (MaRS) development, is a 400,000 sq ft, 15 floor building currently under construction.

Allowing Expansion of UHN Research Programs

UHN researchers will occupy nine floors when completed. "This new space will be a tremendous boon to UHN Research," notes Dr. Christopher Paige, Vice President, Research. "It will allow us to expand critical programs and launch new programs from the ground up." With the building quickly taking shape, occupancy is on track for September 2005.

UHN programs under discussion for creation in TMDT include a new drug discovery program incorporating medicinal chemistry and structural biology...a research program in infectious diseases/immune system research... a convergence centre bringing together a team of engineers, physicists, biologists and clinical researchers to work on multi-disciplinary problems...a home for the McEwen Regenerative Medicine Centre for gene, cell and tissue therapy...a satellite of the McLaughlin Centre for Molecular Medicine including programs in global health and stem cell research...an imaging program for testing new imaging modalities on small to large animal models...and a number of smaller initiatives proposed by research groups.

UHN Research will occupy nine floors in this new state-of-the-art building

State-of-the-Art Construction for Research

The tower has been designed as a fully integrated research facility with significant flexibility on a floor by floor basis. Unique features include 100% fresh air, independent air handlers on each floor, a highly stable structure (minimal vibrational/sway impact), a central reverse osmosis water system, and specialty exhaust risers.

The base building construction for the Toronto Medical Discovery Tower is expected to be complete by the end of 2004, with interior fit-out already underway. TMDT will be ready for full occupation by September 2005.

TMDT MILESTONES

BASE BUILDING

May 04
Concrete structure completed

Oct 04
Glass enclosure completed

Jan 05
Base building systems completed

INTERIOR FINISH

Oct 03
Concept design completed

Jan 04
Schematic design completed

Aug 04
Interior construction initiated

Dec 04
Detail design completed

Sept 05
Full occupancy for UHN Research

TMDT STATISTICS

Workers on site each day	140	Exterior glass	15,600 m^2
Volume of excavated earth	29,750 m^3	Window frames	2,500
Concrete poured	20,000 m^3	Doors and frames	295
Structural steel	179,000 kg	Elevators	9
Reinforcing steel	2,770,000 kg	Historical bricks salvaged	50,000
Indiana limestone (exterior)	11,800 ft^2	New trees planted	43

New Institute for Breast Cancer Research Opens

A first in Canada, new institute will attack disease on basic, translational and clinical research fronts

June 2004 marked the launch of UHN's newest research initiative, the Institute for Breast Cancer Research. Fuelled by generous donor and Foundation support, led by one of Canada's top scientists, and including a stellar scientific team, the new program promises significant future breakthroughs against a disease that strikes one in nine Canadian women.

Making an Impact

"Advances in basic research have created a new opportunity ready for translation into the clinic. Scientists now have the tools—knowledge of the molecular and genetic factors in the development of breast cancer—to make an impact on the treatment of breast cancer," says Dr. Tak Mak, director of the new initiative.

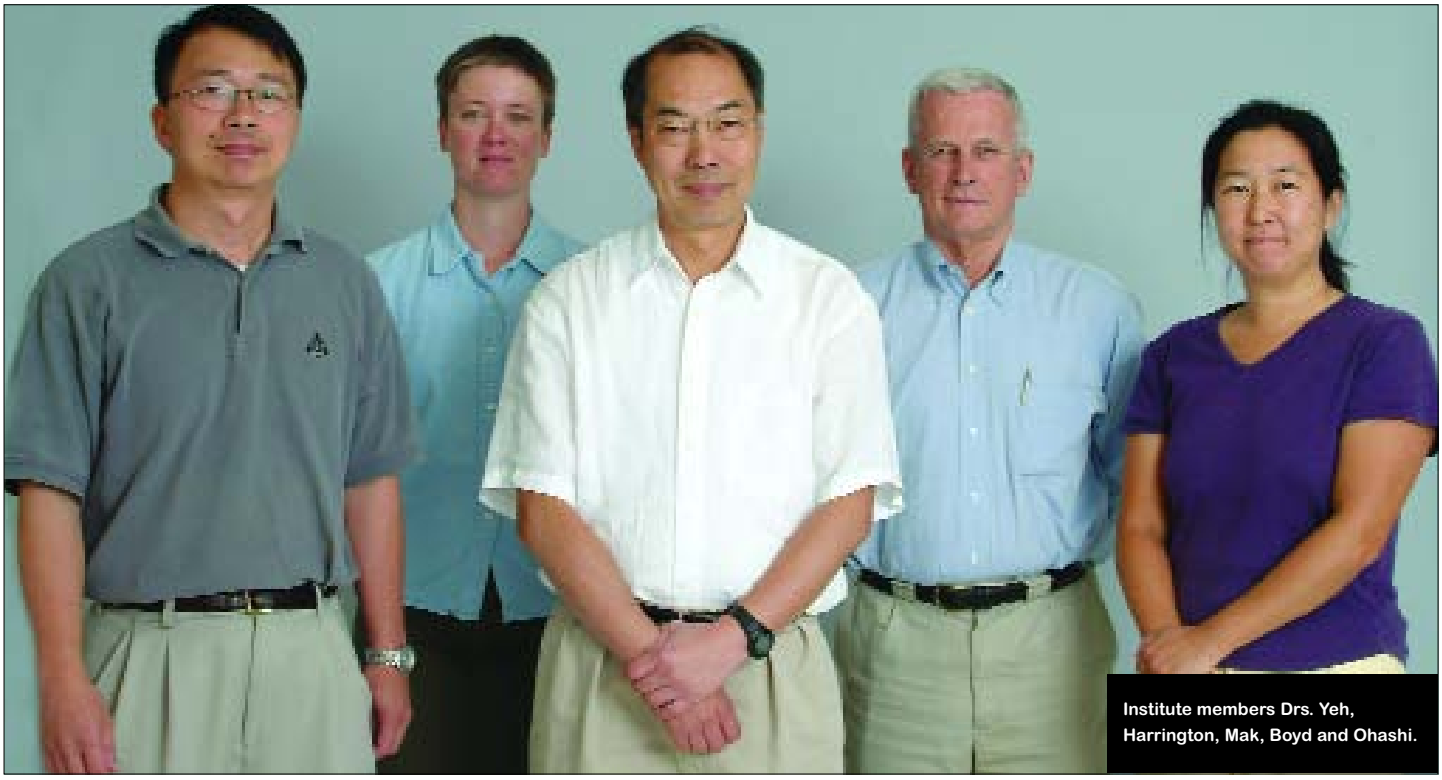
Mechanistically-based drugs—drugs which offer the promise of better treatment with fewer side effects—are rapidly becoming a reality as scientists reveal new insights into the genetic and cellular mechanisms of cancer development.

> Mechanistically-based drugs offer the promise of better treatment with fewer side effects

Within the past three to five years, these drugs have become available for many types of cancers—including leukemia and colon and stomach cancers. Based on the pioneering work done by Dr. Mak and others, new mechanistically-based treatments for breast cancer are not far behind.

Scientific Leadership

Dr. Mak is one of Canada's most prolific researchers and is most famous for his 1984 landmark scientific paper on the cloning of the T cell receptor genes, a key component of the human immune system. He is a Senior Scientist with the hospital's research arm, the Ontario Cancer Institute, as well as a University Professor with the University of Toronto, an Officer of the Order of Canada, and one of a handful of Canadians elected a Foreign Associate of the National Academy of Sciences (USA) and a Fellow of the Royal Society. His international recognition includes the King Faisal Prize for Medicine, the Gairdner Foundation International Award, the Sloan



Institute members Drs. Yeh, Harrington, Mak, Boyd and Ohashi.

Prize of the GM Cancer Foundation, and, most recently, Germany's top scientific award, the Paul Ehrlich and Ludwig Darmstaedter Prize.

Dr. Mak's studies of mice deficient in genes involved in tumorigenesis, including MSH2, DPC-4, PTEN and the breast cancer genes BRCA1 and BRCA2, have furthered our understanding of cancer development. Using mutant mice that have been disrupted in the genes encoding FADD, Apaf-1, TNFR1, and several TRAFs and caspases, he and his colleagues have dissected pathways of cellular survival and programmed cell death.

Innovative Collaborations

Also key to this program is its translational and clinical research slant. The new initiative will bring together many types of cancer researchers—scientists, clinicians and others—to conquer breast cancer. Already on board are noted epidemiologist Norman Boyd, MD, DSc, FRCPC; Terry Fox Young Investigator Lea Harrington, PhD; recent AAAI Investigator Award winner Pam Ohashi, PhD; and noted investigator Dr. Wen-Chen Yeh, MD, PhD.

Up to six investigators to be recruited in the coming months will provide additional clinical and translational research expertise.

The new Institute was launched with a goal of raising a total of $125M. Already, $60M is committed, with part of the money coming from funds raised by thousands of walkers in the annual Weekend to End Breast Cancer event in Toronto held in September. The Princess Margaret Hospital Foundation is pledging to raise an additional $65M from private donors, corporations and other sources to fund the Institute.

ADVISORY BOARD OF THE INSTITUTE FOR BREAST CANCER RESEARCH

Paul Alofs
Robert Bell
Carole Grafstein
Audrey Loeb
Tak Mak
David McCready
Christopher Paige
Lionel Robins
Katherine Vallis

Toronto Western Research Institute Welcomes New Director

World-renowned neurologist and molecular geneticist Dr. Peter St George-Hyslop appointed

Dr. Peter St George-Hyslop, Director of the Toronto Western Research Institute

This year UHN was pleased to welcome Peter St George-Hyslop, MD, as new Director of the Toronto Western Research Institute.

Dr. St George-Hyslop's pioneering genetics research into susceptibility and neurodegeneration in Alzheimer's disease has had a major impact, establishing him as an international authority in the field.

He has published more than 200 papers in leading peer-reviewed journals, and he has won numerous prestigious awards, including two Howard Hughes International Scholar Awards (1997 and 2002) and a Distinguished Scientist Award from the Canadian Institutes of Health Research in 2001. Most recently he was appointed to the Royal Society.

"I am excited by the opportunity to provide leadership here," says Dr. St George-Hyslop. "The research institute has a strong tradition in neuroscience research, and the Toronto community is also recognized internationally for research in this area."

Dr. St George-Hyslop received his MD degree from the University of Ottawa prior to doing postgraduate training at Ottawa, Toronto and Harvard. His first staff appointment was at Massachusetts General Hospital, and he returned to Toronto in 1991 as Assistant Professor, Department of Medicine (Neurology).

Currently Director of the Memory Disorders Clinic at TWH, Dr. St George-Hyslop is also Director of the Centre for Research in Neurodegenerative Diseases and Professor in the Department of Medicine at the University of Toronto. He also speaks extensively to public audiences about Alzheimer's disease.

A leader in the field of Alzheimer's disease research, Dr. St George-Hyslop has published more than 200 scientific papers in his lifetime.

Strategic Planning in Research at UHN

Platform strategic planning process launched; new plans in progress

Scientific breakthroughs occur daily. How can a research hospital best position itself to be at the forefront of scientific and clinical change?

This is the main question underlying strategic planning at UHN.

Beginning with the hospital-wide strategic plan approved in 2001, and including the draft research plan drafted in 2002 and finalized in 2004, UHN Research has been involved with scanning the horizons of the biomedical research field and gauging new opportunities for development.

Progress in 2003/04

This year marked the launch of *The Future Project* Phase II. Its goal is to develop detailed tactics for implementing the strategies detailed in Phase I.

A core of 12 Platform executives, aided by Task Forces, led this process. From January to June, they embarked on an extensive consultation process involving input from UHN investigators, Research Councils and Platform Task Forces. This process included discussion forums, focus groups and the online survey *Call for Ideas!*

Future Steps

The draft plan will become available in late 2004 for review and feedback by researchers and research leadership as well as the UHN International Research Advisory Board.

UHN thanks the Platform Chairs and Task Forces for their efforts to date:

GENES, PROTEINS & PEOPLE

Penn, Linda **(Chair)**
Bremner, Rod **(Site Leader)**
Kain, Kevin **(Site Leader)**
Arrowsmith, Cheryl
Barr, Cathy
Cheung, Peter
Downey, Greg
Fehlings, Michael
Fish, Eleanor
Floras, John
Inman, Robert
Jongstra, Jan
Jurisica, Igor
Kaul, Rupert
Keating, Armand
Lewis, Peter
Mak, Tak
Minden, Mark
Monnier, Philippe
Schimmer, Aaron
Siminovitch, Katherine
Stanley, Elise
Stewart, Keith
Woodgett, Jim

HEALTH INFORMATICS

Maetzel, Andreas **(Chair)**
Miyasaki, Janis **(Site Leader)**
Siu, Lillian **(Site Leader)**
Bacchus, Maria
Badley, Elizabeth
Bombardier, Claire
Borger, Michael
Bournes, Debra
Crawford, Lindsey
Gallie, Brenda
Gospodarowicz, Mary
Heathcote, Jenny
Jadad, Alex
Levinson, Wendy
Martino, Rosemary

MEDICAL TECHNOLOGY INNOVATION

Davis, Karen **(Chair)**
Jaffray, David **(Site Leader)**
Rao, Vivek **(Site Leader)**
Bell, Robert
Chan, Christopher
Cybulsky, Myron
Fehlings, Michael
Feindel, Chris
Husain, Mansoor
Inman, Robert
Irish, Jonathan
Kapoor, Shitij
Kucharczyk, Walter
Langille, Lowell
Levy, Gary
McAndrews, Mary Pat
Raghibizadeh, Sasan
Ruda, Harry
Sefton, Michael
Siewerdsen, Jeffrey
terBrugge, Karel
Wilson, Brian

REGENERATIVE MEDICINE

Waddell, Thomas **(Chair)**
Medin, Jeffrey **(Site Leader)**
Schlichter, Lyanne **(Site Leader)**
Bell, Robert
Benchimol, Sam
Brotchie, Jonathan
Fehlings, Michael
Feindel, Christopher
Fish, Eleanor
Kelvin, David
Levy, Gary
Stanley, Elise
Woodgett, Jim

Breakthroughs
Ontario Cancer Institute

The stories below showcase some of the many breakthroughs that occurred this year at UHN.

Many post-menopausal breast cancer survivors take tamoxifen to ensure that the cancer does not return. However, tamoxifen is only effective for about five years, leaving the survivors with no effective therapies to follow.

Breast Cancer: New Drug So Promising That Trial Cut Short

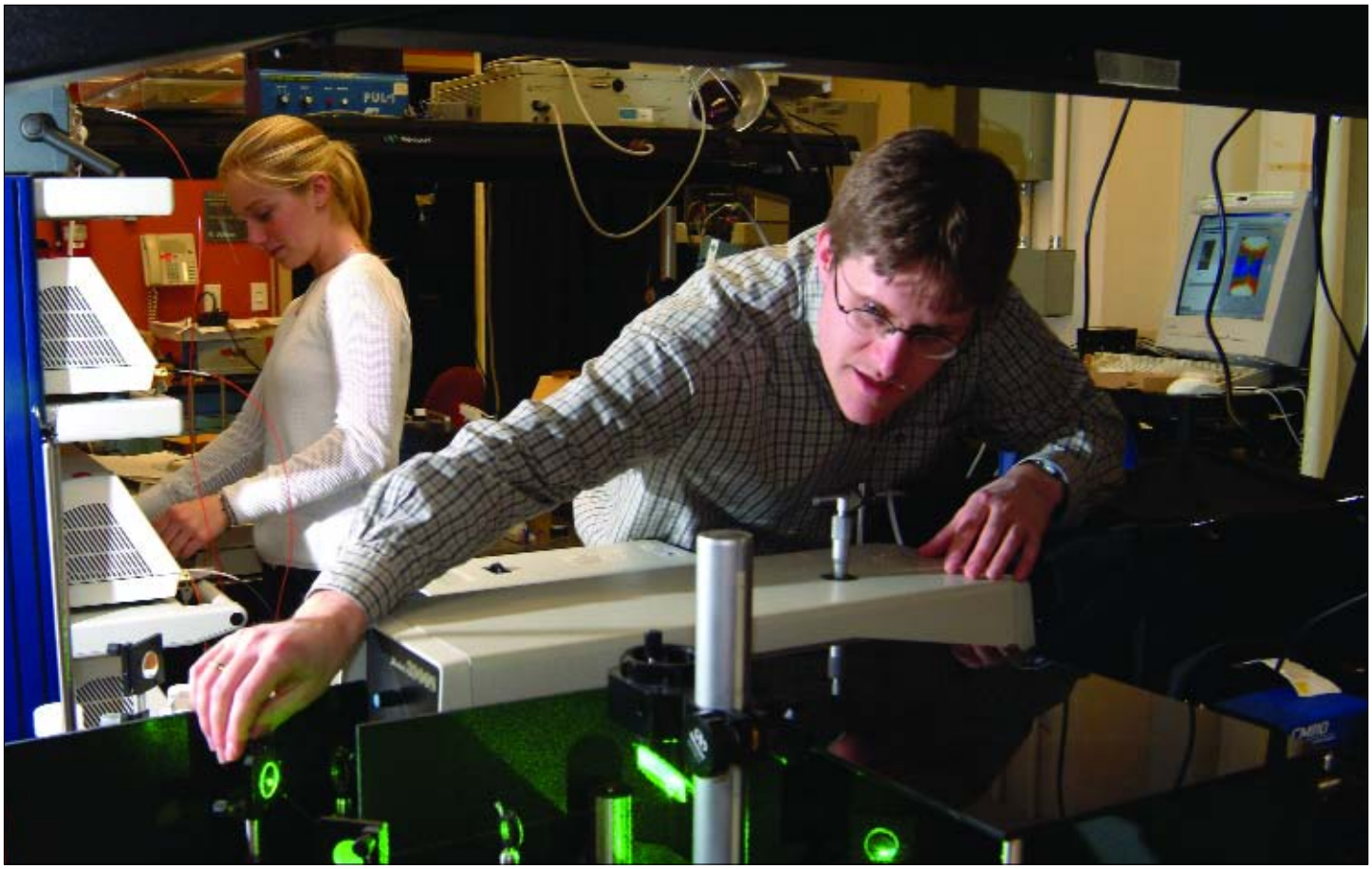
IN a surprise action by a panel of experts, a major international clinical trial conceived and led by Dr. Paul Goss involving 5,187 women across nine countries was recently halted early because the results were so astoundingly positive.

The trial was conducted under the auspices of the National Cancer Institute of Canada's Clinical Trials Group, the US NCI and the Breast International Group in Europe.

The study, reported as an expedited on-line publication, showed that a new drug (letrozole), given after a round of treatment with tamoxifen, cut the risk of breast cancer returning by 44% in post-menopausal women. *"Having ended the trial, we are now able to offer letrozole to women who were receiving placebo, so that they too may benefit from the treatment," says Dr. Goss. "This is the first time we have proof of an effective treatment after tamoxifen that will keep cancer at bay in women who are at substantial ongoing risk of suffering a relapse."*

The study showed letrozole to be more effective than chemotherapy at preventing the recurrence of breast cancer. "*This finding will change the way breast cancer is treated worldwide, and it offers significant new hope to women," says Dr. Goss.*

N Engl J Med. 2003 Nov 6; 349(19): 1793-802.



Head and Neck Cancer: New Therapy Delivers Killer Genes

New research from a large team of UHN investigators may bring us one step closer to gene therapy for a type of cancer that affects people with Southeast Asian or Mediterranean backgrounds.

A team led by Drs. Fei-Fei Liu, Jeff Medin, Peter Neligan, Pat Gullane, Brian O'Sullivan, Ralph Gilbert, Chris Richardson and Wen-Chen Yeh, postdoctoral fellow Dr. Jian-Hua Li and graduate student Ken Yip have developed a new way of making nasopharyngeal cancer cells more vulnerable to radiation.

Nasopharyngeal cancer affects predominantly a young population, and current methods of control have a five-year survival rate of only 70%.

Exploiting the ability of genes such as FasL or Bim_S to cause these cancer cells to commit suicide, the team has modified these genes to make them safer by targeting their expression only in the cancer cells, and then delivered them by direct injections into tumours in mice. These genes stopped the growth of tumours without noticeable toxicity, implying that this strategy may be very promising for future development of treatments for human patients.

FasL and Bim_S can both trigger cellular apoptosis, or cell death–an effect that is useful in treating cancer cells

Mol Ther. 2003 Dec; 8(6):964-73.

Mol Ther. 2004 Sept; 10(3):533-544.

Breast cancer survivors sometimes report symptoms of chemo-fog, a cognitive impairment that is a real issue for quality of life during recovery.

Breast Cancer: Effects of Chemotherapy Revealed

DR. Ian Tannock and his colleagues recently published a study showing that breast cancer patients receiving chemotherapy scored more poorly on tests of memory and language than did healthy women.

Many breast cancer survivors report memory difficulties and being unable to concentrate. The study, which is a follow-up of Dr. Tannock's 2000 study of the same phenomenon, also showed that the women receiving chemotherapy experienced more fatigue and menopausal symptoms than did healthy women.

Although the results of these studies can be used to advise patients about the adverse effects of chemotherapy, Dr. Tannock stresses that women shouldn't stop using chemotherapy to treat their cancer.

"The negative side effects of chemotherapy certainly don't outweigh the benefits. We are currently working to identify strategies that will ease these side effects, and hopefully improve quality of life for these women," he says.

J Clin Oncol. 2003 Nov 15;21(22):4175-83.

Holliday Junctions are structures allowing DNA to recombine and "cross-over"—generating the genetic diversity that is one of the keystones of the evolutionary process.

Genetics of Cancer: Missing Gene an Early Cancer Alert

A team of OCI/PMH scientists stunned the cancer research world in June, 2004, with their announcement that a protein discovered in yeast is a powerful tumour suppressor.

Drs. Razq Hakem, Rama Khokha and postdoctoral fellows Peter McPherson and Bénédicte Lemmers showed that a loss of one or both copies of the Mus81 gene led to the development of lymphomas and other cancers in mice.

"This finding was surprising because everyone had thought that this protein was required for the processing of DNA structures called 'Holliday Junctions' that form during DNA repair. Our work disproves this theory, and reveals an important function for Mus81 as a tumour suppressor," explains Dr. Hakem.

The next step is to determine whether cancer patients have a mutated form of the protein. *"If this is shown to be true in humans, we will have a way of screening for people at risk," he says.*

Science. 2004 Jun 18;304(5678):1822-26.

PTEN is a tumour suppressor gene that is essential for normal cell growth and has been implicated in over 50% of all types of human tumours.

Prostate Cancer: Loss of PTEN Implicated

A key cancer gene is critical for the development of prostate cancer, says a recent report authored by Drs. Tak Mak, Vuk Stambolic, Ming-Sound Tsao, and William Chapman and student Stephanie Backman.

"Prostate cancer is the second leading cause of cancer deaths in men, and there is currently no known single cause of its initiation," says Dr. Chapman. "Our finding is the first to show that PTEN is critical for suppressing tumour development in the prostate. In the future we may be able to target preventive measures towards restoring this gene, or reactivating it."

PNAS. 2004 Feb 10;101(6):1725-30.

Photodynamic Therapy: How Much is Enough?

New research from the lab of Dr. Brian Wilson may help solve the problem of how to dose photodynamic therapy (PDT), an emerging treatment for cancer.

PDT is based on a drug that is activated by light. After application, the drug zeroes in on cancer cells, accumulating in large concentrations. When activated by laser light, the drug produces toxic molecules that destroy the cancer cells.

To determine exactly how much PDT is needed for effective treatment, Dr. Wilson and graduate student Mark Niedre took an approach never taken before.

"Rather than measuring the amount of PDT administered to the cancer cells, we measured the concentration of toxic molecules produced," Dr. Wilson explains. "We found that the number of cancer cells that were destroyed was proportional to the concentration of toxic molecules produced, a finding that suggests that this method could be used to measure PDT."

The group plans further studies to test the feasibility of using this non-invasive technique to optimize PDT treatments in a clinical setting.

Cancer Res. 2003 Nov 15; 63(22):7986-94.

Photodynamic therapy is a new treatment being used to treat some types of esophageal and lung cancers.

Lymphoma: New Study Confirms Treatment Choice in MALT Lymphoma

Emphasizing Princess Margaret Hospital's leading role in cancer treatment advances, a team of radiation oncologists and radiation physicists led by Dr. Richard Tsang and including Drs. Mary Gospodarowicz, Woodrow Wells, Alexander Sun, Michael Crump, David Hodgson and Bruce Patterson and statistician Melania Pintile has studied optimal treatment strategies for a puzzling cancer called localized mucosa-associated lymphoid tissue (MALT) lymphoma.

Associated with various organs in the body, including stomach, tissues surrounding the eye, salivary glands and thyroid glands, this type of cancer is slow growing and not prone to metastasis, indicating that it may be an excellent candidate for radiation therapy.

The team studied responses of 85 patients to radiation therapy, and determined that 84 of these patients had responded "extremely well" to moderate-dose radiation therapy, showing that radiation therapy is an excellent choice for controlling this disease.

J Clin Oncol. 2003 Nov 15;21(22):4157-64.

Radiation therapy is often used to treat localized cancers at specific sites; chemotherapy is often the treatment of choice for cancers which have metastasized, or dispersed.

Breakthroughs
Toronto General Research Institute

AIDS and malaria are twin public health scourges of African countries. It is estimated that 22M Africans are infected with HIV and at least 500M have malaria.

AIDS: New Study Shows Complexity of Treatment Response

For those co-infected with both AIDS and malaria, the effect(s) of antiretroviral drugs for the treatment of HIV on the clinical course of malaria are unknown. New research by Dr. Kevin Kain and postdoctoral fellow Lena Serghides has now shown that ritonavir and saquinavir—two antiretroviral drugs commonly used to treat HIV—impair the immune response to malaria.

Immune cells treated with the antiretrovirals showed decreased amounts of CD36, a protein that is crucial for macrophages to eliminate red blood cells infected with the malaria-causing Plasmodium parasite. The loss of CD36 caused a 50-60% reduction in the number of parasitised red blood cells that were purged from the blood, as part of the body's protective immune response.

This study calls attention to the potential for antiretroviral drugs to worsen malaria, which in turn could worsen HIV disease progression and transmission, a potentially serious public health issue.

Lancet. 2003 Sep 27;362(9389)1039-41.

SARS: UHN Develops World's First Treatment

A new treatment devised by Dr. Eleanor Fish and based on antiviral proteins called interferons has shown great promise against SARS in preliminary tests. Interferons are produced by the immune system to fight viral infections.

During Toronto's second SARS outbreak, the new treatment was administered to 19 patients with the help of Dr. Mona Loutfy at North York General Hospital. Only the four most critically ill died—suggesting that early treatment may be the key to its effectiveness.

Patients who received interferon showed faster improvement of their disease based on their lung X-rays, and they required less oxygen than did comparable patients during the first phase of the outbreak (who did not receive interferon).

"Although our findings are still preliminary, they are extremely encouraging. A global strategy for SARS preparedness is being developed, and it includes further examination of the potential therapeutic benefit of early treatment with interferon," says Dr. Fish.

The study also involved UHN researchers Drs. Kathy Siminovitch, Kevin Kain and Gary Levy.

JAMA. 2003 Dec 24;290(24):3222-8.

The World Health Organization has adopted Dr. Fish's new treatment as the first standard treatment for this baffling disease.

Lung Transplant: New Treatments on the Horizon for Transplant Patients

Recent findings from the labs of Drs. Shaf Keshavjee, Li Zhang, and Tom Waddell have important implications for preventing reperfusion injury—a severe side effect that can develop after transplantation.

Based on the knowledge that the immune system's T cells are involved in mediating this injury, the research team performed lung transplants on two groups of animals: those with their T cells intact, and those missing their T cells. Following transplant, it was clear that the mice with T cells had fared worse—their new lungs didn't function as well, and there was evidence that the T cells were preparing to launch an attack on the transplanted lungs.

These findings provide evidence that it is the transplant recipient's own T cells that mediate reperfusion injury following transplant, a finding that has implications for how doctors might prevent and treat this type of injury.

J Immunol. 2003 Nov 15; 171 (10):4995-5002.

According to the International Society for Heart and Lung Transplantation, there are more than 1600 lung transplants performed each year around the world. Reperfusion injury is a common side effect involving an immune reaction between the organ and its recipient.

Arthritis costs the Canadian healthcare system $4.4B annually, representing more than one quarter the total cost of musculoskeletal diseases.

Arthritis: Balancing Treatment Costs with Benefits

BY the year 2026, it is estimated that more than 6M Canadians will have arthritis. To examine the skyrocketing costs associated with this disease, Dr. Andreas Maetzel—a specialist in the field of pharmacoeconomics—assesses the benefits of arthritis medications.

Recently, two of the drugs under scrutiny were rofecoxib for the treatment of osteoarthritis, and celecoxib for the treatment of rheumatoid arthritis. Using a variety of assessment tools including mathematical modeling techniques and Canadian databases, the team found that both drugs are economically attractive, but only for elderly and "high risk" patients. Thus, the message for physicians is clear: exercise discretion when prescribing these medications, since the benefits may not justify the costs in all patients.

Arthritis Rheum. 2003 Jun 15;49(3):283-92.

Heart disease, obesity, and diabetes: all are conditions associated with high levels of fats (triglycerides) in the blood and low levels of HDL cholesterol, or "good" cholesterol.

Cholesterol Levels: Obesity and Physical Inactivity Quell Good Cholesterol

IN an aging population concerned with preserving good circulatory health, a question that continues to plague researchers is how do individuals lose HDL, or "good" cholesterol.

A study published by Dr. Gary Lewis and his team suggests that the answer may lie in the interaction between triglycerides and the liver enzyme hepatic lipase (HL).

Using an animal model, the team found that HL eliminated the good cholesterol from the body at a faster rate in the presence of elevated triglycerides—not the case in animals whose good cholesterol was not enriched with triglycerides.

"This suggests that high levels of fats in the blood change the structure of the good cholesterol molecules, making them easier for HL to target and destroy—an important finding for controlling the harmful effects of fat in the diet," says Dr. Lewis.

Circulation. 2003 Jun 24;107(24):3066-72.

Stem cells are powerful progenitor cells. They are the "mother cells" that give rise to many different types of "offspring" during growth and maintain the body as it ages.

Leukemia: Targeting "Hidden" Cells for Successful Treatment

New research by Dr. John Dick, graduate student Kristin Hope, and research associate Liqing Jin may help explain why 60-90% of leukemia patients suffer a recurrence following treatment.

Using his pioneering method of studying human stem cells, Dr. Dick and his team learned that there are many different types of leukemia stem cells (LSC), just as there are different types of regular, healthy blood stem cells. Some LSCs are fast acting, while others can lie dormant for a long time before they become reactivated.

"Our research suggests that leukemia recurs because chemotherapy isn't designed to target these dormant cells," says Dr. Dick. "Now that we know they're there, we need to figure out how to eliminate them."

Dr. Dick predicts that similar cancer stem cells will be found for solid tumours, such as breast cancer.

Nat Immunol. Jul 5(7):738-43.

Lymphoma: Special T Cells May Improve Treatment Success

A recent finding by a UHN investigator may overcome a major hurdle in the development of immune-based therapies for cancer.

Bone marrow transplants are a common and successful treatment for cancer. However, a battlefield can potentially develop as donor and recipient immune cells wage war in the recipient. One type of battle is "graft-versus-host disease", in which immune cells from a cell donor attack the recipient's tissues, leading to serious disease. Another type of battle is "graft-versus-lymphoma", in which donor cells attack the cancer, resulting in cancer regression. The current challenge is to trigger the beneficial effects of the graft-versus-lymphoma phenomenon without exposing the transplant recipient to an increased risk of graft-versus-host disease.

A team led by Dr. Li Zhang and graduate student Kevin Young has now identified a special type of immune T cell, the DN T cell, which can trigger the healing graft-versus-lymphoma effects without causing graft-versus-host disease. In a mouse model, these DN T cells can directly kill lymphoma cells in vitro and prevent growth of the cancer. Thus the DN T cells may offer a new treatment approach for cellular therapy of cancer.

Cancer Res. 2003 Nov 15;63(22):8014-21.

Despite the fact that hematopoietic stem cell transplants are widely used to treat lymphoma, graft-versus-host disease remains a barrier to successful treatment. New immune-based therapies must overcome this risk.

Heart Failure: Protein Lures Immune Cells, Damaging Heart

High levels of the endothelin ET-1 in the heart lead to an increased risk of heart failure, and the findings of a recent study by Drs. Mansoor Husain and Avrum Gotlieb may tell us why.

Drs. Husain and Gotlieb compared heart function in normal mice to heart function in mice with high levels of ET-1. *"The heart tissue of mice with high amounts of ET-1 was full of immune cells," explains Dr. Husain. "Since there was no real infection, the chemicals released by the immune cells were damaging the heart, causing heart failure."*

When the researchers treated these mice with drugs to block ET-1, they were able to reduce the incidence of heart failure, proving that ET-1 was responsible for luring the immune cells to the heart. The research points to a potential new strategy for treating this condition.

Circulation. 2004 Jan 20;109(2):255-61.

Endothelins are molecules that exert powerful control over the activities of our blood vessels. They play a role in hypertension and other circulatory illnesses.

Breakthroughs
Toronto Western Research Institute

Controlling neurotransmitters and their receptors is one activity of successful anti-depressants, anti-anxiety drugs, drugs for high blood pressure and heart disease, and nerve toxins including snake and spider venom.

Molecular Complexes Control Brain Function

The cells of our nervous system communicate with each other by sending messages via chemicals called neurotransmitters. The release of these chemicals, though, requires several steps and involves several proteins, and new research by Dr. Elise Stanley and post-doctoral fellows Qi Li and Anthony Lau reveals that this process is far more complicated than once thought.

Using state-of-the-art imaging technology, the research team found that the many proteins involved in releasing these chemicals—once thought to be separate from one another—are actually part of a single complex.

"Our research shows that the point of transmitter release contains highly evolved, miniscule molecular machines designed to transfer information between nerve cells under very tight control," says Dr. Stanley.

J Neurosci. 2004 Apr 21;24(16):4070-81.

Childhood Cancer: Clue May Help Understand Cancer Development

Featured as the cover story in the June issue of *Cancer Cell,* new research by Dr. Rod Bremner and postdoctoral fellows Danian Chen, Izhar Livne-bar and Mahima Agochiya will lead to the development of new treatments for retinoblastoma, the most common eye cancer in children.

Using mice that have retinoblastoma, Dr. Bremner found that some retinal cells exhibit abnormal survival patterns—patterns that are the hallmark of cancer cells.

Says Dr. Bremner, "These cells may be partially cancer-like to begin with. They may explain why retinoblastoma, as well as other childhood cancers, develop in fewer steps than typical adult cancers. It may also help us develop drugs that interfere with the cellular development of cancers of many types."

Cancer Cell. 2004 Jun;5(6):539-551.

Retinoblastoma is the most common childhood eye cancer. It can run in families or occur "sporadically" (without previous family history).

Internal Clock: Tick-Tock of the Body Clock Under Tight Control

Research by neuroscientist Dr. Qi Wan provides new clues regarding how our body's internal clock keeps such good time.

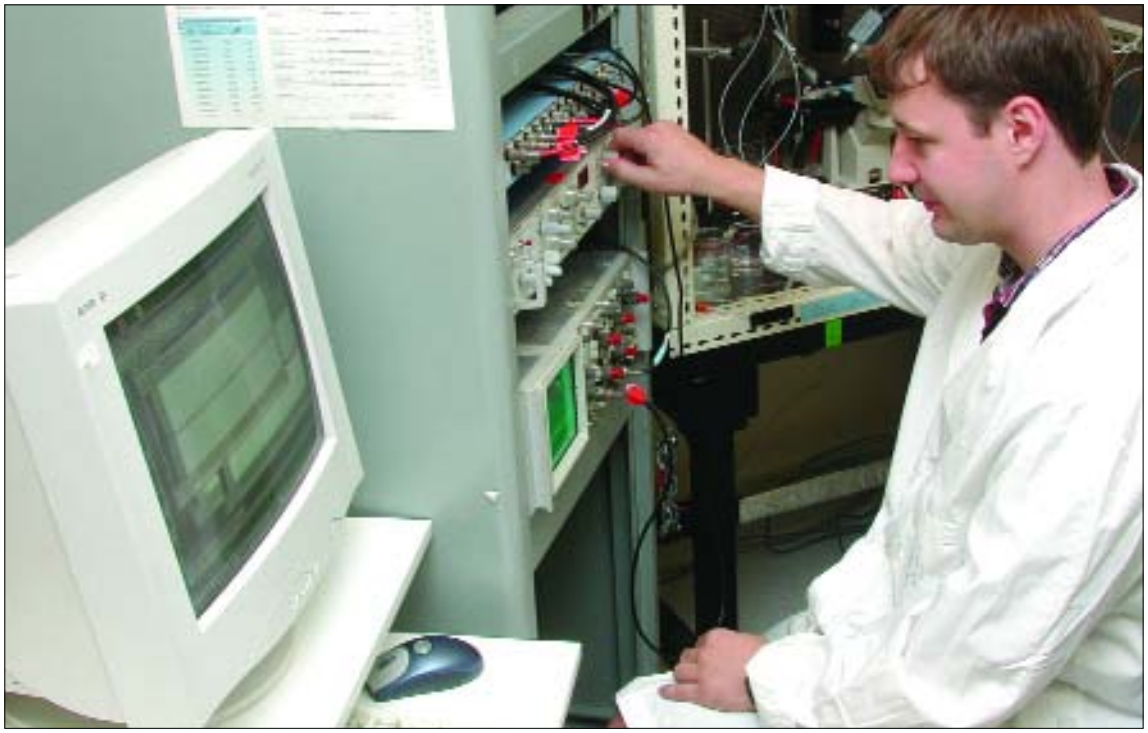
Our internal clock is made up of numerous "clock cells" that all work together to control the timing of rhythmic functions such as sleeping, waking, and digestion, to name a few.

Dr. Wan's research shows that proteins called $GABA_A$ receptors—long believed to be the principal clock regulators—are actually controlled by another protein called CKIϵ-CKIδ.

"Our research provides evidence of an intracellular mechanism for regulating synchronization of our body's clock," explains Dr. Wan. "It is relevant for the future development of treatments for people with health problems associated with insomnia, shift work, and jet lag."

Nat Neurosci. 2004 May;7(5):489-90.

The body clock is involved in insomnia, jet lag, response to shift work and other rhythmic functions and dysfunctions.



Systemic lupus erythematosus, commonly called lupus, is an autoimmune disease affecting primarily women.

Lupus and Heart Disease: Risk Greater in Women With SLE

IN the first large-scale study of its kind, Drs. Dafna Gladman and Murray Urowitz and TGRI/TGH's Dr. George Steiner looked for risk factors for coronary artery disease in women with systemic lupus erythematosus (SLE). Women with SLE are known to have a greater risk for heart disease than other women.

The researchers compared the number of heart disease risk factors in women with and without SLE, and found that based on classic heart disease risk factors, the 10-year risk of heart attack was the same in both groups of women.

However, the researchers did find that women with SLE had higher levels of fat molecules in their blood, including triglycerides (the major form of fat) and VLDL cholesterol (the "bad" cholesterol), which may be related to their basic disease process or its therapy.

"Problems related to lipid metabolism are characteristic of SLE," explains Dr. Gladman, "and further studies are needed to understand exactly how this contributes to the increased risk of heart disease in this high-risk patient group. Although many patients can reduce their risk using screening and intervention procedures, more research is needed to learn how to accurately predict the risk of heart disease in these patients."

Arthritis Rheum. 2003 Nov; 48(11):3159-67.

Hepatitis: Body Weight, Dosing Closely Related

A new study by Drs. Jenny Heathcote and Brian Bressler and TGRI/TGH's Dr. George Tomlinson shows that a person's body mass index (BMI)—a measurement that describes a person's weight relative to their height—may be a risk factor for determining their degree of responsiveness to antiviral treatment for hepatitis C infection.

A total of 253 hepatitis C patients were treated with antiviral therapies between 1989 and 2000. At six months post-therapy, their conditions were assessed to determine if the medications had been effective.

The results showed that the therapy was less effective in patients with a high body fat content (BMI>30) than in patients with a BMI of less than 30. *"This research shows how important it is to maintain a healthy body weight," says Dr. Heathcote, "and we are currently investigating how weight-based dosing may optimize treatment success."*

This research has spurred the FDA to request that pharmaceutical companies who make therapies for hepatitis C conduct further tests to examine the effect of body weight on drug efficacy.
Hepatology. 2003 Sep;38(3):639-44.

New research from a UHN group is making the medical community re-examine the relationship between body weight and drug efficacy.

Stroke: Main Source of Brain Damage Identified

Exciting new research conducted by a team of researchers led by Dr. Michael Tymianski and colleague Dr. John MacDonald has provided a better understanding of how stroke causes brain damage.

Reported in *Cell*, the research shows that when brain cells are deprived of oxygen and nutrients—as in a stroke—an ion channel on the surface of brain cells (called TRMP7) is activated. This releases toxic molecules, which then kill other, healthy brain cells in the vicinity.

"Now that we know that TRMP7 is the culprit, we can focus on developing medications that will prevent these consequences and improve patient outcome," says Dr. Tymianski.
Cell. 2003 Dec 26; 115(7):863-877.

Much of the damage in the brain associated with stroke occurs hours and days after the initial incident—leaving a window of time for preventive treatment.

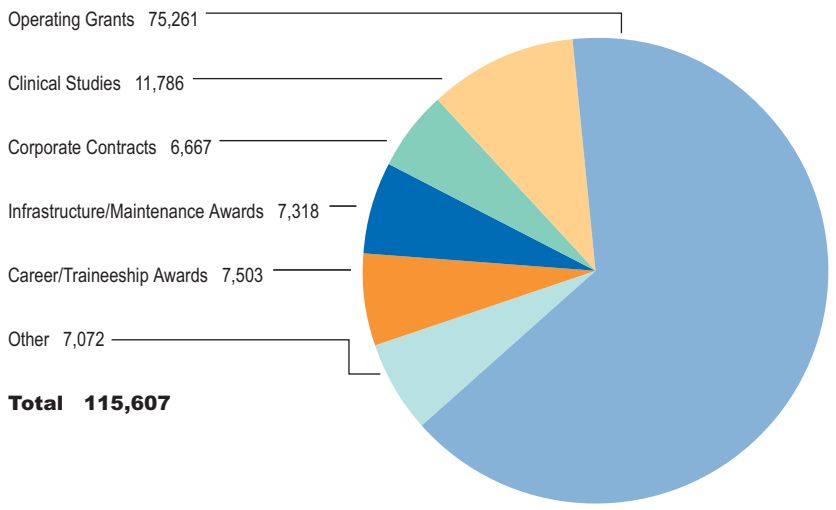
Research Funding

Revenues

All figures represent fiscal year 2003/04 and include Ontario Cancer Institute (Princess Margaret Hospital); Toronto General Research Institute (Toronto General Hospital) and Toronto Western Research Institute (Toronto Western Hospital). These figures have been provided by UHN Research Financial Services and Research Grant and Contract Services.

UHN Research Core Funding	Total ($1,000s)
Princess Margaret Hospital Foundation	14,500
Toronto General & Western Hospital Foundation	4,000
Arthritis & Autoimmunity Research Centre Foundation	1,500
Recoveries	5,859
Investment Income	3,859
Ministry of Health & Long Term Care	2,816
Other	7,835

Total External Funding Awarded by Purpose of Funding ($1000's)



Major Sources of External Funding	Total ($1000s)
Canadian Institutes of Health Research	20,542
National Cancer Institute of Canada	9,886
Ontario R & D Challenge Fund	6,256
National Institutes of Health (U.S.)	6,234
Ontario Innovation Trust	6,198
Ontario Cancer Research Network	6,054
Heart and Stroke Foundations	4,438
Canada Foundation for Innovation	3,624

Research Funding
External Agencies

Abbott Laboratories
Achillion Pharmaceutical
Actelion Pharmaceuticals
Agouron Pharma
Alcon Research
Allergan Sales
Alteon
Alzheimer Society of Canada
Alzheimer's Disease and Related Disorders Association
AmCyte
American Association for Thoracic Surgery
American Association of Neurological Surgeons and Congress of Neurological Surgeons
American College of Surgeons Oncology Group
American Digestive Health Foundation
American Foundation for AIDS Research
American Society of Clinical Oncology
American Society of Echocardiography
American Society of Hematology
American Society of Interventional & Therapeutic Neurology
Amersham
Amgen
AO-ASIF Research Foundation
Arius Research
Arthritis Community Research & Evaluation Unit
Arthritis Society
Associated Medical Services Incorporated
Astra Pharma
AstraZeneca
Aventis Pasteur
Banting and Best Diabetes Centre
Bausch and Lomb
Baxter Healthcare Corporation
Bayer
Beckman Coulter
Berlex Laboratories
Biochem Therapeutic
BioMedicines
Bloorview Epilepsy Research
Boehringer Ingelheim
Boston Scientific Corporation
Brahms Diagnostica
Breast Cancer Society of Canada
Bristol-Myers Squibb Pharmaceutical Research Institute
Broncus Technologies
C.R. Younger Foundation
Canada Foundation for Innovation
Canadian Anesthesiologists Society
Canadian Association of Radiation Oncologists
Canadian Breast Cancer Foundation
Canadian Breast Cancer Research Initiative
Canadian Cancer Etiology Research Network
Canadian Cancer Society (Ontario)
Canadian Coordinating Office for Health Technology Assessment
Canadian Cystic Fibrosis Foundation
Canadian Dermatology Foundation
Canadian Diabetes Association
Canadian Foundation for AIDS Research
Canadian Health Services Research Foundation
Canadian Institutes of Health Research
Canadian Liver Foundation
Canadian Lung Association
Canadian Prostate Centre
Canadian Society of Hospital Pharmacists
Canadian Urologic Oncology Group
Cancer Care Ontario
Cancer Research Institute
Cancer Research Society
Cangene Corporation Canadian
Chiropractic Protective Association & National Chiropractic Mutual Insurance Company
Celgene Corporation
Cell Therapeutics
Cervical Spine Research Society
Change Foundation
Ontario Ministry of Health
CLP Research (Switzerland)
Cook (Canada)
Corgentech
Corvita Canada
Covance
Crohn's and Colitis Foundation of Canada
Cyanamid
Defense and Civil Institute of Environmental Medicine
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ECHO Research
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Glaxo
GlaxoSmithKline
GlycoDesign
Government of Canada-Canadian Space Agency
Guidant Europe
Health Canada
Heart and Stroke Foundation
Hemosol
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Susan G. Komen Breast Cancer Foundation
Synbiotics
T Cell Sciences
Taylor & Frances Group Publishing
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Tiffin Trust Fund
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Research Support Services at UHN

Research Support Services provides a supportive collaborative infrastructure for research across UHN's institutes. Approximately 240 RSS staff support UHN's researchers, staff and trainees.

Animal Resource Centre: Provides facilities, care and technical services for animal models used in research as well as experimental design support and ethics review

Grant and Contract Services: Reviews clinical trial agreements, tracks information regarding employees and grants, and processes documents for hiring new research staff

Clinical Studies Resource Centres (PMH and TGH/TWH): Assists clinical investigators in initiating, conducting, managing and analyzing investigator-driven and industry-sponsored clinical research

Research Business Development Office: Commercializes research discoveries that help investigate, treat and diagnose disease, to generate revenue for inventors and research reinvestment

Research Communications and Proposal Development: Develops print and electronic communications in consultation with internal and external stakeholders for various audiences

Research Ethics Board: Oversees research involving human subjects to ensure it meets scientific and ethical standards to protect patients, investigators and the institution

Research Information Systems

Research Facilities: Involves the management of office and lab space, relocations and renovations, core equipment and general equipment, maintenance, and safety

Research Financial Services: Provides financial information and services to investigators, research administration and sponsors related to research funding and disbursements

Research Information Systems: Provides researchers a full range of computing services from email and file storage to remote access and the power of high processing clusters

Research Program Planning and Analysis: Provides analyses of research activity and supports performance evaluation activities of research programs and departments

Sterilization, Sera and Media Services: Co-ordinates the purchase, cleaning and sterilization of laboratory glassware and the provision of tissue culture and bacteriological media

Vice President's Office: Provides strategic leadership for UHN Research in consultation with the Research Councils

Analysis of Research Activity at UHN

Nearly every paper published in a peer-reviewed journal contains a list of citations: references to earlier papers which helped the authors define and answer their current research question. A paper which is influential in its field will be cited frequently by other authors over the months and years following its publication.

Citation analysis is used by institutions around the world as one way of measuring research productivity and success. UHN Research has over the past three years begun collecting citation analysis information to determine its usefulness as a method of measuring scientific impact over time.

Citation analysis uses computer databases to search and count all references to a certain paper to determine its impact on a field. We can also do this for all papers published by a scientist or group of scientists over a defined time period.

Citation Data for Papers Published by UHN Researchers 2001/03

2001/03	Total Papers	Citations to Date	Cites/Paper	Papers in Top Journals*	Top Papers*
OCI	1040	9753	9.4	142 (14%)	283 (37%)
TGRI	1620	12243	7.6	157 (10%)	518 (32%)
TWRI	1068	5524	5.2	49 (5%)	200 (19%)
UHN	3613**	24621	6.8	338 (9%)	930 (26%)

***Where papers are collaborations between scientists at different UHN research institutes, papers are counted only once in the "UHN" total*

**"Top Journals" are those journals with an impact factor>10, and "Top Papers" are papers in the top 10% of cited papers (as defined by the Institute for Scientific Information)*

Benchmarking to Peer Institutions, 2001/03

	Top Papers
Cleveland Clinic	22%
UHN	26%
Johns Hopkins	27%
Massachusetts General Hospital	30%

Endowed Chairs at UHN

Much of the research at UHN is made possible through the generosity of donors, who contribute to UHN's work through the three UHN Foundations and their fund-raising efforts.

Among the most generous of contributions is an endowed Chair, established at a minimum level of $2M. The income from this endowment provides ongoing funding for the Chairholder. There are currently 53 endowed Chairs established at UHN or held by UHN investigators.

Dr. Jim Woodgett
The AMGEN Chair in Cancer Research
Dr. Brian O'Sullivan
The Bartley-Smith/Wharton Chair in Radiation Oncology
Dr. Ian Tannock
The Daniel E. Bergsagel Chair in Medical Oncology
(to be appointed)
BMO Financial Group Chair in Health Professions Education Research
Dr. Jeremy Squire
The JC Boileau Grant Chair in Oncologic Pathology
Dr. Christopher Paige
The Ronald N. Buick Chair in Cancer Research
Dr. Charles Tator
The Robert Campeau Family Foundation Chair in Brain and Spinal Cord Research
Dr. Ming Tsao
M. Qasim Choksi Lung Cancer Chair in Translational Research
Dr. Ori Rotstein
Peter A. Crossgrove Chair in General Surgery
Dr. Glenn Regehr
Richard & Elizabeth Currie Chair in Health Professions Education Research
Dr. James Rutka
The Dan Family Chair in Neurosurgery
(to be appointed)
Angelo & Lorenza DeGasperis Chair in Cardiovascular Surgery Research
(to be appointed)
Alfredo & Teresa DeGasperis Chair in the Surgical Management of Heart Failure
(to be appointed)
Antonio & Helga DeGasperis Chair in Clinical Trials and Outcomes Research
Dr. Fei-Fei Liu
Dr. Mariano Antonio Elia Chair in Head and Neck Cancer Research
Dr. Scott Beattie
The R. Fraser Elliott Chair in Cardiac Anaesthesia
Dr. Gregory Downey
The R. Fraser Elliott Chair in Transplantation Research
Dr. K. Wayne Johnston
The R. Fraser Elliott Chair in Vascular Surgery
Dr. Armand Keating
The Gloria & Seymour Epstein Chair (in Cell Therapy & Transplantation)
Dr. David Jaffray
The Orey and Mary Fidani Family Chair in Radiation Physics
Dr. John Trachtenberg
The Fleck/Tanenbaum Chair in Prostatic Diseases
Dr. David McCready
Gattuso Chair in Breast Surgical Oncology
Dr. Malcolm Moore
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Dr. Michael Baker
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James Wallace McCutcheon Chair in Surgery
(to be appointed)
Robert & Cheryl McEwen Chair in Cardiac Regenerative Medicine
Dr. Tirone David
The Melanie Munk Chair in Cardiovascular Surgery
Dr. Mark Minden
The Philip S. Orsino Chair in Leukemia Research
Dr. John Parker
The Pharmacia Chair in Cardiovascular Research
Dr. Allan Kaplan
Loretta Anne Rogers Chair in Eating Disorders
(to be appointed)
Sandra Rotman Chair in Health Care Management at University of Toronto and University Health Network
(to be appointed)
RBC Financial Group Chair in Cardiovascular Nursing Research
Dr. Doris Howell
RBC Financial Group Chair in Oncology Nursing Research
Dr. Keith Stewart
The J. Gerald Scott/David G. Whitmore Chair in Haematology and Gene Therapy Research
Dr. Nizar Mohammed
The Smith & Nephew Chair in Orthopaedic Surgery Research
(to be appointed)
The Joey and Toby Tanenbaum/Brazilian Ball Chair in Prostate Cancer Research
Dr. Andres Lozano
The R.R. Tasker Chair in Stereotactic and Functional Neurosurgery
Dr. Frances Shepherd
The Scott Taylor Chair in Lung Cancer Research
(to be appointed)
Tyco Chair in Minimally Invasive Surgery
Dr. Pat Gullane
The Robert E. Wharton Chair in Head & Neck Surgery
Dr. Peter Neligan
The Robert E. Wharton Chair in Reconstructive Plastic Surgery

U of T Chairs Held by UHN Appointed Staff

Dr. Elise Stanley
The Anne and Max Tanenbaum Chair in Molecular Neurosciences
Dr. Chris Wallace
The Fondation Baxter and Alma Ricard Chair (in Cerebrovascular Neurosurgery)
Dr. Peter Liu
The Heart & Stroke Foundation Polo Chair in Cardiovascular Research
Dr. Anthony Lang
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Informatics, Stanford
University

Malcolm Pike, PhD
Professor in the Department
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University of Southern
California

The third IRAB meeting will take place November 2004.

2004
RESEARCH REPORT

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