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UHN Research Report

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Achieving with Partnerships

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University Health Network

CONTENTS

About Research at University Health Network

Total Number of Researchers	**465**
Senior Scientists	152
Scientists	47
Affiliate Scientists	46
CRU/CSRC Members	220
Total Number of Trainees	**881**
Fellows	387
Graduate Students	364
Other Students	130
Staff	**1083**
Research Space	**480,000 sq ft**
Publications	**1191**
Total Research Funding	**$160,700,000**

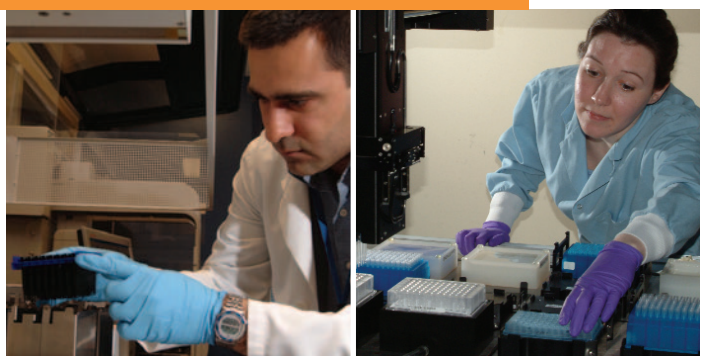
2005

Contents

PARTNERSHIPS

COMING TOGETHER TO ACHIEVE COMMON ENDS

Research at University Health Network is built on partnerships.



New research facilities, new research programs, new resources for research and new research staff—all have been achieved through partnerships.

Partners include public and private agencies; donors and foundations; companies; other research organizations such as universities and hospitals; and governments at the municipal, provincial and federal levels.

In these pages UHN salutes its partners.

FROM THE PRESIDENT & CEO

Welcome to the University Health Network *Research Report* for 2004/05. This year's *Report* has the theme of "Partnership", and so it is fitting that we are pairing up to introduce this year's edition.

UHN is a landmark in the Canadian health care system, and UHN Research is the largest hospital-based research enterprise in the country.

As a network of teaching hospitals, research institutes, and other affiliates, University Health Network has from the beginning embraced the concept of partnership. Partnering with other hospitals to streamline care delivery through IT and other strategies. Partnering with stakeholders and care providers in the community. Partnering with our three Foundations for fundraising in a very successful Campaign. Partnering with our staff to implement patient-centred care. Partnering with the University of Toronto and the Toronto Academic Health Sciences Network to fulfill our research and teaching mandates. In these ways and many others, UHN is a prime example of collaboration in action.

In UHN Research, particularly, the list can be extended. Research continues a long tradition of partnering with public funding agencies to explore novel research avenues. Scientific collaboration is also a key ingredient in many UHN research breakthroughs. In the past few years, Research has also built capacity to partner with private sector representatives for commercialization of new technologies and development of innovative new funding mechanisms.

No institution, not even an institution the size of UHN, can do it all alone. In working with partners we build on our strengths and minimize our weaknesses. Together we achieve much more than we could achieve independently.

UHN realized many partnership successes in 2004/05. This *Report* outlines some of them. Please read on to learn more.

Tom Closson
President and CEO
University Health Network
(2000-2005)

Robert S. Bell,
MD CM, MSc, FRCSC, FACS
President and CEO
University Health Network
(2005-)

FROM THE VICE PRESIDENT

Research plays a vital role in achieving UHN's vision of "global impact"—and I am convinced that we will achieve this goal only through partnership.

For Research, global impact means that our basic science discoveries will influence the course of scientific thinking around the world; our translational discoveries will spur the development of new treatments and diagnostic tools; and our clinical discoveries will be adopted world wide, resulting in improved patient outcomes at every level.

We will only achieve this vision by establishing productive partnerships: partnerships with other leading academic institutions, with communities and governments, with the private sector, and with the help of engaged supporters who work with our Foundations to allow researchers to realize their ambitious dreams.

UHN enjoys membership in one of the most vibrant medical research communities in the world—the Toronto Academic Health Sciences Network (TAHSN). Composed of the University of Toronto and 9 research hospitals, TAHSN provides researchers with access to collaborative expertise across the medical disciplines. Major joint initiatives such as the R.S McLaughlin Centre for Molecular Medicine, the Toronto Centre for Phenogenomics, and BioDiscovery Toronto serve to focus research talent drawn from diverse institutions on common research problems.

Another important set of partners are funding agencies and governments. There has been an extraordinary commitment on the part of federal and provincial governments to increase Canadian competitiveness in biomedical research. This has translated into major increases in UHN's annual research spending.

The ultimate goal of biomedical research is to improve health. Striving to achieve this goal is the foundation of the knowledge-based economic engine. UHN values its relationships with private sector partners whose complementary skills and funding capacity help us to achieve our goals.

Philanthropy also plays a big part in our success. The three UHN Foundations—the Princess Margaret Hospital Foundation, Toronto General & Western Hospital Foundation and Arthritis & Autoimmunity Research Centre Foundation—help fund core research programs and provide the base upon which UHN investigators were able to raise more than $160M in total research funding last year.

Most importantly, UHN Research's success rests on the success of our many internal "partners": our scientists and clinician-scientists, our technical and support staff, and our students and fellows. They are the creative force that is changing the face of health care.

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

PRINCESS MARGARET HOSPITAL

Ontario Cancer Institute

Research Space	222,000 sq ft
Publications	402
Total External Funding	$65,392,000

Staff and Students

Total Number of Researchers	**146**
Senior Scientists	44
Scientists	16
Affiliate Scientists	3
CRU Members	83
Total Number of Trainees	**387**
Fellows	164
Graduate Students	184
Other Students	39
Staff	**455**

Applied Molecular Oncology

SENIOR SCIENTISTS
Asa, Sylvia*
Hedley, David *
Hill, Richard
Liu, Fei-Fei*
Miller, Richard
Moore, Malcolm*
Squire, Jeremy*
Tannock, Ian*
Tsao, Ming *

SCIENTISTS
Bristow, Robert*
Done, Susan*
Vallis, Katherine*

AFFILIATE SCIENTIST
Kamel-Reid, Suzanne*

Biophysics & Bioimaging

SENIOR SCIENTISTS
Chakrabartty, Avi
Hunt, John
Jaffray, David
Lepock, James
Sherar, Michael
Vitkin, Alex
Wilson, Brian

SCIENTISTS
Lilge, Lothar
Siewerdsen, Jeff

Cancer Genomics & Proteomics

SENIOR SCIENTISTS
Arrowsmith, Cheryl
Benchimol, Sam
Gallie, Brenda
Gariépy, Jean
Pai, Emil
Penn, Linda
Privé, Gilbert
Richardson, Christopher
Rose, David

SCIENTISTS
Harrington, Lea
Schimmer, Aaron*
Tillier, Elisabeth

AFFILIATE SCIENTIST
Bradley, Grace

Epidemiology, Statistics & Behavioural Research

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

AFFILIATE SCIENTIST
Ritvo, Paul

Signaling Biology

SENIOR SCIENTISTS
Ikura, Mitsu
Khokha, Rama
Manoukian, Armen
Ohashi, Pam
Woodgett, Jim

SCIENTISTS
Cheung, Peter
Hakem, Razq
Jurisica, Igor
Koch, Anne*

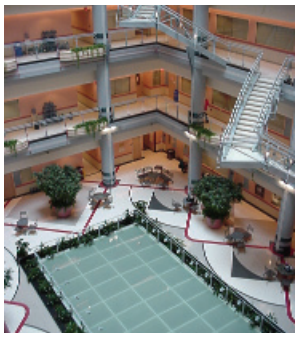
OCI includes the Advanced Medical Discovery Institute and The Campbell Family Institute for Breast Cancer Research

Stambolic, Vuk
Vaziri, Homayoun
Yeh, Wen-Chen

Stem Cell & Developmental Biology
SENIOR SCIENTISTS
Barber, Dwayne
Iscove, Norman
Mak, Tak
McCulloch, Ernest
Messner, Hans*
Minden, Mark*
Paige, Christopher
Rottapel, Robert
Stewart, Keith*

SCIENTIST
Medin, Jeffrey

Clinical Research Unit (CRU)
MEMBERS
Bayley, Andrew
Bell, Robert
Bezjak, Andrea
Brandwein, Joseph
Brierley, James
Brown, Dale
Catton, Charles
Catton, Pam
Chen, Christine
Chen, Eric
Chetty, Runjan
Cho, John
Chung, Peter
Crook, Juanita
Crump, Michael
Cummings, Bernard
Darling, Gail
Dawson, Laura



de Perrot, Marc
Dodge, Jason
Easson, Alexandra
Edelstein, Kim
Elliott, Mary
Evans, Andrew
Feld, Ronald
Finelli, Tony
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, Jeffrey
Manchul, Lee
Mason, Warren
McCready, David
McLean, Michael
McLean, Linda
Menard, Cynthia
Mikhael, Joseph
Millar, Barbara-Ann
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
Wei, Alice
Wells, Woodrow
Wong, Rebecca
Zimmermann, Camilla

**these researchers are also members of the Clinical Research Unit*

Research Council

Director
Christopher J. Paige

Division Heads
Applied Molecular Oncology
Fei-Fei Liu
Biophysics & Bioimaging
Brian Wilson
Cancer Genomics & Proteomics
Linda Penn
Epidemiology, Statistics & Behavioural Research
Norman Boyd
Signaling Biology
Mitsu Ikura
Stem Cell & Developmental Biology
Robert Rottapel

Vice President, Research
Christopher J. Paige

Clinical Representatives
Armand Keating
Mary Gospodarowicz
Jonathan Irish

Site Representative
Robert Bell

TORONTO GENERAL HOSPITAL

Toronto General Research Institute

Research Space	153,000 sq ft
Publications	541
Total External Funding	$46,623,000

Staff and Students

Total Number of Researchers	**188**
Senior Scientists	64
Scientists	22
Affiliate Scientists	30
CSRC Members	72
Total Number of Trainees	**327**
Fellows	149
Graduate Students	119
Other Students	59
Staff	**435**

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, M Jane
Katz, Mark*
McVey, Gail
Reid, Graham
Ritvo, Paul
Robinson, Gail
Styra, Rima
Woodside, Blake

Cell & Molecular Biology

SENIOR SCIENTISTS
Backx, Peter
Berger, Stuart
Cardella, Carl
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
Rubin, Barry
Schuh, Andre*
Whiteside, Catherine
Zacksenhaus, Eldad
Zhang, Li

SCIENTISTS
Belsham, Denise
Cattral, Mark
Husain, Mansoor
Irwin, David
Jin, Tianru
Volchuk, Allen
Waddell, Thomas*

AFFILIATE SCIENTISTS
Branch, Donald
Clark, David
Cole, Edward
Ojha, Matadial
Wen, Xiao-Yan
Wilson, Gregory

Clinical Decision–Making & Health Care

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

SCIENTISTS
Alibhai, Shabbir
Cheung, Angela
Krahn, Murray
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
Kucharczyk, Walter
Lewis, Gary
Logan, Alexander
Miller, Judith
Olivieri, Nancy
Steiner, George
Walmsley, Sharon
Zamel, Noe

SCIENTISTS
Reilly, Raymond
Wong, Florence

AFFILIATE SCIENTIST
Easty, Anthony

Experimental Therapeutics

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

SCIENTISTS
Rao, Vivek
Yau, Terrence

AFFILIATE SCIENTISTS
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, Katherine
Sole, Michael

SCIENTISTS
Osborne, Lucy

AFFILIATE SCIENTISTS
Boright, Andrew
Denomme, Greg

Clinical Studies Resource Centre (CSRC)

MEMBERS
Ali, Mohamed
Bacchus, Maria
Bargman, Joanne
Beattie, Scott
Borger, Michael
Bradley, John
Bril, Vera
Brister, Stephanie
Cameron, Douglas
Chan, Charles
Chan, Christopher
Chauhan, Vijay
Colman, Jack
Cooper, Richard
Daly, Paul
David, Tirone
Djaiani, George
Dzavik, Vladimir
Fedorko, Ludwik
Fenton, Stanley
Fisher, Joseph
Gardam, Michael
Girgrah, Nigel
Gold, Wayne
Goldszmidt, Eric
Granton, John
Grigoriadis, Sophie
Harris, Louise
Herridge, Margaret
Humar, Atul
Ing, Douglas
Jaigobin, Cheryl
Jassal, Vanita
Jewett, Michael*
Johnston, Michael*
Kachura, John
Kapral, Moira
Karkouti, Keyvan
Karski, Jacek
Kennedy, Sidney
Keystone, Edward
Lapinsky, Stephen
Lilly, Leslie
Loke, Julian
Manktelow, Ralph
McCluskey, Stuart
McLaughlin, Peter
McRae, Karen
Merchant, Naeem
Neary, Mary Ann
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, Leonard
Seidelin, Peter
Sherman, Morris
Singer, Lianne
Siu, Samuel
Slinger, Peter
Straus, Sharon
Sutton, David
Sweet, Joan
Wilson, Stephanie
Wolman, Stephen
Yeo, Erik

** these researchers are also cross-appointed as members of the Clinical Research Unit at PMH*

Research Council

Director
Richard Weisel

Division Heads
Behavioural Sciences & Health
Gary Rodin
Cell & Molecular Biology
Eleanor Fish
Clinical Decision-Making & Health Care
Claire Bombardier
Clinical Investigation & Human Physiology
Richard Weisel
Experimental Therapeutics
David Kelvin
Genomic Medicine
Katherine Siminovitch
Clinical Studies Resource Centre
John Parker

Vice President, Research
Christopher J. Paige

Clinical Representatives
Carl Cardella
Christopher Feindel
Gary Levy

Site Representative
TBD

TORONTO WESTERN HOSPITAL

Toronto Western Research Institute

Research Space	105,000 sq ft
Publications	342
Total External Funding	$16,600,000

Staff and Students

Total Number of Researchers	**132**
Senior Scientists	45
Scientists	9
Affiliate Scientists	14
CSRC Members	65
Total Number of Trainees	**167**
Fellows	74
Graduate Students	61
Other Students	32
Staff	**193**

Applied & Interventional Research

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

SCIENTISTS
Hudson, Christopher
Kucharczyk, Walter
Roberts, Timothy
Wong, Agnes

AFFILIATE SCIENTISTS
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, Rod
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
Wither, Joan

SCIENTISTS
Monnier, Philippe
Sugita, Shuzo
Wan, Qi
Zhang, Liang

AFFILIATE SCIENTISTS
El-Beheiry, Hossam
Gallie, Brenda

Outcomes & Population Health

SENIOR SCIENTISTS
Badley, Elizabeth
Carette, Simon

Cassidy, David
Fortin, Paul
Gladman, Dafna
Urowitz, Murray

SCIENTISTS
Gignac, Monique
Mahomed, Nizar

AFFILIATE SCIENTISTS
Cott, Cheryl
Lineker, Sydney

Clinical Studies Resource Centre (CSRC)
MEMBERS
Anastakis, Dimitri
Bernstein, Mark
Bookman, Arthur
Buys, Yvonne
Chan, Vincent
Chapman, Kenneth
Chung, Frances
Davey, Roderick
del Campo, Martin Jose
Devenyi, Robert
Epstein, Trina
Escallon, Jaime
Etlin, David
Evans, Michael
Farb, Richard
Fung, Ken
Gentili, Fred
Graham, Brent
Hawa, Raed
Heathcote, Jenny
Iwanochko, Mark
Lam, Robert
Lam, Wai-Ching
Manninen, Pirjo

Massicotte, Eric
McCartney, Colin
McGuire, Glenn
McIntyre, Roger
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
Saltzman-Benaiah, Jennifer
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

Research Council

Director
Peter St George-Hyslop

Division Heads
Applied & Interventional Research
Andres Lozano
Cellular & Molecular Biology
Rod Bremner/Cathy Barr (acting)
Outcomes & Population Health
Elizabeth Badley
Clinical Studies Resource Centre
Jenny Heathcote

Vice President, Research
Christopher J. Paige

Clinical Representatives
Michael Fehlings
Nizar Mahomed
Martin Steinbach

Site Representative
Catherine Zahn

Record Donation Accelerates Breast Cancer Research

October 2004: Marking the country's largest private gift to cancer research, a $25M gift this month launched The Campbell Family Institute for Breast Cancer Research at Princess Margaret Hospital.

The gift will assist the Institute in becoming a world-leading program by leveraging basic, translational and clinical research into dramatic breast cancer breakthroughs. The funds were donated by Audrey Campbell, daughter of the late Roy Thomson, and her three daughters.

Institute Director Dr. Tak Mak has received numerous international accolades for his scientific discoveries and is most famous for his landmark 1984 cloning of the T-cell receptor genes, a key component of the human immune system.

New Federal Funding Supports Transplant and Cancer Research

October 2004: New funding from the Canada Foundation for Innovation announced this month will help accelerate three projects under the new Research Hospital Fund. The projects are led by Drs. David Jaffray, Gary Levy and Tak Mak, and awards totalled $18M.

Advisory Board Guests at UHN Research Day

November 2004: This year UHN Research Day welcomed the International Research Advisory Board as guests to its annual Research Day.

This year's Inventor of the Year, selected by the Research Business Development Office's Strategic Advisory

UHN+PARTNERS=

A "Brain Gain" for UHN

March 2005: A memorandum of understanding signed this month with the Shanghai Institute of Health Sciences will allow UHN and Canada to tap into valuable resources for health research on an international scale. The Shanghai institute is affiliated with a major medical school and a leading cancer hospital in China, and the new international partnership will provide access to skilled experts in critical areas for the development of new anti-cancer drugs.

The Shanghai collaboration is an example of UHN Research's "preferred partnership" strategy. UHN Research seeks out groups and institutions with complementary areas of expertise, establishing collaborative relationships to achieve ambitious "win-win" outcomes.

Committee, was Dr. Dan Drucker, selected based on his contributions to research in diabetes and intestinal disorders through his discovery and commercialization of the glucagon-like peptides GLP-1 and GLP-2.

A New Look for UHN Research

December 2004: UHN Research made its mark on the world wide web with the re-launch of its website at www.uhnresearch.ca. The re-design features a custom search engine and profiles of more than 400 individual researchers. The new site receives more than 25,000 visits per month.

TGRI Welcomes Dr. Richard Weisel to the Helm

January 2005: Following an international search, cardiovascular surgeon, TGRI Senior Scientist and Chair of the Division of Cardiac Surgery at the University of Toronto Dr. Richard Weisel is named the new Director of the Toronto General Research Institute. With a distinguished UHN career spanning nearly 30 years, Dr. Weisel in his new role commits to providing enhanced support for research at TGRI.

Platform Recommendations Released

April 2005: After a year-long consultation process, *UHN Platforms: Strategies for Global Impact*, representing phase II of UHN strategic planning for Research, is released.

Dr. David Naylor Appointed University President

April 2005: Dr. David Naylor, former Dean of the University of Toronto Faculty of Medicine and Vice Provost, Relations with Health Care Institutions, is appointed to the top University post. Dr. Naylor's extensive experience combines academia and health care and he is a member of the UHN Board of Trustees.

Dr. Robert Bell Appointed as new UHN CEO

May 2005: Dr. Robert Bell, formerly Chief Operating Officer at Princess Margaret Hospital and Medical Director of the UHN Oncology program (2000-2005) was named successor to Tom Closson, outgoing President and CEO of UHN. Dr. Bell is an orthopedic surgeon with a specialized practice in oncology and a successful career in cancer research and education.

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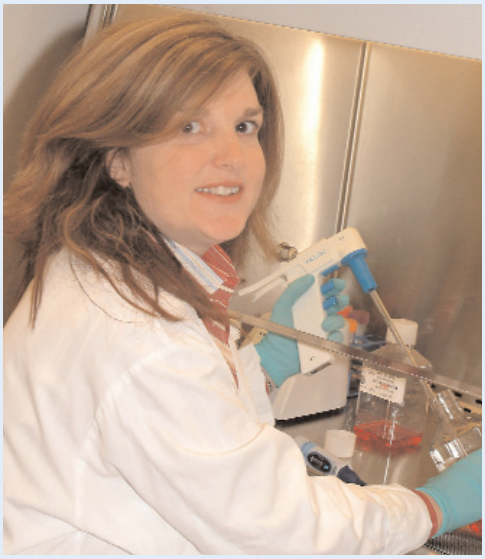

Recruiting New Expertise

Dr. Suzanne Trudel is one of UHN's newest scientists, and she was recruited through the **McLaughlin Centre for Molecular Medicine (MCMM)**, a $150M "virtual centre" established in 2001 "to advance the basic biomedical sciences of genetics and molecular biology and translate them into new strategies for disease diagnosis, treatment and prevention."

The McLaughlin Centre is itself a partnership comprising the **University of Toronto Faculty of Medicine**, the **Hospital for Sick Children, Mount Sinai Hospital, Sunnybrook** and **Women's College Health Sciences Centre**, and **University Health Network**. Significant funding is provided by the Ontario Innovation Trust and the McLaughlin Foundation.

Her research focuses on new drug development for the treatment of mature B–cell malignancies based on molecular targets.

Dr. Trudel is a member of the MCMM Program in Molecular Therapeutics, and her research focuses on new drug development for the treatment of mature B–cell malignancies based on molecular targets. Her work has recently resulted in the validation of a new clinical target in myeloma, and the first clinical trial of drugs targeting this molecule.

She did her medical training at the University of Toronto, and was lured back to the city, and to UHN, after further training in the United States. "I was attracted by the opportunity to work at an institute with state-of-the-art tools, world-renowned scientists, one of the top clinical programs in mature B–cell malignancies in North America and with a vision to apply molecular discovery to clinical care of patients ."

In recent years the UHN-McLaughlin partnership has been successful in recruiting two other new investigators, Drs. Xiao-Yen Wen and Aaron Schimmer, both part of the MCMM Program in Molecular Therapeutics.

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New Clinical Products

Metastasis of tumours to the spine is a debilitating outcome for many women with breast cancer, as well as for women and men with several other types of cancer. UHN researchers, in partnership with **Sunnybrook and Women's College Health Sciences Centre** and **University of California-Davis**, as well as the private sector, are working on a revolutionary new way to treat such patients.

The method involves photodynamic therapy, or PDT, in which a targeted laser is used to specifically activate a drug (photosensitizer) that is localized in cancer cells—while causing only minimal damage to surrounding healthy cells.

"PDT is a powerful treatment and its uses against tumours in various parts of the body are only beginning to be shown. The challenge, in each case, is to find a way to shine the light directly on the affected organ. Since laser light does not easily penetrate deeply into tissues, access is simpler in some organs, like the lungs, gastrointestinal track and eye, but more difficult in organs with no external access. Our technology addresses this in the spine," says Dr. Brian Wilson of OCI/PMH, who, with colleagues Drs. Shane Burch, Stuart Bisland and Jeff Siewerdsen, is leading the program.

Their invention, the bone screw, resembles a metallic straw. The screws can be implanted in affected vertebrae and used to place optical fibers to deliver the light deep into the bone. This device also allows subsequent vertebroplasty—injection of a plastic compound into the vertebra—in order to stabilize and strengthen the bone to improve mobility.

A **Canadian biopharmaceutical company, QLT Inc**, has a focus in PDT for cancer and other diseases and has joined forces with the group to sponsor a preclinical safety study. "The results of this study are very promising in terms of effectiveness and safety and we're hoping to move to clinical trials in humans within the next year," says Dr. Wilson.

Working with the UHN Research Business Development Office, the group has applied for a patent on the device and has also attracted the interest of companies interested in developing guidance and imaging software for the treatment.

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Training the Next Generation

University Health Network is a teaching hospital, meaning that it takes very seriously its mandate to train the next generation of health care providers and biomedical researchers.

Funding for training comes from a variety of sources. One of UHN's innovative programs is the Strategic Training Grant in Regenerative Medicine, funded by the **Canadian Institutes of Health Research.**

Regenerative medicine embraces ground-breaking new treatments for organ failure—stem cell therapy, therapeutic cloning, tissue engineering, tolerance research, and gene therapy. Led by world-famous transplant physician and researcher Dr. Gary Levy, the CIHR training program is a multi-site (**University of Toronto, McMaster University** and **University of Ottawa**), multidisciplinary accredited course for students interested in obtaining a Master's or PhD in regenerative medicine.

Launched in 2002, the program has enjoyed steady growth. It now boasts fifteen faculty at UHN and other hospitals, and in 2005 the program funded a total of 24 trainees in 16 labs: four postdoctoral fellows, fourteen graduate students and six summer students.

UHN researchers also lead two other training grants funded under the same CIHR program: a group led by Dr. Fei-Fei Lui providing training in radiation medicine and a group led by Dr. Ming Tsao in molecular oncologic pathology.

NEW DIRECTOR

Esteemed Scientist Takes on New Challenge of TGRI Leadership

This year Toronto General Research Institute welcomed its new Director, Dr. Richard Weisel. A cardiovascular surgeon, TGRI Senior Scientist and Chair of the Division of Cardiac Surgery at the University of Toronto, Dr. Weisel brings a great deal of leadership experience to this role.

"I was attracted to the Director position for the opportunity to focus the activities of the TGRI and enhance the environment for the excellent researchers in our institution," says Dr. Weisel. "We have an opportunity to take a giant step forward by coordinating our research efforts and consolidating around our strengths."

"Among its many leading programs, TGRI has specific strengths in cardiovascular, transplant, arthritis and immunity, diabetes, pulmonary, stem cells, genomics and extensive clinical research. The new initiatives will attempt to implement the recommendations of *The Future Project* and create the collaborations suggested by the four UHN Priority Platforms. The availability of new resources from our successful infrastructure grants and new space in the MaRS Discovery Tower provides a unique opportunity to achieve global impact in research."

Dr. Weisel's major research interests lie in cardiac regeneration and tissue engineering. He has more than 170 publications in peer-reviewed journals, and is the recipient of numerous awards, including the Research Achievement Award from the Canadian Cardiovascular Society, the Wilfred Bigelow Award from the Canadian Society of Cardiac Surgeons, the Career Investigator Award from the Heart and Stroke Foundation of Ontario, the Earl Bakken Scientific Achievement Award of the Society of Thoracic Surgeons, the Honored Guest Lecturer, American Association for Thoracic Surgery and the Distinguished Scientist Award from the American Heart Association.

He is proudest of his role in mentoring approximately a dozen clinician-scientists in their research and clinical careers, and he has received the Charles Tator Surgeon-Scientist Mentoring Award from the University of Toronto and the Mentoring Award from the Council on Cardiovascular Surgery, American Heart Association.

DISCOVERY TOWER

New Tower Will Stretch UHN Research Capacity

Not only is the Toronto Medical Discovery Tower (TMDT) a shining example of partnership, it is also an amazing opportunity for growth and expansion of UHN Research.

UHN-MaRS Priorities Aligned

The story starts in June 2001, when UHN sold lands to the Medical and Related Sciences (MaRS) Discovery District, a non-profit group mandated to bring together research, capital and industry.

"UHN was very involved in the process from day one," says Dr. Christopher J. Paige, Vice President, Research. "We selected MaRS because we knew it provided much-needed space to expand our research programs, and their vision of accelerating commercialization was completely aligned with our priorities."

Ultimately UHN became a full partner in the development of the main research tower, which came to be called the

Laboratories in the Toronto Medical Discovery Tower are nearing completion for occupancy in late 2005.

Toronto Medical Discovery Tower. Design took place over much of 2003 and 2004, with construction commencing in Sept 2004.

Building on Track for Occupancy within Months

Fast forward to summer 2005. The TMDT has been built and stands fifteen stories high above the corner of Elizabeth and College Streets in downtown Toronto. This key location is on a corner of the UHN campus, across the street from the provincial legislature and less than one block from the University of Toronto. UHN occupancy is expected in late 2005.

There are many things unique about the building—the open-concept lab spaces, the high-end lab finishes, the powerful mechanical systems that make it all possible—but the defining feature of the tower is not its design but its occupants.

At TMDT a range of disciplines will be brought to bear on disease. TMDT research programs incorporate physics, chemistry, informatics and knowledge management, and engineering—along with expertise in basic and clinical biomedicine.

Funding Partners Key to Tower's Framework

The range and breadth of research expertise is evident in the floor plan. UHN, with leadership from the scientists and the UHN Foundations, sourced funding for the creation of significant new centres and programs not before seen in Toronto.

One such centre is the T. Robert

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A "Towering" Success

UHN's expansion into the Toronto Medical Discovery Tower was made possible by the following agencies:

- **Canada Foundation for Innovation**
- **Province of Ontario**

Special leadership support provided by:

- **Campbell Family** & **Weekend to End Breast Cancer Walkers for Breast Cancer Research**
- **Robert & Cheryl McEwen** for Regenerative Medicine
- **Sandra Rotman** for Global Health
- **WB Family Foundation** for Convergence Centre

Ongoing support provided by:

- **Princess Margaret Hospital Foundation, Toronto General & Western Hospital Foundation** and **Arthritis & Autoimmunity Research Centre Foundation**

Beamish Family Convergence Centre of Medical Discovery, bringing together more than 60 investigators and staff in the areas of genomics, proteomics, systems biology and informatics, and locating them on one floor in the TMDT.

"The power of this Centre will lie in its ability to integrate a flood of data from genomics and proteomics studies and translate it into real, usable information—patterns and trends—for application to clinical care," says Dr. Jim Woodgett, a leading scientist in the centre.

Funded by a generous donation from the WB Family Foundation, the Convergence Centre will be one of the first TMDT programs to open, and is slated for occupancy in fall 2005.

Structural Biology and Medicinal Chemistry a "One-Two Punch"

Another breakthrough centre at the TMDT will house two 800 MHz nuclear magnetic resonance (NMR) units, currently among the most powerful in the world. Similar technology to an MRI machine, the NMR is used to take "snapshots" of molecular structure at very high resolution.

The major goal of the program is to investigate specific cancer targets. "We are interested in protein-protein interactions, and specifically the protein interaction network that underlies signaling cascades. Many cancer targets are part of this network and NMR will help researchers to decipher in detail what can go wrong with those targets," explains Dr. Mitsu Ikura, head of the Division of Signaling Biology and co-leader of the NMR centre with Dr. Cheryl Arrowsmith.

NMR-based structural biology, combined with an emerging medicinal chemistry program that is part of the UHN's international agreement with Shanghai, will constitute a one-two punch for cancer molecules, using knowledge of molecular structure to devise targeted drug compounds.

A major funder of the NMR centre was a grant from the Canada Foundation for Innovation and the province of Ontario to the Advanced Medical Discovery Institute.

Regenerative Medicine Centre Cuts Across Boundaries

A third centre is the McEwen Centre for Regenerative Medicine, funded through the visionary leadership of donors Robert and Cheryl McEwen.

"Regenerative medicine cuts across traditional research areas by engaging cell biology, engineering, materials science, and surgery. Together these fields can transform how we treat and prevent human diseases through new and innovative therapies," says Dr. Richard Weisel, who is providing interim leadership for the Centre.

The McEwen Centre will be a hub for this type of research in Canada and will drive collaborative, multidisciplinary research with a focus on new options for cure.

Schematic of UHN spaces within the Toronto Medical Discovery Tower

9
T. Robert Beamish Family Convergence Centre of Medical Discovery
genomics, proteomics and informatics

8
McLaughlin Centre for Molecular Medicine
stem cells and global health

7
STTARR
research in radiation medicine

6
experimental therapeutics

5
structural biology/drug development

4
structural biology/drug development

3
McEwen Centre for Regenerative Medicine

2
Research in Immune Tolerance in Transplantation
McLaughlin-Rotman Centre
infectious diseases/immune system

1
public spaces

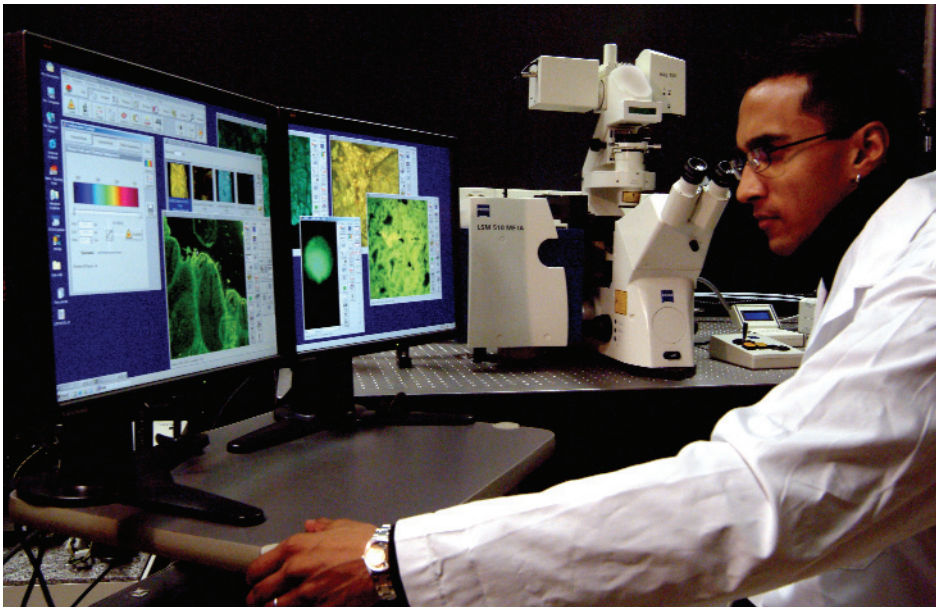
TMDT a "Powerhouse of Innovation"

These three centres will be joined by, among others, the McLaughlin-Rotman Centre — Molecular Solutions for Global Health, a new initiative led by Dr. Kevin Kain and focusing on research in diagnosing and treating emerging and infectious diseases. The TMDT will also allow creation of the STTARR centre for research enhancing the delivery of radiation therapy, as well as RITT, a new program in infectious diseases/immune system research. Both are funded by the Canada Foundation for Innovation and the province of Ontario.

"Individually, each program is very very strong," says Dr. Paige. "Any institute would be proud to claim a single one. Together, though, the TMDT programs will be a powerhouse of innovation. The TMDT mission, in brief, is to accelerate cures. With the support of our partners, we're bringing together the expertise and the equipment to achieve that."

Ontario Cancer Institute

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



Tamoxifen blocks the effects of the estrogen hormone.

Combined Drug-Radiation Therapy Dramatically Cuts Risk of Breast Cancer Recurrence

In a ground-breaking new multi-centre study Drs. Anthony Fyles, David McCready, and Lee Manchul have found that the use of the drug tamoxifen combined with radiation therapy to treat breast cancer following surgery reduced the likelihood of cancer relapse to virtually zero at five years.

In this study, half the women received the combined treatment, and half received tamoxifen alone. Less than 1% of the women who received the combined treatment had suffered a relapse five years after surgery, compared to almost 8% of the women who received tamoxifen alone.

Says Dr. Fyles, "We didn't expect to see such a dramatic difference, but the results definitely show that post-surgery radiation therapy offers a significant benefit. Women should continue to discuss the risks and benefits of treatment with their doctors, and make decisions based on what will best work for them."

The study also involved researchers from Toronto Sunnybrook Regional Cancer Centre (Sunnybrook and Women's College Health Sciences Centre), University of Toronto, and the British Columbia Cancer Agency.

N Engl J Med. 2004 Sep 2; 351(10): 963-70.

In an autoimmune disease, the immune system responds to bodily tissue the same way it would respond to an invader —with harmful consequences.

Research Points to Cause of Autoimmunity

Why are some people more likely to develop an autoimmune disease than others? Although many believe it may be due to a process called molecular mimicry, Dr. Pam Ohashi's research suggests otherwise.

According to the theory of molecular mimicry, people who develop autoimmune diseases such as diabetes or arthritis may have a naturally occurring protein that looks very much like a protein from a virus or bacteria. If these people ever became infected with a "look-alike" pathogen, their immune cells could be spurred to attack their normal proteins as well as the real pathogen. This results in autoimmune disease.

Says Dr. Ohashi, "Our model shows for the first time that there must be a very tight bond between the infecting pathogen and the attacking immune cells before autoimmune disease can develop. It also shows that most people have genes that protect them from this process, indicating that molecular mimicry likely isn't the cause."

Nat Med. 2004 Oct 3; 10(11): 1234-39.

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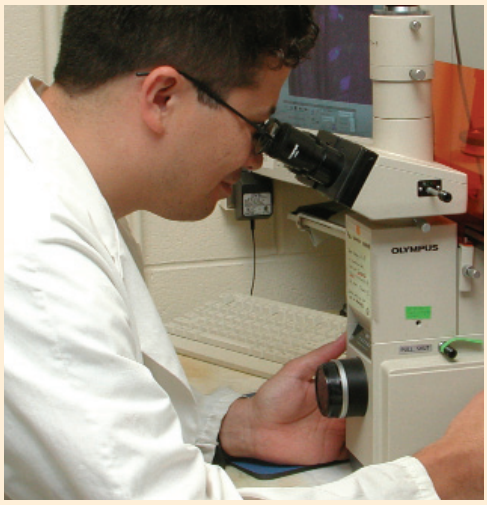
New Standards of Evidence-Based Care in Prostate Cancer

This year a UHN researcher led an international study which pointed to a new standard of treatment for men with advanced, incurable prostate cancer.

One of the many challenges in clinical trials is to enrol a sufficiently large number of patients to get definitive proof for a conclusion. In this case, PMH's Dr. Ian Tannock led a phase III trial supported by the **drug company Aventis which enlisted 43 oncologists with practices in 24 countries on six continents** to test a new treatment regime for advanced prostate cancer.

The two-year study involving 1,000 men has proven that a drug called docetaxel, when taken in combination with prednisone, improved survival by an average of three months when compared to the current treatment regime. It also had a greater chance of reducing pain and improving quality of life in patients with symptoms from their disease, although there was some increase in toxicity.



"Overall, treatment with docetaxel resulted in many patients feeling better and living longer," says Dr. Tannock. "It is for this reason that we're recommending docetaxel every three weeks, with daily prednisone, as the new standard of treatment for patients with prostate cancer resistant to hormone therapy."

In this case, the international, industry-supported partnership generated new hope for men with prostate cancer.

N Engl J Med. 2004 Oct 7; 351(15): 1502-12.

Controlling the level of calcium in the cell is crucial for many physiological functions including the regulation of our heart beat and brain function.

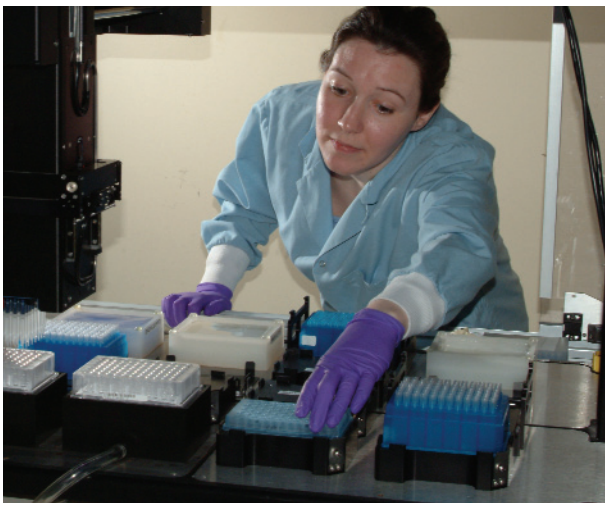
Finding Will Lead to Targeted Therapies for Heart Disease and Brain Disorders

A groundbreaking discovery by Dr. Mitsu Ikura and PhD candidate Ivan Bosanac will lead to the development of new therapies for treating and preventing heart and brain disorders.

In collaboration with Dr. Katsuhiko Mikoshiba of the University of Tokyo, Dr. Ikura used special molecular imaging techniques to visualize the IP_3 receptor (IP_3R) molecule in three dimensions. Along with its cousin receptor the ryanodine receptor (RyR), the IP_3R is responsible for regulating the levels of calcium in our cells.

Says Dr. Ikura, "This is a big step towards understanding how the calcium level in the cell is controlled so precisely. The structure of this part of the IP_3R is the same in the RyR receptor. Since the IP_3R functions in the brain and the RyR functions in the heart, this information could be used to develop drugs for heart problems and brain disorders in the future."

Mol Cell. 2005 Jan 21; 17(2): 193-203.



Inflammation is the way in which the body defends itself against injury and infection, but if it is not switched off when the job is done, it can cause more harm than good.

Inflammatory Switch May Turn Off Disease

In a paper called a landmark in the inflammation field, UHN researchers have identified a switch important in controlling the body's inflammatory response. The switch—actually a gene called Timp3—was identified by Drs. Rama Khokha and Wen-Chen Yeh and graduate student Dr. Fazilat Mohammed.

As reported in *Nature Genetics*, the researchers found that mice missing the Timp3 gene were unable to turn off their inflammatory response following tissue injury.

"Our research has identified the gene we need to target to gain control of an excessive inflammatory response," says Dr. Khokha. "Also, it points to Timp3 as a potential treatment for inflammatory conditions. At least one arthritis drug has been shown to increase Timp3 in the body, and this finding has important implications for treating a multitude of diseases including rheumatoid arthritis, diabetes, hepatitis, and cancer, to name just a few."

Nat Genet. 2004 Sep; 36(9): 969-77.

A woman with an altered BRCA1 or BRCA2 gene is estimated to have a 3-7 times greater risk of developing breast cancer over her lifetime.

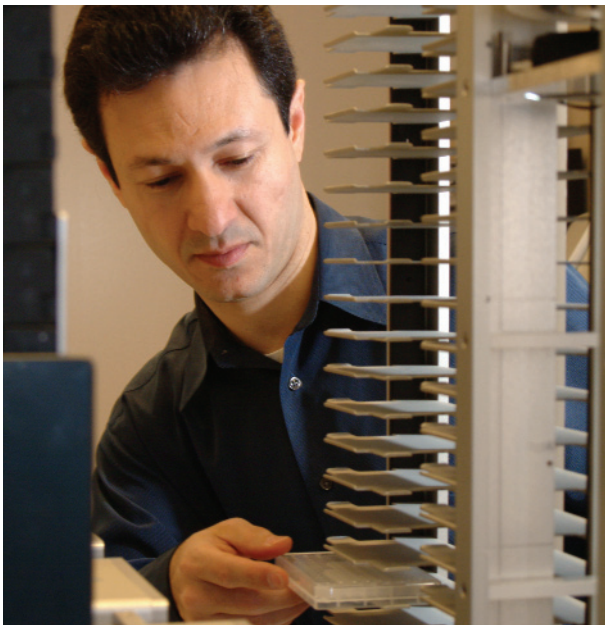
Group Therapy Eases Breast Cancer Fears

Group therapy improves anxiety, depression, and psychosocial functioning in women who are at higher risk for breast and ovarian cancer because they carry mutations in BRCA1/BRCA2, according to a recent study conducted by Dr. Mary Jane Esplen.

To determine if psychosocial supports would help women deal with their diagnosis, 70 women were recruited to take part in 12 sessions of group therapy. All 67 women who completed the sessions had fewer cancer worries and less depression and anxiety.

Says Dr. Esplen, "Our findings reveal that a support group is extremely beneficial for women who carry mutations in BRCA1/BRCA2. By giving them an opportunity to discuss their concerns and also share thoughts around their decisions regarding prophylactic surgery, it decreased their stress significantly."

Cancer. 2004 Nov 15; 101(10): 2327-40.



DJ-1 has been intensely studied due to its role in familial Parkinson's disease. This is the first study to determine its mechanism of action in cancer.

DJ-1 Molecule Newly Implicated in Cancer

A team of researchers including Drs. Tak Mak, Fei-Fei Liu, Armen Manoukian, Ming Tsao and student Raymond Kim have discovered that a molecule called DJ-1 plays a role in the development of cancer.

Using a genetic screening method in fruit flies, they discovered that DJ-1 prevents the tumour suppressor molecule PTEN from doing its job. With PTEN out of commission, cell growth can rage out of control and cancer can develop. Human breast and lung cancer cells also have high levels of the molecule, and lung cancer patients with high levels of DJ-1 are more likely to suffer a relapse.

Says Dr. Mak, "Our results suggest that DJ-1 does play a role in the development of cancer, and in the future it may represent a valuable new target for cancer therapy."

Cancer Cell. 2005 Mar; 7(3): 263-273.

Toronto General Research Institute

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

The current treatment for Fabry's Disease is enzyme replacement therapy—to administer doses of manufactured alpha-Gal-A enzyme.

Fabry's Disease Treatment Successfully Tested

There is good news for sufferers of Fabry's disease, a hereditary disorder caused by a faulty gene. People with the disease are missing the activity of the alpha-Gal-A enzyme and, as a result, fats accumulate in their blood vessels damaging the kidneys, heart, and other organs.

Fortunately, Dr. Jeffrey Medin and colleagues have discovered a way to stop the disease. Using gene therapy tools, they gave the alpha-Gal-A enzyme to 1-2 day-old Fabry mice. The treatment proved successful: alpha-Gal-A levels increased, and the levels of accumulated fats dropped. Moreover, the effects were long lasting.

"The problem with current treatments is that they are given to patients after the damage is done and they aren't long-term solutions," says Dr. Medin. "We needed to find a way to treat Fabry's patients sooner, to avert the irreversible damage before it happens and also provide sustained therapy."

Further testing is required before the therapy can be used in humans.

Proc. Natl. Acad. Sci. USA. 2004 Nov 30; 101(48): 16909-14.

In people with heart problems, anxiety can be both dangerous—putting them at risk for future heart attacks—and beneficial—causing them to adopt healthier behaviours.

Anxiety Under-Treated in Heart Patients

A recent study by Drs. Donna Stewart, Sherry Grace, Susan Abbey and Jane Irvine reveals that anxiety symptoms may be ignored in heart patients—something which may negatively impact their recovery and health.

Using surveys, the research team assessed anxiety in 913 heart patients over one year of recovery. More than one third of patients suffered from anxiety at the time of their coronary event, and approximately 50% of them continued to report it at six months and one year post-event.

"Surprisingly, we found that only 38% of patients with anxiety were asked about anxiety symptoms by their healthcare providers during the course of the year," says Dr. Grace. "This tells us that anxiety symptoms are likely under-recognized and under-treated in heart patients, and that anxiety-reducing interventions are needed to improve quality of life."

Psychother Psychosom. 2004 Nov-Dec; 73(6): 344-52.

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New Diabetes Treatments

Type 2 diabetes is a disease characterized by high levels of blood glucose and low levels of insulin and/or defective insulin action. TGH/TGRI's Dr. Daniel Drucker is one of a handful of researchers in the world studying the protein GLP-1 (glucagon-like peptide-1), which plays a key role in controlling blood glucose levels.

A recent study by Dr. Drucker's group sheds further light on GLP-1's role. His team examined the effects of GLP-1's glucose-regulating actions in mice lacking a factor called Pdx-1—a regulator of insulin production in the pancreas. They observed that the presence of Pdx-1 was essential for GLP-1's ability to control blood glucose levels.

Says Dr. Drucker, "Our study predicts that subtypes of diabetes associated with genetic or acquired defects in Pdx-1 action—in maturity-onset diabetes of the young or other forms of type 2 diabetes—may result in sub-optimal responses to treatment with drugs mimicking GLP-1's actions."

Based on the work of Dr. Drucker and others, **pharmaceutical companies** are developing drugs mimicking the action of GLP-1. These drugs are currently being evaluated for their efficacy in treating diabetes. The first GLP-1-related drug was approved for the treatment of type 2 diabetes in the United States in April 2005.

Diabetes. 2005 February; 54: 482-491.

The majority of Wiskott-Aldrich Syndrome patients are male, as it is inherited as an X-linked genetic disorder.

One Step Further to Finding the Cause of a Rare Genetic Disorder

Wiskott-Aldrich Syndrome is a rare, inherited disorder that is characterized by repeated infections due to malfunctions in the immune system. Scientists have identified defects in the WASP (Wiskott-Aldrich Syndrome protein family) gene to be a key factor in the cause of this disorder.

TGRI's Dr. Katherine Siminovitch is a world expert in this disease and is particularly interested in its genetic basis. As part of her studies, she and her team recently examined the role of WASP by studying the interactions of WAVE-2—a WASP-related molecule—with the molecule Abi-1 in immune cells.

Her team showed that Abi-1 association to WAVE-2 is essential for many immune cell functions. "Any mutations in Abi-1 would therefore impede these important functions—including those required to fight infection," says Dr. Siminovitch. "Knowing this, we are one step closer to understanding how the immune system works and how it might be manipulated to prevent disease."

Proc. Natl. Acad. Sci. USA. 2005 Jan; 102(4): 1098-1103.

Coxsackieviruses are part of the enterovirus family, which also includes polio and hepatitis A viruses.

Molecule Critical for Fighting Viral-Induced Heart Disease

Myocarditis is an inflammatory disease of the heart muscle that is often caused by infection by coxsackievirus. In serious cases, it can lead to heart failure. Previous studies by others indicated that the immune molecule called IFN-beta plays an important role in fighting the virus, and Drs. Eleanor Fish and Peter Liu further assessed its role by comparing the severity of infection in mice missing the IFN-beta molecule, to mice with the IFN-beta molecule intact.

"Our results clearly show that the viral infection was more aggressive in mice missing IFN-beta," says Dr. Fish. "The data confirm a critical role for IFN-beta in mediating protection from coxsackievirus infection and subsequent heart problems."

Circulation. 2004 Dec; 110(23): 3540-3.

Hepatitis C can lead to liver damage, cirrhosis and cancer. The current therapy has negative side effects and isn't effective in many patients.

Genes Predicting Hep C Treatment Response Identified

New research by UHN's Drs. Ian McGilvray and Jenny Heathcote has put health care providers one step closer to providing personalized care for the 230,000 Canadians with hepatitis C.

The research team used advanced genomics techniques and microarray technology to identify a subset of 18 genes that can predict a patient's response to therapy. The study followed 31 patients with the disease who were treated at TWH.

Says Dr. McGilvray, "Our results show that a small number of genes can predict how a patient will respond to therapy, and it suggests that these genes may be important for helping the patient eliminate the virus. In the future we might be able to manipulate the products of these genes to improve how patients respond to treatment."

Gastroenterology. 2005 May; 128(5): 1437-44.

Excess weight, lack of exercise, and genetic factors can all contribute to developing insulin resistance (IR). The NIH calls IR a "stepping-stone" to type 2 diabetes.

Hepatic Lipase Enzyme Pinpointed in Abnormal Fat Metabolism in Pre-Diabetic States

Insulin resistance syndrome—in which many cells in the body, in particular muscle, fat, and liver cells, do not respond to insulin properly—is linked with an increased risk for developing type 2 diabetes and coronary artery disease.

Recent studies by Dr. Gary Lewis revealed that high levels of an enzyme called hepatic lipase, which is made in the liver and regulates cholesterol levels in the blood, are associated with the abnormal fat metabolism of pre-diabetic states and type 2 diabetes.

"Increases in this enzyme in pre-diabetic and diabetic states may play a key role in developing abnormal fat metabolism and coronary artery disease associated with these conditions, particularly in the formation of small, dense LDL (so-called "bad" cholesterol) and the reduction in HDL ("good" cholesterol)," says Dr. Lewis.

"This is the first time that we've been able to show that this enzyme's gene expression level in the liver and blood level increases in an animal model that is made insulin-resistant by feeding high fructose (a sugar). We've also shown that the levels are corrected by treatment of the insulin resistance. We look forward to studying these observations in patients."

Diabetes. 2004 November; 53(11): 2893-2900.

Cardiovascular disease remains the number one killer in Canada. In 2002, 74,626 Canadians died as a result of cardiovascular diseases.

Gene Therapy Boosts Cell Transplantation Success in Injured Hearts

A heart attack leaves injured tissue that prevents proper heart function and may lead to heart failure. Transplanting healthy cells into damaged heart tissue has shown promising results in the lab—however, the low survival rate of these cells remains a concern in developing this treatment for patients.

Pioneering research by Dr. Ren-Ke Li and his group at TGRI/TGH showed that using gene therapy in transplanted cells could be the answer to this problem. This group compared transplanting normal cells with transplanting cells that had the IGF-1—a molecule that increases cell growth and survival—gene inserted in them. They obtained a significant increase in cell survival after transplantation and found that IGF-1 gene therapy led to improved blood vessel formation in the injured tissue.

"We're very pleased with these results, and we are continuing to study whether implanting these modified cells can actually improve heart function in the long term," says Dr. Li.

Am. J. Physiol. Heart Circ. Physiol. 2004; 287(6): 2840-49.

Toronto Western Research Institute

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

"Secondary" brain injuries occur minutes, hours or days after the initial insult. Much research is focused on reducing damage stemming from secondary injuries.

Research Describes Mechanism of Secondary Brain Injury

Mild brain injuries rarely cause neuronal death, but they do make the brain's neurons more vulnerable to secondary injuries. To determine the cause of this increased sensitivity, Dr. Michael Tymianski simulated mild brain injury in cultured neurons by mechanically stretching them. This caused the neuronal cells to produce very high levels of a toxic chemical called ROS, making them abnormally sensitive to glutamate, a neurochemical involved in secondary injuries and stroke. Blocking the actions of ROS and glutamate prevented neuronal cell death.

This study describes the mechanism by which secondary brain injury occurs, and highlights the importance of this type of injury to the ultimate outcome of neurons following mild brain injury.

J Neurosci. 2004 Sep 15; 24(37): 8106-23.

Although early studies of dyslexia focused on the ability to recognize letters, current studies focus on the ability to work with the individual sounds that make up words.

Risk Factor for Dyslexia Identified

Dyslexia is an inherited language-based learning disability and new research by Dr. Cathy Barr provides evidence that the region containing the gene called EKN1 may be a risk factor for the disorder.

Following up on studies by others, Dr. Barr examined the relationship of the EKN1 gene to dyslexia in children aged six to sixteen, who were recruited from 148 families with known reading difficulties. Her genetic analysis revealed that the chromosomal region containing this gene contributes to reading ability and reading-related processes.

Says Dr. Barr, "Our findings support the idea that the region of the EKN1 gene may be involved in dyslexia, but further studies are necessary to determine the precise relationship of the gene to the disorder."

Mol Psychiatry. 2004 Dec; 9(12): 1111-21.

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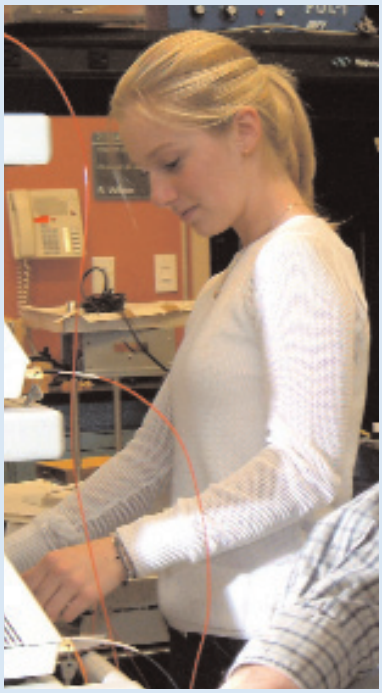
Insight into the Cause of Parkinson's Disease

Malfunctions in the parkin gene are a major cause of Parkinson disease, and new research by TWRI/TWH's Dr. Andres Lozano, student Suneil Kalia, and post-doctoral fellow Sang Lee, along with colleagues at the **University of Ottawa, McGill University** and the **University of Toronto**, reveals another way in which the parkin gene can be compromised. The finding may lead to new drugs for treating the disease.

If not removed from the cell, damaged proteins clump together forming aggregates—a lethal consequence found in many neurodegenerative diseases. Part of the cell's "garbage disposal system," parkin tags these damaged proteins for destruction.



The research team found that a protein called BAG5 prevents parkin from doing its job. BAG5 also inhibited parkin's helper-protein, Hsp70.

"High levels of BAG5 inhibited the actions of parkin and Hsp70 resulting in enhanced neuronal cell death," says Dr. Lozano. "Our results propose a mechanism for the cause of neurodegeneration in Parkinson's disease and other diseases, and points to BAG5 as a potential therapeutic target for Parkinson's patients."

Neuron. 2004 Dec 16; 44(6): 931-45.

Functional MRI allows researchers to study brain activation-induced changes in blood flow, oxygenation, and volume.

Cognitive Therapy May Diminish Pain

Using functional MRI techniques, Dr. Karen Davis and PhD student David Seminowicz have found evidence to support the idea that, in some people, a busy brain may divert their attention away from a painful experience.

The researchers applied a mildly painful stimulus to 16 healthy volunteers who were busy concentrating on a task, and measured how their brains perceived the stimulus. They found that while the stimulus made some people lose their focus, it sharpened the concentration of others.

In this latter group of people, it also reduced their pain-related brain activity.

"The fact that there are two different types of responders suggests that different people deal with pain in different ways," says Dr. Davis. "Our results show a biological basis for the finding that cognitive therapies may be useful for treating pain in some people."

Pain. 2004 Nov; 112 (1-2): 48-58.

Up to 20% of people with depression fail to respond to medications or psychotherapy. For this group, there is a clear need for new treatment options.

Parkinson's Disease Treatment Also Alleviates Depression

In collaboration with a team of Toronto scientists, Drs. Andres Lozano and Sidney Kennedy and Dr. Helen Mayberg (Emory University School of Medicine) recently showed that deep brain stimulation (DBS)—a procedure usually reserved for treating Parkinson's disease and epilepsy—alleviates severe depression.

Based on the team's previous findings that an area of the brain called Cg25 is important for mood regulation, the research team suspected that DBS might be useful to "retune" this area of the brain. The treatment was successful: changes observed in four of the six patients treated resembled changes that are seen when patients respond successfully to the standard treatment.

Says Dr. Lozano, "Our study shows that DBS can lead to striking and sustained remission of depression in some patients. It further suggests that DBS may become a standard therapy for treating severely depressed people who are resistant to drug therapy."

Neuron. 2005 Mar 3; 45(5): 651-60.

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 been collecting citation analysis information to determine its usefulness as a method of measuring scientific impact over time.

Citation analysis uses 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
(2002/04 inclusive)

	# of Papers (2002/04)	Citations to date	Papers in Top Journals †	Top Papers §
OCI	1203	10703	159 (13%)	317 (26%)
TGRI	1553	12682	150 (10%)	416 (27%)
TWRI	1024	6845	51 (5%)	208 (20%)
UHN	3497*	28515	340 (10%)	881 (25%)

* 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 (as defined by the Institute for Scientific Information)

§ "Top Papers" are papers in the top 10% of papers (as defined by the Institute for Scientific Information)

UHN Research Support Services

Research Support Services provides a supportive collaborative infrastructure for research across UHN's institutes. Approximately 260 support staff provide a range of services for 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 Research Unit (PMH) and Clinical Studies Resource Centres (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 the highest scientific and ethical standards to protect patients,

New Service Strategy

UHN Research Support Services is in year three of a five-year project to improve client service and streamline processes.

The new Service Strategy involves significant re-tooling of support processes. In 2004/05, a number of new initiatives were implemented to meet new client service objectives. These included

- New user committees to enhance user input to key service departments
- New online administrative tools for faster response and feedback

RSS User Committees

Grant & Contract Services (GCS)

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Malcolm Moore
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Pat Clark, GCS
Angela Fong, GCS
Ken Woo, Human Resources

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Shelley Malton
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Brenda Gallie
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Lucy Teves
Neil Winegarden
Christopher Adams, Manager, RFS
Marcellus Arokium, RFS
Dianne Billows, RFS
David Fernandes, RFS
Frances Guglielmo, SHSS
Bala Kumbakonam, RFS
Ashley Taylor, Accounts Payable

Research Business Development Office (RBDO)

Brian Barber
Tony Easty
Micheline Gravelle

investigators and the institution

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 Training Development and Information Services: Designs and implements research orientation and training programs and collaborates with other departments to develop applications, procedures and policies

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

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Kelly Holman
Bob McArthur, Director, RBDO
Jodi Braunton, Manager, Research Communications
Thomas Parsons, Senior BDO

Research Information Systems (RIS)

Gerald Devins
Linda Mills
Janis Miyasaki
Mary Jane Salpeter
Neil Winegarden
Leigh Revers
Philippe Monnier
Robert Rottapel
Bill Wassenaar

Tom Goldthorpe, Director, RIS
David Huh, Operations Manager, RIS
Joe DeLeon, Manager, Project Management, RIS

New Online Tools from RSS in 2004/05

Animal Protocol Management & Ordering
The first fully online tool for submitting and tracking new animal use protocols and ordering animal stocks for studies

Staff Directory
Fully searchable database of contact information on all Research staff and trainees

Process Improvement Log
Online feedback form allowing client input on services and processes. Also features a survey tool to elicit feedback on specific services

Financial Information System from Research Financial Services
Online access to researcher accounts information relating to grants funding and operating expenses

"My Account" Application from Research Information Systems
One-stop tool to manage and edit all RIS computer account preferences in one location

FUNDING

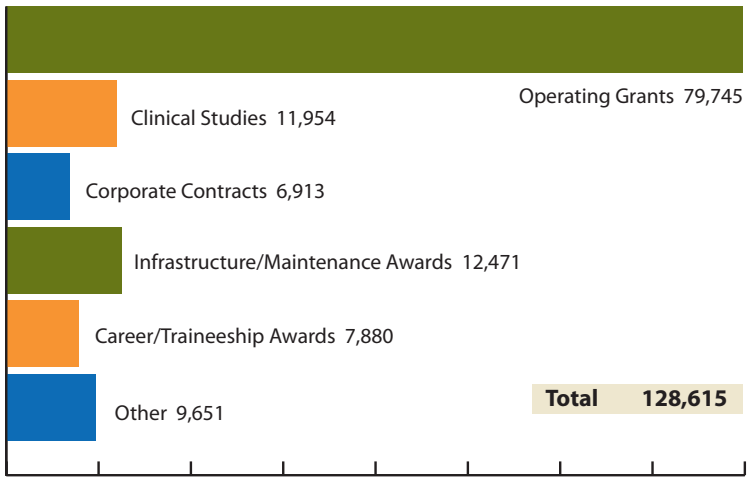
Research Funding Revenues

All figures represent fiscal year 2004/05 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. 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.

Total External Funding Awarded by Purpose of Funding

(thousands of dollars)



UHN Research Core Funding

(thousands of dollars)

Princess Margaret Hospital Foundation	13,200
Toronto General & Western Hospital Foundation	2,500
Arthritis & Autoimmunity Research Centre Foundation	1,250
Ministry of Health & Long Term Care	2,816
Recoveries	5,839
Investment income	3,256
Other	8,883
TOTAL	**37,744**

Major Sources of External Funding

(thousands of dollars)

Canadian Institutes of Health Research	21,706
Ontario R&D Challenge Fund	16,003
National Cancer Institute of Canada	10,627
National Institutes of Health (US)	7,481
Canada Foundation for Innovation	6,857
Heart and Stroke Foundations	4,168
Ontario Cancer Research Network	4,049
Ontario Innovation Trust	3,370

External Agencies Funding UHN Research

Abbott Laboratories • Achillion Pharmaceutical Inc. • Actelion Pharmaceuticals Ltd • Agouron Pharma Inc. • Alcon Research Ltd • Allergan Sales Inc. • Alliance Pharmaceutical Corp. • Allos Therapeutics • Alteon Inc. • Alzheimer Society of Canada • Alzheimer's Disease and Related Disorders Association • AmCyte • American Association for the Study of Liver Diseases • 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 Foundation for Urologic Disease • American Society of Clinical Oncology • American Society of Echocardiography • American Society of Hematology • American Society of Interventional & Therapeutic Neurology • American Society of Regional Anesthesia • Amersham • Amgen • Amyotrophic Lateral Sclerosis Society of Canada • Anemia Institute for Research and Education • AO-ASIF Research Foundation • Argos Therapeutics Inc • Arius Research • Arthritis Center of Excellence • Arthritis Community Research & Evaluation Unit • Arthritis Health Professions Association of Ontario • Arthritis Society • ArthroLab Inc. • Associated Medical Services Inc. • Astra Pharma • AstraZeneca • Aventis Pasteur • Axcan Pharma • Banting and Best Diabetes Centre • Bausch and Lomb • Baxter Healthcare Corporation • Bayer • Beckman Coulter • Berlex Laboratories • BioAxone • 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 • Burroughs Wellcome • C.R. 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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.

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(to be appointed)
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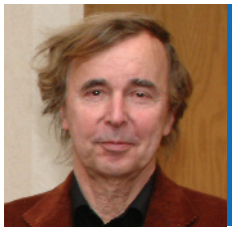

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and Tumor Biology Center,
Karolinska Institute, Sweden

Mark Musen, MD, PhD
Head, Stanford Medical
Informatics, Stanford
University

(Photo not available)

The fourth annual IRAB meeting is scheduled for October 2005.

Achieving with Partnerships
University Health Network Research Report 2005
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UHN Research Report

2005

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