University Health Network

Toronto General Hospital | Toronto Western Hospital | Princess Margaret Hospital

Research Report 2009

Achieving Global Impact

UHN Advanced Therapeutics Research Platform

Snapshot of UHN Research

Affiliate Scientists	71
Scientists	44
Senior Scientists	152
CSRC/CRU Members	269
Total Researchers	**536**
Fellows	437
Graduate Students	406
Total Trainees	**843**
Technical and Support Staff	**1,330**
Research Space	**735,000 sq ft**
Publications	**1,665**
Total Funding	**$261,113,000**

UHN International Research Advisory Board

Philip Branton, Chair: Scientific Director, Institute of Cancer Research, CIHR; Gilman Cheney Professor of Biochemistry, Faculty of Medicine, McGill University

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Hans Wigzell: Professor of Microbiology, Tumor Biology Center, Karolinska Institute

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University Health Network Research Report 2009
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Photographs courtesy of various sources, including Yuan Lew and UHN

Some figures may be rounded and/or may include data not represented in institute data. Publications jointly authored by investigators at multiple UHN institutes are counted only once in UHN total. Institute space figures are approximate due to ongoing construction.

Welcome Messages

Robert S. Bell, MDCM, MSc, FACS, FRCSC
President & CEO,
University Health Network

UNIVERSITY HEALTH NETWORK HAS LONG been recognized for its outstanding research programs. Recently, a significant part of this recognition translated into a $119.9M grant awarded to us from the Canada Foundation for Innovation. This award—the largest single research grant in UHN history—will provide crucial cutting-edge equipment and facilities, which will enable us to continue our internationally renowned research. Combined with the strengths of our researchers, this funding will help transform health care for our patients, our community and the world. I invite you to learn more about our vision of the Advanced Therapeutics Research Platform and how we are making it a reality.

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

OUR AMBITION AS A RESEARCH HOSPITAL IS to build powerful platforms where patients, health professionals and researchers can interact to solve the medical mysteries of our time. To accomplish this, we need platforms equipped with the latest advances in medical technology, which allow UHN investigators to yield new insights into the cause and cure of disease. By organizing around these platforms, we drive innovation within the hospital and with public and private sector partners. In 2009, we received a strong endorsement of our ambition when the UHN Advanced Therapeutics Research Platform (ATRP) was funded by the Canada Foundation for Innovation—$119.9M in support from the Canadian government, matched by UHN's own Foundations and donors.

Many factors contribute to our ability to build and use our platforms. **First: Research excellence.** Our strengths are demonstrated in the amazing discoveries that take place at UHN—discoveries that span the spectrum of health research, from basic science to clinical application. Along with our local, national and international colleagues, including those at the University of Toronto and our other Toronto Academic Health Science Network (TAHSN) hospital partners, we are advancing novel clinical approaches for some of the most complex diseases based on new information emerging from our labs and clinics.

Second: Strong funding partners. Our internationally acclaimed researchers win support from many different funding agencies and groups, including those from the Government of Canada, the Government of Ontario and our three UHN Foundations. Our Foundations channel the strong desire of generous donors who want to make a difference in health in Ontario and beyond.

Third: Integration across institutes and disciplines. Over 70 investigators across our three institutes—Ontario Cancer Institute (OCI), Toronto General Research Institute (TGRI) and Toronto Western Research Institute (TWRI)—lent their vision and insights towards the formation of the ATRP, creating UHN-wide programs that will enable our research teams to lead the global scientific community in biomedical discovery.

Taken together, these elements strengthen our position as a leader in innovative health research—now and in the future. With this funding, UHN will build the Krembil Discovery Centre—a 400,000 square foot facility that will house research programs in arthritis, rheumatism, autoimmune disease, stroke, neurodegenerative disorders and visual sciences. In addition, new cutting-edge equipment and further enhanced research space will be established across UHN. This ability to provide first-rate facilities and equipment will enable us to attract and retain the top researchers, clinicians and trainees, ensuring that our ATRP will result in discoveries that will lead to improvements in human health.

UHN Advanced Therapeutics Research Platform

Achieving Innovation Through Integration

UHN IS PROUD TO BE A RESEARCH HOSPITAL—NOT JUST A HOSPITAL WHERE INDIVIDUALS do research. Our mission of impacting health care through innovation drives strategic decisions across the institution. The Advanced Therapeutics Research Platform (ATRP) was designed to enable this by accelerating scientific breakthroughs through fully integrated research themes. This Platform, in combination with our large and diverse patient base, will bring unparalleled opportunities to understand disease, develop interventions and improve health on a global level.

In August 2008, the Canada Foundation for Innovation (CFI) announced a $119.9M Research Hospital Fund Large-Scale Institutional Endeavours award in support of UHN's ATRP. This award—the largest single research award in UHN's history—includes $92M in new funding towards construction projects across UHN's institutes.

This initiative—led by VP of Research Dr. Christopher Paige and theme leaders Drs. Benjamin Neel, David Jaffray, Eleanor Fish, Claire Bombardier, Gordon Keller, Emil Pai and Pamela Ohashi—also sourced nearly $28M in operating funding to implement this Platform.

Since the award announcement, UHN Research has been working closely with CFI and local industry partners to begin the early stages of project implementation. Key construction initiatives on the UHN campus include:

- **Building the new Krembil Discovery Centre at the Toronto Western Hospital.** The new nine-floor building will be home to dry and wet laboratories. Construction is set to begin in December 2009.
- **Renovation of laboratory space in the Toronto Medical Discovery Tower (TMDT)**—a 400,000 square foot, 15 floor, state-of-the-art research facility. Since investigators began to move their laboratories into TMDT in 2005, research programs have significantly grown. Current offices and laboratories will be expanded to accommodate new staff.
- **Significant space renovations within the Peter Munk Cardiac Centre at the Toronto General Hospital.** These improvements include space to house specialized imaging equipment and support space required for clinical research. Improvements will also be made to provide open research space for specialized laboratories in the Max Bell Research Centre.
- **Several floors at the Ontario Cancer Institute at the Princess Margaret Hospital will also be developed with open research laboratories similar to those found currently in TMDT.** Creating these interactive spaces will facilitate research collaborations and foster innovative ideas.

In addition to new construction initiatives, this award will establish new state-of-the-art equipment across seven research themes: Signal Transduction & Disease, Image-Guided Discovery in Health & Disease, Biomarkers, Clinical Studies, Stem Cells & Tissue Engineering, Immunity in Health & Disease and Drug Discovery & Development. Four of the seven research themes are classified as "Foundational"—the building blocks of a Research Hospital—while the remaining three themes are described as "Specialty"—areas that are poised to yield significant medical advances. Together, these seven themes form an integrated framework that yields the UHN Advanced Therapeutics Research Platform.

Foundational Themes

Signal Transduction & Disease: A theme that will focus on the identification of molecular/biochemical pathways that explain the mechanisms underlying disease.

Image-Guided Discovery in Health & Disease: Cutting-edge imaging systems interconnected by a storage network to advance multidisciplinary research programs in neural, cardiac and cancer imaging.

Biomarkers: A comprehensive and centralized resource for basic/clinical scientists who strive to identify biomarkers in cardiology, hepatology, rheumatology, oncology, infectious diseases, transplant medicine and the neurological sciences.

Clinical Studies: Infrastructure linking clinical and research data that will foster the development of research tools, increasing information content and spurring the pace of clinical studies. These resources will leverage the robust clinical programs at UHN and Toronto's diverse patient population.

Specialty Themes

Stem Cells & Tissue Engineering: A facility that will provide essential cells and tissues to researchers at UHN and across Ontario for studies in neuroscience, cardiology, diabetes and transplantation.

Immunity in Health & Disease: An expansion of current facilities for research with highly infectious pathogens, clinical grade expansion of human cells for innovative therapy, cell analysis capacity and comprehensive clinical databases. These resources will enable key advances in the fields of cancer, autoimmune rheumatic diseases and infectious diseases.

Drug Discovery & Development: A sub-platform for identifying potential molecules for drug development from early stage to clinically relevant compounds. This will support strong programs in neuroscience, cancer, infectious disease, cardiovascular disease, autoimmunity and many other areas.

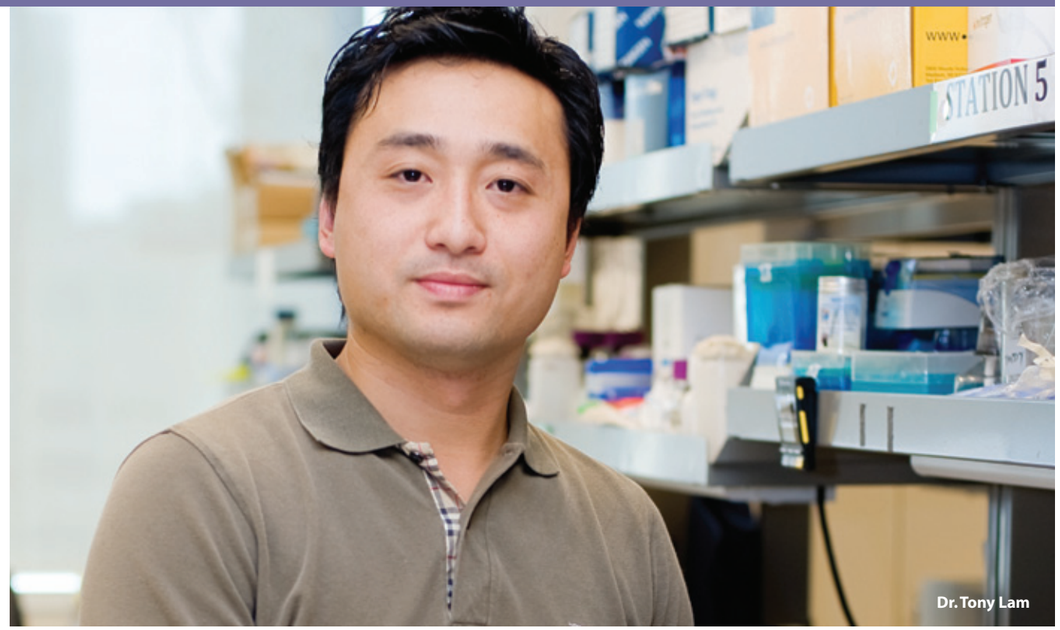
These seven themes offer the greatest potential for medical advances. Each theme has an organizational framework designed to maximize impact: Discover, Develop, Deliver and Evaluate, as detailed below.

UHN Advanced Therapeutics Research Platform – At a Glance

		DISCOVER	DEVELOP	DELIVER	EVALUATE
FOUNDATIONAL THEMES	**Signal Transduction & Disease**	• Biochemical pathways, their switches and influence of intervention	• Pathway-based disease models • New biomarkers & drug targets	• Indirect pathways • Assess outcomes	• Define & control critical pathways
	Image-Guided Discovery in Health & Disease	• New imaging modalities	• Integrate imaging with diagnostic (Dx) and treatment (Rx) protocols	• Image-guided treatment trials • Image-guided diagnosis • Real-time disease progression	• Better Dx, Rx • Improved understanding
	Biomarkers	• New markers & techniques	• Prognostic & predictive markers • Integrate clinical & molecular analysis	• High content/biomarker-designed trials • Biomarker-guided intervention • Biomarker-guided assessment	• Diagnostic, prognostic, therapeutic value
	Clinical Studies	• New trial methods	• Informatics tools & databases	• High content/biomarker-designed trials • Image-guided therapy/diagnostics	• Outcomes, quality of life, cost
SPECIALTY THEMES	**Stem Cells & Tissue Engineering**	• New biomaterials, tissue repair • Cell growth & development	• Good Manufacturing Practice (GMP) stem cell & biomaterials production • Develop useful animal models	• Functional analysis in pre-clinical models • Clinical trials	• Functional or clinical improvement
	Immunity in Health & Disease	• Gene/protein/cell controls of immune response (IR) • Host-pathogen reactions	• Modulate innate & adaptive IR • Establish gene/disease linkages	• Cell-based immunotherapy trials • Anti-malaria field trials	• Define role of IR, enhance treatment
	Drug Discovery & Development	• Target identification • Rational drug design • High-throughput screening	• New applications of known drugs • Process chemistry, toxicology, lead development	• Pre-clinical studies • Partnerships with industry	• Efficacy

Foundational Theme:

Signal Transduction & Disease



Dr. Tony Lam

DIABETES: SWEET AND SMART COMMUNICATION

EXCITING NEW FINDINGS out of UHN have revealed a three-organ sensory network relaying vital information responsible for the regulation of glucose levels.

"It's a completely new circuit, which begins with the intestines serving as a remote control device that signals the brain to regulate glucose production," says Dr. Tony Lam, TGRI Scientist and study lead of the paper, which appeared in *Nature*.

Dr. Lam and colleagues used a mouse model to show for the first time that an axis of communication exists between the gut, brain and liver, whereby the accumulation of fats in the upper intestine triggers a wave of information to pass to the brain and then off to the liver. This signals the liver to decrease glucose production and maintain appropriate levels of blood glucose.

Notes Dr. Lam, "It's far easier to design drugs to 'hit' the gut than either the liver or the brain, with the latter being especially difficult to target because of the blood-brain barrier. This new finding is very significant for potential diabetes treatments."

Nature. 2008 Apr; 452(7190): 1012-6. This work was supported by the Canadian Institutes of Health Research.

IMMUNE SYSTEM: TAKING APART THE 'ENGINE'


Dr. Rod Bremner

A NEW LEVEL OF CONTROL for interferon-gamma (IFN-gamma)—an important 'engine' of the immune system involved in a variety of human diseases including cancer, multiple sclerosis, heart disease and arthritis—has been recently uncovered by a TWRI team.

"It's a bit like discovering that your car needs more than an ignition switch to start," says Dr. Rod Bremner, study author. Using a variety of molecular and biochemical strategies, Dr. Bremner and his team have been able to demonstrate that the BRG1 protein, critical for IFN-gamma-mediated gene expression, works with five remote switches to activate the CIITA gene, which is responsible for mobilizing a very important class of molecules involved in ramping up the immune response.

Dr. Bremner notes, "In cancer, the goal is to 'fix the engine' by reactivating a broken IFN-gamma pathway. But, in arthritis, the goal is to turn the engine down to reduce an overactive immune system. Ours is a critical finding towards the development of novel treatments that will have significant impacts on diseases requiring either level of control."

Nat Immunol 2008 Jul; 9(7): 785-93. This work was supported by the National Cancer Institute of Canada, the Canadian Cancer Society, the Krembil Foundation Seed Fund, the Vision Science Research Program, the Frank Fletcher Memorial Fund, the Dr. R. Dittakavi & Dr. P. Rao Graduate Award and the Krembil Foundation.

CANCER: NEW TARGET IDENTIFIED


Dr. Stuart Berger

c-Myc IS ONE OF THE MOST commonly implicated genes in human cancer. Yet unravelling how c-Myc promotes cancer has been challenging as it mediates its effects by turning on or off literally thousands of other genes. Dr. Stuart Berger and colleagues at TGRI have uncovered an exciting new twist in the c-Myc story. They discovered that c-Myc activates an enzyme called calpain. Calpain activation appears to be an important part of how c-Myc promotes cancer as inhibition of calpain kills c-Myc-transformed cancer cells but has no effect on normal cells. c-Myc was found to regulate calpain by suppressing a natural inhibitor of the enzyme. When this natural inhibitor, called calpastatin, was suppressed in normal cells, the cells took on many of the properties of c-Myc-transformed cells, indicating that calpastatin may be a natural tumour suppressor.

"These findings provide important new insight into how c-Myc promotes cancer formation," comments Dr. Berger. "Just as exciting is the possibility that inhibiting calpain may be a potent new strategy for targeting c-Myc-transformed cells."

With support from the Canadian Institutes of Health Research, the Leukemia and Lymphoma Society of Canada and the Lymphoma Foundation, Dr. Berger and his group are currently investigating the role of calpain and calpastatin in leukemias and lymphomas. "We are finding elevated levels of calpain activity in many leukemia samples," says Dr. Berger. "Although we are only at the start of this project, we are optimistic that calpain will turn out to be an important part of the cancer puzzle."

J Biol Chem. 2008 Aug; 283(31): 21371-81. This work was supported by the National Cancer Institute of Canada, the Canadian Institutes of Health Research, the Leukemia and Lymphoma Society of Canada and the Lymphoma Foundation.

BLOOD CANCER: EXCITING NEW MODEL


Dr. Benjamin Neel

JUVENILE MYELOMONOCYTIC leukemia (JMML)—a cancer of the white blood cells of the immune system—is a rare and lethal disorder of early childhood that often (in 35% of cases) involves the mutation of the *PTPN11* gene. To gain deeper understanding into how JMML develops, Dr. Benjamin Neel and his team at OCI created a new model to study the disease—using mice that had a specific mutated form of the *PTPN11* gene associated with leukemia.

The team showed that mice with the mutated *PTPN11* gene developed a fatal condition like JMML, and featured abnormally high levels of white blood cells, low levels of red blood cells (anemia) and enlargement of the liver and spleen. Other key observations in this mutant mouse model revealed that only cells carrying the mutated gene showed these abnormalities and that the changes that occurred in the blood cells were dependent on the types of cells from which they descended.

"This model is highly relevant and yields new insights into JMML pathogenesis," comments Dr. Neel. "It will enable further studies into the molecular basis for leukemia as well as provide an excellent platform for the evaluation of potential therapeutic strategies."

Blood. 2009 Apr; 113(18): 4414-24. This work was supported by the National Institutes of Health.

STROKE: POTENTIAL NEW DRUGS FOR BRAIN PROTECTION


Dr. Michael Tymianski

DESPITE ITS ENORMOUS socioeconomic implications, stroke has not yet been significantly impacted by neuroprotectants—drugs that prevent or dramatically slow down the deterioration of brain cells. An exciting series of studies conducted by Dr. Michael Tymianski and colleagues at TWRI, the University of Western Ontario, the Hospital for Sick Children, the University of PEI and the University of British Columbia provides new hope in this direction for patients suffering from stroke.

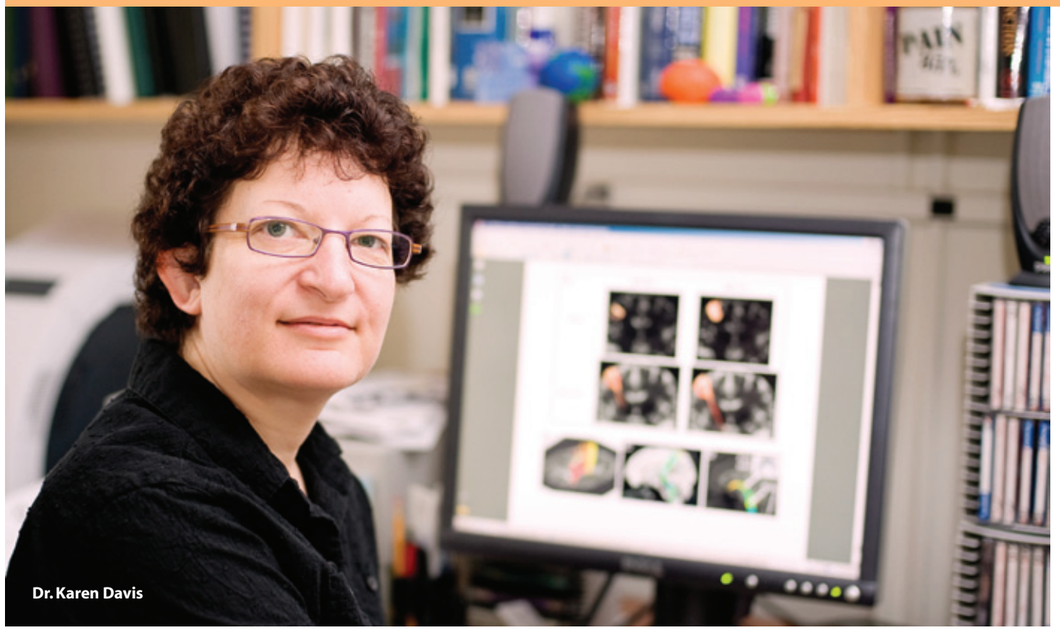
The team tested the use of special drugs that suppress the interactions of postsynaptic density-95 (PSD-95) protein with other signaling proteins. PSD-95 is an important structural brain cell protein. When the drugs were administered to rats after stroke was induced, the team observed reductions in the sizes of infarcts (areas of dead tissue caused by a loss of blood supply) and improved long-term behaviour in a wide therapeutic window.

"To our knowledge, PSD-95 inhibitors are among the first pharmacological compounds that effectively produce neuroprotection when administered within hours following stroke," notes Dr. Tymianski. "Continued evaluation of this class of drugs will be key in helping to find a neuroprotective drug therapy for stroke patients."

Stroke. 2008 Sep; 39(9): 2544-53. This work was supported by the Canadian Institutes of Health Research, the National Institutes of Health, the Canadian Stroke Network, and the Ontario Research Fund (Ministry of Research and Innovation).

Foundational Theme:

Image-Guided Discovery in Health & Disease


Dr. Karen Davis

NERVE INJURY: CUTTING YOUR NERVE CHANGES YOUR BRAIN

A RECENT STUDY PERFORMED by Drs. Karen Davis and Dimitri Anastakis, as well as PhD student Keri Taylor, provides exciting new evidence that the human brain changes functionally and structurally after a nerve is cut and surgically repaired.

The TWRI team used powerful magnetic resonance imaging techniques to assess functional and structural modifications (i.e., plasticity) in the brains of 14 patients who had had their median and/or ulnar nerves completely cut (as a result of various accidental and work-related injuries) and subsequently surgically repaired at least 1.5 years prior to study enrolment. These patients showed impaired function of their repaired nerves, reduced grey matter and white matter (major structural components of the brain) and functional changes in key areas of the brain that process information related to touch and pain. Furthermore, the magnitude of cortical thinning in the somatosensory cortex reflected the severity of sensory loss.

"Many of these types of patients suffer a long life of disability and economic difficulties," comments Dr. Davis. "Understanding the ramifications of nerve injury provides insight into the mechanisms of brain plasticity and its relation to sensory function and may help to facilitate the development of new therapeutic strategies and intervention programs."

Brain. 2009 Nov; 132(11): 3122-33. This work was supported by The Physicians' Services Incorporated and a joint seed grant from the University of Toronto Centre for the Study of Pain/AstraZeneca.

BONE CANCER: RELIEVING PAIN

THE SPREAD OF CANCER TO the bone, also referred to as bone metastases, is commonly associated with debilitating pain that does not often respond to standard available therapeutic options. A TGRI team, led by Dr. David Gianfelice, conducted a study to evaluate the safety and efficacy of using magnetic resonance (MR) imaging-guided focused ultrasound to alleviate pain caused by bone metastases in patients with whom standard available treatments were ineffective or not feasible.

Informed consent was obtained from 11 patients (seven women and four men of average 58.6 years) with pain related to non-weight bearing bone metastases. These patients were treated with MR imaging-guided focused ultrasound, and efficacy was evaluated by changes in visual analog scale scores, pain medication use and quality of life. The safety of this approach was evaluated by recording the incidence and severity of related adverse events for three months post-treatment. All patients reported a progressive decrease in pain in treated regions and a reduction in pain medication use during the three month follow-up period.

"No adverse events were recorded during physical examination or follow-up imaging and five of the patients had increased bone density at the site of treatment," says Dr. Gianfelice. "Our results show that MR imaging-guided focused ultrasound is an effective noninvasive technique that allows for palliative treatment of bone metastases with little or no morbidity."

Radiology. 2008 Oct; 249(1): 355-63.

BREAST CANCER: ASSESSING RISK EARLY IN LIFE

AN OCI TEAM, LED BY DR. Norman Boyd and in collaboration with colleagues at Sunnybrook Health Sciences Centre and the Population Health Alberta Cancer Board, has conducted a unique mother-daughter study that provides further understanding of breast density, an inheritable characteristic known to be a strong risk factor for breast cancer, and suggests that risk assessment and prevention of breast cancer might start early in life.

The team recruited 400 pairs of mothers and daughters and used magnetic resonance imaging (MRI) to examine breast tissue in daughters, aged 15-30 years, as well as a random sample of 100 of the mothers. Results showed that percent breast water variation was higher in 15-19 year olds than in 20-30 year olds and that this variation decreases with age.

Height and weight, the mothers' breast tissue characteristics and elevated blood growth hormone concentrations were also linked to higher percent breast water. The team found that each additional 5 cm in the daughters' heights was associated with a 3% increase in percent breast water, suggesting a mechanism by which growth might affect the risk of cancer.

"Our findings indicate that differences in breast tissue composition in early life may be a potential mechanism for this increased susceptibility to the effects of carcinogens at early ages," comments Dr. Boyd. "By identifying the environmental and genetic factors that influence breast tissue composition early in life, we may be able to develop safe and effective methods of prevention."

Lancet Oncol. 2009 Jun; 10(6): 569-80. This work was supported by the Canadian Breast Cancer Research Alliance.

Image-Guided Discovery in Health & Disease

CANCER IMAGING: BUILDING NEW TREATMENT DOSE PRACTICES


Dr. David Jaffray

FINDINGS FROM A STUDY conducted by OCI's Dr. David Jaffray and colleagues from Sweden have shed new light on our understanding of dosage for radiotherapy in addition to radiosurgery used in the treatment of head and neck cancers.

Explains Dr. Jaffray, "With the advent of new imaging technologies, it is important to revisit the concept of appropriate radiation dosage—specifically, as it pertains to reachable radiation volumes and efficient treatment. In terms of our research, with the Leksell Gamma Knife Perfexion unit now established at UHN, we felt this was the perfect opportunity to answer these kinds of questions for patients undergoing treatment of head and neck cancers."

Dr. Jaffray and his team used a series of investigations to evaluate the extent of radiation spread to surrounding areas of the body when targeting tumours in the skull-base or upper-spine region of the body with the new Leksell Gamma Knife Perfexion unit. Study findings show that with increased tumour size, the area of healthy tissue irradiated increases as well, primarily due to an increased radiation time.

"With continued research, our findings will help to establish appropriate levels of radiation dosage for newer technology that minimizes radiation exposure to healthy tissue surrounding tumours," says Dr. Jaffray. "Cancer research is a highly competitive field and new advances are being made everyday. It is extremely important that we stay abreast of these discoveries to bring them to patients as quickly and safely as possible."

Med Phys. 2009 Jun; 36(6): 2069-73. This work was funded in part by Elekta Instrument, AB, Stockholm, Sweden.

NEUROLOGY: A DIFFERENT WAY OF SEEING THE BRAIN

A NEW WAY TO VISUALIZE blood vessels in the brain that also overcomes current limitations may be possible, thanks to findings from a TWRI team led by Dr. David Mikulis. Conventional imaging of abnormal blood vessels of the brain requires the injection of contrast agents into the blood. The images show defects in the column of blood caused by abnormalities that actually lie within the blood vessel wall. However, defects in the blood column can look similar even when caused by different diseases. A new approach uses a more powerful magnetic resonance imaging (MRI) system that is able to image the blood vessel wall directly to enable a more accurate diagnosis of the disease affecting the blood vessel.

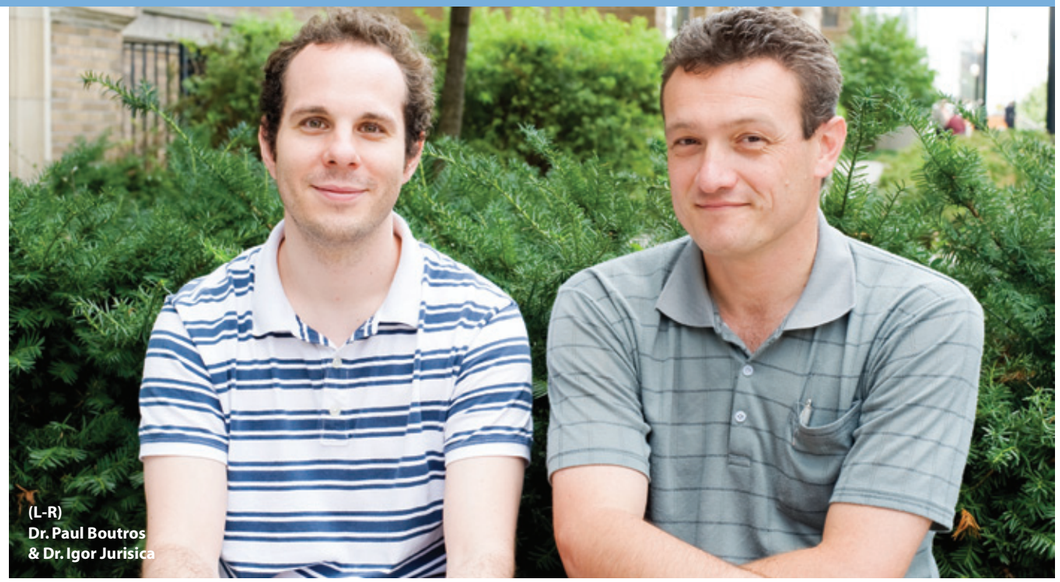
Investigators from TWRI and Johns Hopkins Hospital recruited 37 patients with various blood vessel diseases including atherosclerosis, dissecting aneurysms (tears in blood vessel walls) and inflammation. Using a powerful form of MRI—specifically, 3T MRI—they demonstrated higher definition and improved image clarity of blood vessels in the brain.

"The 3T MRI technology was quite useful in providing clear imaging of blood vessel wall architecture that was specific to the disease," says Dr. Mikulis. "The ability to make a more accurate diagnosis will allow physicians to initiate more timely and definitive treatment preventing brain injury from deficits in blood flow (stroke). Future studies will examine a broader range of patients to determine how sensitive, specific and predictive a tool like 3T MRI can be in terms of the best treatment strategy for each patient."

Neurology. 2009 Feb; 72(7): 627-34.

Foundational Theme:

Biomarkers



(L-R)
Dr. Paul Boutros
& Dr. Igor Jurisica

CANCER: DECIPHERING IMPORTANT GENE PATTERNS

TUMOUR STAGE IS CURRENTLY the best predictor of patient survival in non-small cell lung cancer (NSCLC), but new evidence from a team of OCI investigators may provide important prognostic information—independent of tumour stage—that may affect treatment strategies.

Explains Dr. Igor Jurisica, "Many useful molecular markers have been identified for several cancers, including NSCLC. However, for many technical reasons these small predictive sets of genes usually have poor overlap across studies. Our recent study provides another explanation for this lack of overlap and is the first comprehensive study of predictive signatures."

Dr. Jurisica and colleague Dr. Paul Boutros, along with team members Drs. Frances Shepherd, Ming-Sound Tsao and Linda Penn, developed an algorithm and used it to analyze data from four previous lung cancer studies—a follow-up study to one led by Dr. Tsao in 2007. The team found that the algorithm could accurately predict patient survival outcomes, a result validated in four external datasets, and later again validated in a pooled data set from eight NSCLC studies comprising 589 patient samples.

"Based on our calculations, we've found another half million different six-gene signatures—gene activity between six genes—that could predict NSCLC," comments study author Dr. Boutros. "The six-gene signatures we've found have the potential to help us understand the biology of NSCLC and provide alternative markers for identifying patients with poor prognosis."

Proc Natl Acad Sci USA. 2009 Feb; 106(8): 2824–2828. This work was supported by the National Cancer Institute of Canada, the Natural Sciences and Engineering Research Council of Canada, the Princess Margaret Hospital Foundation, Genome Canada through the Ontario Genome Institute, IBM, and fellowships from the PreCarn Foundation and the Canadian Institutes of Health Research's Excellence in Radiation Research for the 21st Century Strategic Training Initiative in Health Research Program.

MALARIA: UNCOVERING DIAGNOSTIC TOOLS

Dr. Kevin Kain

IN A WORLD FIRST FINDING, TGRI investigators have discovered promising biomarkers for cerebral malaria (CM) that may one day serve as a prognostic test for severe malaria, according to study lead Dr. Kevin Kain. Currently, there are few tools that can determine which individuals infected with *Plasmodium falciparum*—the parasite responsible for causing malaria in humans—will progress to severe and potentially fatal complications such as CM.

With colleagues from Thailand and Uganda, Dr. Kain's team analyzed blood samples from malaria-infected and non-infected Thai adults, as well as Ugandan children, for changes in proteins including angiopoietin-1 (ANG-1) and angiopoietin-2 (ANG-2). The team selectively chose to investigate these proteins because of their intimate involvement with maintaining vascular integrity.

Findings showed that ANG-1 and the ratio of ANG-2:ANG-1 had a sensitivity and specificity of 100% for distinguishing CM in Thai adults and 70% and 75% respectively for Ugandan children. Low levels of the ANG-1 protein were also able to predict subsequent mortality in children.

"Specifically, we found that ANG-1 and ANG-2 proteins may play a role in the pathogenesis of CM and are accurate biomarkers to discriminate CM from uncomplicated malaria," says Dr. Kain. "Of particular interest, they also help to predict survival in African children and may assist health care providers in triaging critically ill patients and in individualizing treatments in the future."

PLoS ONE. 2009 Mar; 4(3): e4912. This work was supported by the Canadian Institutes of Health Research, Genome Canada through the Ontario Genomics Institute, Canada Research Chairs, the NIH Fogarty International Center, Sandra A. Rotman Laboratories, the McLaughlin-Rotman Centre for Global Health and the McLaughlin Centre for Molecular Medicine.

PRIMARY BILIARY CIRRHOSIS: EXAMINING DISEASE GENETICS

(L-R) Technician Jennifer Yuan
and Dr. Katherine Siminovitch

FINDINGS FROM A UHN-LED study published in the *New England Journal of Medicine* highlight the significant association between primary biliary cirrhosis (PBC)—an autoimmune disease of the liver targeting the small bile ducts—and genetic predisposition to the disease due to changes or mutations to specific genes.

Led by UHN's Drs. Katherine Siminovitch, Jenny Heathcote and Gideon Hirschfield, DNA samples from over 2,000 North American subjects, with and without PBC, were analyzed. The genomewide studies showed that changes in the *HLA*, *IL12A* and *IL12RB2* genes were strongly associated with risk for this disease.

Comments Dr. Siminovitch, "The proteins these genes produce are critical components of the immune response, so our findings confirm a major role for the immune system in development of this disease. Our study also identifies the IL12 pathway as a potential therapeutic target in PBC and may subsequently lead to a new approach to treating PBC patients."

N Engl J Med. 2009 Jun; 360: 2544-55. This work was supported by the Canadian Institutes of Health Research, the Ontario Research Fund, the Canadian Primary Biliary Cirrhosis Society, the National Institutes of Health, the American Gastroenterological Association, and the A.J. and Sigismunda Palumbo Charitable Trust.

THYROID CANCER: IDENTIFYING MARKERS OF DISEASE

OCI'S DRS. SYLVIA ASA AND Shereen Ezzat, with colleagues in Mexico, have identified a new research tool that may one day be used to help physicians assess patients with thyroid cancer.

Led by Dr. Asa, the team used a battery of molecular techniques to analyze thyroid cancer tissue samples from more than 350 patients and found that a member of the melanoma-associated (MAGE) family of cancer-testis antigens plays a role in thyroid cancer development and metastasis. High levels of the MAGE protein were detected in primary and metastatic thyroid tumours.

"We were also able to detect levels of MAGE protein relating to the number of lymph node metastases," says Dr. Asa. "These findings are clinically important because in the future, we could use MAGE levels as a marker of disease that could be used to refine diagnostic procedures, or to help with prognosis by enabling treating physicians to decide between an aggressive or conservative approach to therapy."

Endocr Relat Cancer. 2009 Jun; 16(2): 455-66. This work was supported by the Canadian Institutes of Health Research, the Canadian Breast Cancer Research Alliance, the Toronto Medical Laboratories and the Rita Banach Thyroid Cancer Research Fund.

VIROLOGY: UNDERSTANDING THE MECHANISMS OF INFECTION

A NEW FINDING FROM TGRI adds important knowledge to our understanding of how virus infections, especially poxviruses, spread throughout the human system and where the spread may potentially be stopped.

The immune system contains chemokines, proteins responsible for relaying messages that trigger T cells into action, launching an immune response. During an immune response, the chemokine receptor CCR5 plays a pivotal role in how the immune system responds to clear an infection. Viruses have evolved to co-opt this chemokine system, using it to their advantage—such is the case with poxviruses.

"Mice who do not have CCR5 are quite resistant to poxvirus infection. When we put back CCR5 using a bone marrow transplant, virus infection occurred in the mice, detected as viral spread from the lungs to the brain and spleen," says study lead Dr. Eleanor Fish.

"This evidence shows that CCR5 is important for the migration of virus infected T cells out of affected lungs following intranasal poxvirus infection," notes Dr. Fish. "We show, for the first time, that CCR5 expression in T cells contributes to the spreading of virus beyond lung tissue, which suggests that CCR5 may in fact be required for whole body poxvirus infection. We now have a target for antiviral drug development: an inhibitor of this receptor that would prevent the spread of poxvirus infection. Since vaccination against smallpox no longer occurs, it is important to develop antiviral drugs that would combat any newly emerging poxvirus or any potential bioterrorist threat of a weaponized poxvirus."


Dr. Eleanor Fish

J Virol. 2009 Mar; 83(5): 2226-36. This work was supported by the Natural Sciences and Engineering Research Council of Canada and the Canadian Institutes of Health Research.

Foundational Theme:

Clinical Studies


Dr. Amit Oza

ENDOMETRIAL CANCER: ASSESSING TREATMENT FEASIBILITY

BETWEEN 36 AND 87 PERCENT of endometrial cancer patients overexpress the epidermal growth factor receptor (EGFR), a protein involved in tumour growth and progression. Recent findings from an OCI-led Phase II study of the drug erlotinib is providing strong evidence for its effectiveness in selectively inhibiting EGFR in patients with recurrent or metastatic endometrial cancer.

Study lead Dr. Amit Oza explains, "Erlotinib is taken orally and has been shown to promote cell death in laboratory studies of cancer. In clinical trials, erlotinib has shown antitumour activities in several cancers such as lung, ovarian, and head & neck, and we wanted to see if the same was true for endometrial cancers."

With colleagues across the country, the team administered erlotinib orally on a daily basis to patients with endometrial cancer who were ineligible for standard treatments. Following the study, the team found that the treatment was well tolerated and that patients only infrequently experienced side effects such as rash, diarrhea, nausea and fatigue. Moreover, a modest response rate of 12.5% was detected with disease stabilization lasting from 1.5 to 11.9 months in another 46.9% of patients.

"In our molecular investigations of EGFR we were unable to detect any mutations resulting in amplified genes that would have contributed to the development of endometrial cancer," says Dr. Oza. "Future studies of erlotinib as a treatment option for patients with endometrial cancer could build on available information of the biology of EGFR, its interactions with chemotherapy, hormonal therapy or other targeted agents which we did not attempt here."

J Clin Oncol. 2008 Sep; 26 (26): 4319-25. This work was supported by the National Cancer Institute of Canada with funds received from the Canadian Cancer Society and the Bras Drug Development Program.

LIVER CANCER: A NEW TREATMENT DIRECTION


Dr. Laura Dawson

FINDINGS FROM A UHN-LED Phase I study are casting light upon a new radiotherapy treatment option that is individualized and does not cause radiation-related liver toxicity, potentially resulting in new treatments for patients with liver metastases that are inoperable and who are not candidates for standard treatment therapies.

To determine the safety and efficacy of individualized six-fraction stereotactic body radiation therapy (SBRT)—which involves delivering high doses of radiation precisely to tumour sites within the body—OCI's Dr. Laura Dawson and colleagues Drs. James Brierley, Rebecca Wong, Bernard Cummings, Jolie Ringash and Jennifer Knox recruited 68 patients with inoperable colorectal, breast or other liver metastases.

Overall, SBRT was well-tolerated by patients and no radiation liver toxicity was observed. The majority of irradiated tumours had a sustained response to SBRT. Among patients who had undergone SBRT, the one-year survival rate was 60%.

"What we've seen here is that with this group of patients with focal liver metastases unsuitable for standard therapies, SBRT was safe, and it led to sustained local control for the majority of patients treated," says Dr. Dawson. "Taking this into Phase II and III studies will help us determine the benefits of SBRT, which may be greatest when delivered earlier in a patient's treatment course."

J Clin Oncol. 2009 Apr; 27(10): 1585-91. This work was supported in part by the Canadian Cancer Society, the National Cancer Institute of Canada, Elekta Oncology Systems, and a 2002 American Society of Clinical Oncology Career Development Award (L.A.D.).

CARDIOLOGY: TAKING TIME TO DETERMINE PATIENT PREFERENCES

DETERMINING PREFERRED treatment strategies is important early in the course of illness for patients dealing with heart failure, according to findings from a TGRI-led study, which show that understanding individual patient preferences will impact the decision-making process.

"The treatment options patients were asked to choose from were standard medical management, oral inotropes and the use of a left ventricular assist device," explains study lead Dr. Heather Ross. "We wanted to know, when given the option of choosing between three very different routes of treatment, which one patients facing heart failure would choose."

Over 90 patients were asked to complete the Minnesota Living with Heart Failure Questionnaire, which measures patient perception of the effects of congestive heart failure on physical, socioeconomic and psychological aspects of life—and it was discovered that two groups of patients exist based on treatment preference. One group preferred treatments that prolonged survival time while the other group favoured strategies that improved quality of life but reduced survival time.

"Our findings show that when presented with three options, 55% of patients chose oral inotropes, preferring a significantly shorter life with fewer symptoms," says Dr. Ross. "Alternatively, 45% of patients chose medical management, preferring longer life with worsening symptoms. Future studies could look at techniques to describe the process of making treatment decisions that explore personal preferences; however, the best method to understanding treatment preferences is to talk to patients about their options."

J Heart Lung Transplant. 2008 Sep; 27(9): 1002-7. This work was supported in part by the Heart and Stroke Foundation of Ontario.

LUPUS: MONITORING THE ADVANTAGES OF METHOTREXATE

RESEARCHERS AT TWRI WITH collaborators across Canada recently revealed advantages in using methotrexate to treat patients with moderately active lupus.

Methotrexate is a commonly prescribed rheumatoid arthritis drug that increases the body's anti-inflammatory and immunosuppressive responses. Findings from the UHN double-blind, randomized, placebo-controlled study of patients with moderate systemic lupus erythematosus (SLE), led by Dr. Paul Fortin, showed that in comparison to study participants using placebo, patients prescribed methotrexate experienced decreasing disease activity and lowered daily prednisone dose.


Dr. Paul Fortin

"Methotrexate was not only significant in reducing time-average prednisone use, but patients also scored significantly better on the mental health component of the quality of life scale," says Dr. Fortin. "As with any medication, there are some common side effects that patients should discuss with their physicians, but our findings show that methotrexate use is beneficial for patients with moderately active lupus, especially in patients without damage—which is a function of the cumulative severity of disease activity since diagnosis."

Arthritis Rheum. 2008 Dec; 59(12): 1796-804. This work was supported by The Arthritis Society of Canada with participation from Faulding Canada, Inc. (now Mayne Pharma [Canada] Inc.), Lupus Canada and the Canadian Institutes of Health Research.

HIV: EVALUATING THE VALUE OF NEW TREATMENT OPTIONS

TGRI'S DR. SHARON WALMSLEY and an international team of colleagues have confirmed that use of the boosted protease inhibitor saquinavir/ritonavir (SQV/r) in HIV-1-infected patients is as effective as existing treatments when used as part of combination HIV therapy.

Currently, the most effective initial treatment for patients with HIV-1 is a combination of drugs aimed at preventing the virus from multiplying as much as possible.

"Our study followed patients who had never been treated for HIV-1 infection for 48-weeks to determine if SQV/r was as effective as the currently widely prescribed lopinavir/ritonavir (LPV/r) treatment strategy when used in combination with Truvada," notes Dr. Walmsley.

In fact, the study findings showed that SQV/r was as effective as LPV/r in keeping HIV-1 levels low and increasing CD4 cell counts in patients.


Dr. Sharon Walmsley

Patients prescribed SQV/r treatment experienced smaller increases in triglyceride levels than those on LPV/r, an important finding as HIV-1 patients are at an increased chance of experiencing metabolic syndrome, and in some cases, coronary artery disease.

"This is very important in terms of future treatment strategies because SQV/r works as effectively as current practices but without as severe risks to the heart," says Dr. Walmsley. "These findings add additional support to current treatment guidelines and reinforce their use as a viable component for first-line therapy of HIV-1-infected patients."

J Acquir Immune Defic Syndr. 2009 Apr; 50(4): 367-74. This work was supported by the Ontario HIV Treatment Network and Roche.

Specialty Theme:

Stem Cells & Tissue Engineering

(L-R) Dr. Charles Tator and graduate student Susan Fan

SPINAL CORD INJURY: USING PROGENITOR CELLS TO IMPROVE FUNCTION

A GROUP OF UHN investigators led by Drs. Charles Tator and Armand Keating have shown that the transplantation of neural stem/progenitor cells (NSPCs)—immature cells found in the spinal cord—may help improve function following spinal cord injury.

NSPCs are naturally found in the spinal cord and help in the repair process immediately after injury; however, their beneficial action is limited to a few days. The researchers sought to determine whether the addition of more NSPCs would help to improve this process. Cells were transplanted into the spinal cords of rats nine days following injury. Animals were tested for locomotor activity twelve weeks later and showed significant functional improvements.

These promising early effects of increased NSPCs at the spinal cord injury site suggest a neuroprotective effect. "Our initial results are very promising," says Dr. Tator. "Future studies will help us determine whether these cells are able to help regenerate tissue at the site of spinal cord injury."

Neuroscience. 2008 Aug; 155(3): 760-770. This work was supported by the Canadian Institutes of Health Research, the International Foundation of Research in Paraplegia and the Christopher Reeve Paralysis Foundation.

CELL THERAPY: PREVENTING HEART FAILURE AFTER INJURY

PATIENTS WHO HAVE suffered a heart attack can be protected from congestive heart failure by the injection of new cells into their heart at the time of coronary bypass. A recent preclinical study from TGRI investigators showed that injecting skeletal myoblasts—undifferentiated muscle cells—improved cardiac function and prevented heart failure after a heart attack. The new information provided in this study was the elucidation of the mechanism responsible for the beneficial effects, which could permit surgeons to devise new therapies.

Dr. Ren-Ke Li

Dr. Ren-Ke Li led a team of investigators, including colleagues Drs. Richard Weisel and Terrence Yau, that injected myoblasts into the injured region (tissue damaged by the heart attack) at 5 or 30 days following heart injury in a preclinical mouse model. Regardless of when or where the cells were injected, they improved global heart function and preserved heart wall thickness as well as the elasticity in the non-injured areas of the heart. The study indicated that cell implantation improved heart function by preventing the remodelling of uninjured heart muscle.

"It's exciting to see that these injected cells were able to improve heart function," notes Dr. Li. "These results suggest that injection of skeletal myoblasts, which have been genetically engineered to preserve the matrix structure of the normal heart muscle, may be a better approach to prevent congestive heart failure."

Circulation. 2008 Sep; 118 (14 Suppl): S130-7. This work was supported by the Heart and Stroke Foundation of Ontario and the Canadian Institutes of Health Research.

REPAIRING INJURED LUNGS: DISCOVERY OF A NEW POPULATION OF BONE MARROW CELLS

A NEW POPULATION OF BONE marrow cells (BMCs) expressing lung epithelial markers and capable of repairing injured airway epithelium has been identified by a group led by Drs. Thomas Waddell and Armand Keating.

This population of cells, found in mouse and human bone marrow, express the Clara cell secretory protein (CCSP)—a marker of airway progenitor and stem cells—along with a number of other stem cell markers. When these CCSP-expressing cells were injected into naphthalene-damaged lungs, they preferentially migrated to the damaged areas and developed into multiple airway cell types.

"For the first time we've been able to show that these CCSP-expressing cells are able to engraft in the lung and grow into different lung epithelium," explains Dr. Waddell. "With continued research, these bone marrow CCSP cells may have substantial value as a cell replacement therapy for lung epithelial diseases. We know these cells do exist in humans and are currently determining whether they change in a variety of lung diseases."

J Clin Invest. 2009 Feb; 119(2): 336-48. This work was supported by the Canadian Cystic Fibrosis Foundation and the Canadian Institutes of Health Research.

CARDIOLOGY: GROWING HEART CELLS FOR REPAIR

IN A GROUNDBREAKING study, an international team of researchers, led by UHN's Dr. Gordon Keller (Director of UHN's McEwen Centre for Regenerative Medicine) has successfully grown human heart progenitor cells—immature heart cells—from embryonic stem cells. This study represents a major step towards creating functional heart tissue.

In an eloquent series of studies, the researchers treated cultures of embryonic stem cells with a combination of growth-promoting proteins. The team was able to direct the stem cells to make three types of heart cells: cardiomyocytes, endothelial cells and vascular smooth muscle cells.

These findings offer a potentially unlimited supply of heart cells, which may be used for basic and clinical research. "The immediate impact is significant," states Dr. Keller.


Dr. Gordon Keller

"It will allow us to test for potential toxic effects of new drugs in petri dishes. Over the longer term, it may represent a new strategy for repairing damaged tissues after a heart attack."

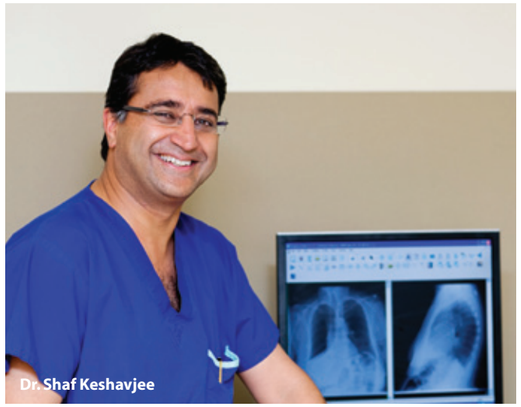
Nature. 2008 May; 453(7194): 524-8. This work was supported by the National Institutes of Health/National Heart Lung and Blood Institute.

(Image courtesy of Gary Rhijnsburger Photography)

LUNG TRANSPLANTATION: INCREASING THE DONOR POOL

AN INNOVATIVE STRATEGY to improve available donor lungs for transplantation has been developed by a group of investigators at UHN. This technique provides a method for preserving lungs before implantation, allowing researchers to evaluate and repair donor lungs prior to transplant.

Leading thoracic surgeon and researcher Dr. Shaf Keshavjee, together with Drs. Marcelo Cypel, Mingyao Liu, Marc de Perrot, and Thomas Waddell, have developed an ex vivo lung perfusion (EVLP) system to protect donor lungs.


Dr. Shaf Keshavjee

By keeping the lungs at normal body temperature and providing them with continuous oxygen and nutrients, the organs demonstrated stable function for 12 hours without causing injury—a significant improvement over the normal 1-2 hours observed in earlier attempts.

While the initial studies were performed using animal models, the EVLP system has since been used successfully in human lung transplantation. Notes Dr. Keshavjee, "This system will have a significant impact towards expanding the pool of donor lungs and improving outcomes following lung transplantation."

J Heart Lung Transplant. 2008 Dec; 27(12): 1319-25. This work was supported by the Canadian Institutes of Health Research and Astellas Canada.

Specialty Theme:
Immunity in Health & Disease


Dr. Joan Wither

AUTOIMMUNE DISEASE: SEARCHING FOR BIOMARKERS

SYSTEMIC LUPUS erythematosus (SLE) is a chronic autoimmune disease in which the body's immune system targets connective tissues. Although no single gene has been identified as the cause of SLE, the presence of certain groups of genes increases the risk of SLE being triggered by environmental factors. To determine whether genes induced by interferons (IFNs; proteins released by immune cells in response to viruses) could be used as a biomarker for lupus activity, Dr. Joan Wither and colleagues at TWRI examined their expression over extended periods of time.

In a study involving 94 SLE patients and 11 healthy control subjects, the team showed that five IFN-responsive genes were expressed to a greater degree in SLE patients versus controls. This expression was poorly correlated with severity of disease—gene expression level changes remained fairly stable over the study period despite marked changes in SLE activity.

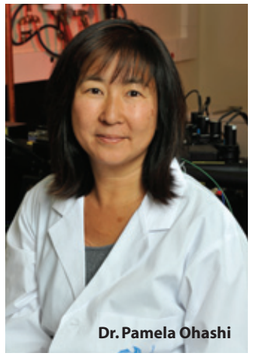
"This study provided very interesting results regarding IFN-induced gene expression in SLE," comments Dr. Wither. "The lack of correlation with disease severity prevents these genes from being suitable disease biomarkers with clinical utility for SLE."

Ann Rheum Dis. 2009 Sep; 68(9): 1440-6. This work was supported by the Canadian Institutes of Health Research and the Arthritis Centre of Excellence of the University of Toronto.

CANCER: NEW TOOL FOR AUGMENTING TUMOUR VACCINE EFFECTIVENESS

AN EXCITING NEW APPROACH to cancer treatment is focused on developing vaccines that can provide immunity against tumours. A breakthrough discovery by Drs. Pamela Ohashi and Tak Mak and colleagues at OCI has highlighted the protein interleukin-7 (IL-7) as a potential therapeutic tool for treating cancer in this manner.

Using a genetically engineered mouse model of cancer that also produced a special viral protein, this team found that the administration of IL-7, following treatment with a live viral antitumour vaccine, led to an enhanced antitumour response that also increased the survival of the mice. The study further showed that this effect was the result of repressing key inhibiting proteins of immune function, and that IL-7, when administered alone, was ineffective.


Dr. Pamela Ohashi

"This enhanced response with IL-7 administration can be harnessed to directly target spontaneously arising tumours," comments Dr. Ohashi. "This has major implications for immunotherapy in the treatment of cancer."

Nat Med. 2009 May; 15(5): 528-36. This work was supported by the Canadian Institutes of Health Research, the Ontario Institute for Cancer Research, the Terry Fox Cancer Foundation and the National Cancer Institute of Canada.

ORGAN TRANSPLANTATION: IMPORTANT MOLECULE FOR PREVENTING REJECTION

DR. GARY LEVY AND colleagues at TGRI have shown that fibrinogen-like protein 2 (FGL2), a protein known to inhibit the maturation and proliferation of specific immune cells, plays an important role in the rejection of transplanted organs or tissues.

Transplant rejection occurs when the recipient's immune system distinguishes the transplanted organ or tissue as foreign material and attacks it in response. This research team showed that FGL2 specifically binds to other proteins (receptors) called Fc-gamma IIB and Fc-gamma III on 'antigen-presenting cells' (APCs; cells that 'present' foreign substances to the immune system). While FGL2 was found to prevent the rejection of transplanted skin grafts in mice, this effect was not present in genetically engineered mice lacking the Fc-gamma IIB receptor.

"Identifying this specific receptor binding is very exciting," comments Dr. Levy. "This finding has very important implications for the pathogenesis of immune-mediated conditions like transplant rejection and suggests FGL2 as a potential target for therapy."

Eur J Immunol. 2008 Nov; 38(11): 3114-26. This work was supported by the Heart and Stroke Foundation of Canada and the Canadian Institutes of Health Research.

IMMUNITY: UNRAVELLING THE MYSTERY OF IMMUNE RESPONSES

TOLL-LIKE RECEPTORS (TLRs) are important proteins that, when stimulated by specific pathogens like bacteria, enable the body to initiate an immune response by triggering the release of special immune system-regulating protein molecules called cytokines. Improper functioning of TLRs can result in sepsis (infection of the blood) or chronic inflammatory disorders.

Dr. Pamela Ohashi and colleagues at OCI recently conducted a study involving proteins called c-Rel and C/EBPbeta/delta—known to be involved in the formation of new blood cells and fat cell development—and showed that stimulation of TLRs did not trigger the production of proinflammatory cytokines in the absence of these proteins.

"This study provides important new knowledge about how TLRs are involved in controlling immune responses," states Dr. Ohashi. "Further understanding of its role and key molecules involved could provide critical, new drug targets for treating inflammatory and immune disorders."

J Immunol. 2009 Jun; 182(11): 7212-21. This work was supported by the Canadian Institutes of Health Research and the National Institutes of Health.

TRANSPLANT REJECTION: UNMASKING THE ROLE OF SPECIAL IMMUNE CELLS

REGULATORY T CELLS ARE special immune cells that play an important role in the development of various immune conditions like transplant rejection and autoimmune diseases. A specific type of this cell, the 'double negative' regulatory T cell, has been shown to prevent transplant rejection and Type I diabetes. How these cells are involved with this action, however, is largely unknown.

Recent studies from the laboratories of Dr. Li Zhang and colleagues at TGRI have shed light on this mystery. They showed that double negative regulatory T cells are involved in a special process called 'trogocytosis'—during which they physically associate with antigen-presenting cells to acquire alloantigens (a foreign substance that stimulates an immune response). Moreover, double negative regulatory T cells that had undergone trogocytosis were able to kill specific types of immune cells that targeted the alloantigens.


Dr. Li Zhang

"These studies provide important insights into how double negative regulatory T cells mediate immune cell suppression," comments Dr. Zhang. "Further understanding into how these cells work may potentially lead to a novel therapy for transplant rejection and autoimmune diseases."

J Immunol. 2008 Aug; 181(4): 2271-5. This work was supported by the Canadian Institutes of Health Research and the Canadian Cancer Society.

Specialty Theme:

Drug Discovery & Development

Dr. Lakshmi Kotra

CANCER: BUILDING MOLECULES TO FIGHT DISEASE

UHN INVESTIGATORS DRS. Lakshmi Kotra, Christopher Paige and Emil Pai have conducted a series of studies to identify novel compounds that show potent anticancer activity against various leukemia and myeloma cells.

Led by Dr. Kotra, the team created a series of compounds directed towards the impairment of the protein ODCase, ultimately affecting the production of nucleic acids (which contain genetic information) in rapidly replicating cancer cells.

When treating different leukemia cells with the synthesized compounds, three specific derivatives were effective in stopping ODCase and thus in promoting cell death.

Explains Dr. Kotra, "When we took a closer look at those cells exposed to these three derivatives, we observed the death of cancer cells at potent concentrations. We were also able to determine that these compounds are effective against leukemia, lymphoma and multiple myeloma in vitro. We are now focusing on developing this class of compounds for the treatment of acute myeloid leukemia and multiple myeloma in collaboration with the clinical teams at the Princess Margaret Hospital."

J Med Chem. 2009 Mar; 52(6): 1648-58. This work was supported by the Canadian Institutes of Health Research and the Natural Sciences and Engineering Research Council of Canada.

PARKINSON'S DISEASE: UNDERSTANDING TREATMENT-RELATED SIDE EFFECTS

PARKINSON'S DISEASE (PD) is characterized by the loss of the key brain chemical dopamine. For decades, patients have been treated with the drug L-DOPA to help restore dopamine levels. Research by TWRI's Dr. Jonathan Brotchie and his team, with collaborators from France, has provided critical insight into whether a by-product of L-DOPA called noradrenaline plays a critical role in dyskinesia (the impaired ability to control movement) or implusive behaviours (such as pathological gambling, hypersexuality or compulsive shopping), which are common side effects of prolonged L-DOPA use.

The team assessed the involvement of alpha1-adrenoreceptors—the molecules targeted by noradrenaline—in the actions of L-DOPA in an animal model of PD. They found that co-administration of prazosin (a drug known to inhibit these molecules) with L-DOPA reduced impulsive behaviours but not the anti-parkinsonian benefits of L-DOPA or dyskinesia. "Although activation of the alpha1-adrenoreceptors plays no major role in the antiparkinsonian and dyskinetic effects of L-DOPA per se," comments Dr. Brotchie," these receptors may be involved in pathological responses to L-DOPA treatment in patients with PD."

Dr. Jonathan Brotchie

J Pharmacol Exp Ther. 2009 Jan; 328(1): 276-83. This work was supported by the Krembil Neuroscience Fund and the Cure Parkinson's Trust.

LEUKEMIA: IDENTIFYING EMERGING TREATMENT OPTIONS

QUINOLINES ARE A CLASS of chemical compounds with emerging anti-cancer properties. UHN researchers Drs. Aaron Schimmer, David Rose and Hans Messner, along with colleagues at the University of Toronto, recently tested a series of quinolines and quinoline-like molecules for anti-cancer activity and identified a new compound—a diquinoline (Q^2)—that could induce death in human and mouse cancer cells.

More importantly, it was found that Q^2 caused death in leukemia, myeloma and solid tumour cancer cells preferentially over normal cells. Studies also showed that it delayed tumour growth in an animal model of leukemia and that the cell death activity was linked to a process called autophagy, the degradation of the cancer cells' own components.

"Q^2 is a new compound with extremely promising preclinical activity," comments Dr. Schimmer. "With further study, it may be a promising new potential drug compound for treating cancers like leukemia and myeloma."

Apoptosis. 2008 Jun; 13(6): 748-55. This work was supported by the Canadian Institutes of Health Research.

CANCER: CHANNELLING LIGHT TO STOP GROWTH

A NEW METHOD OF targeted cancer treatment that harnesses the power of light may be on the horizon thanks to the recent efforts of a team of OCI investigators and colleagues from the University of Toronto and the Fox Chase Cancer Center. Known as activatable photodynamic therapy (PDT), this novel method utilizes molecules that have been created in a 'silenced' form using a physics principle called energy transfer. As such, they cannot produce reactive oxygen and are harmless even when they accumulate in normal tissues and are treated with light. However, a tumour biomarker can 'awaken' these molecules. In reaction with light, these molecules produce reactive oxygen that leads to the destruction of cancer cells only.

Led by Dr. Gang Zheng and in collaboration with Dr. Ming-Sound Tsao, the team generated a PDT approach to killing cancer cells by using fibroblast activation protein (FAP)—chosen as a target due to its high expression in epithelial cancers. Using mouse and human models of cancer, the team was able to show that PDT specifically and effectively targeted FAP-rich cancer cells and was not toxic to surrounding non-cancer cells.

"Our findings show that this newly developed PDT approach is not only a specific probe for the diagnosis of FAP-expressing epithelial cancers but also a promising therapeutic agent for this kind of cancer," comments Dr. Zheng. "With future studies we hope that this FAP-targeted PDT could be potentially useful for fluorescence-guided surgery."

J Med Chem. 2009 Jan; 52(2): 358-68. This work was supported by the Canadian Institutes of Health Research, the Ontario Institute for Cancer Research through funding provided by the Government of Ontario, and the Joey and Toby Tanenbaum/ Brazilian Ball Chair in Prostate Cancer Research.

CANCER: REPOSITIONING OLD DRUGS FOR NEW ANTI-CANCER INDICATIONS

UHN RESEARCHERS DRS. Aaron Schimmer, Hans Messner and Suzanne Trudel, in collaboration with investigators in Toronto and the US, recently found evidence that the drug cyproheptadine—which has been used for treating migraines, anorexia and atopic dermatitis—can induce death in human cancer cells. Using mouse models of myeloma and leukemia, the team also showed that cyproheptadine could inhibit tumour growth without significant toxicity and that this activity was likely due to the activation of molecules (caspases) involved in events leading to cell death.


Dr. Aaron Schimmer

"Cyproheptadine represents an exciting approach to cancer drug discovery," says Dr. Schimmer. "By identifying old drugs with previously unrecognized anti-cancer activity, we can leverage their prior safety records to move them rapidly and safely into clinical trials for cancer."

Blood. 2008 Aug; 112(3): 760-9. This work was supported by the Multiple Myeloma Research Foundation, the Canadian Institutes of Health Research, and the Leukemia and Lymphoma Society of Canada.

The Research Pipeline at the UHN Board of Trustees Retreat

Transforming Discovery to Impact Health

TRANSFORMATION IS A CENTRAL THEME IN RESEARCH AT UHN: OUR SCIENTISTS AND clinicians take breakthrough discoveries from their laboratories and transform them into products, processes or policies to improve health. This requires commitment to an interactive pipeline (illustrated below) of discovery and development stages including basic research, translational research, clinical research and commercialization, that result in contributions that change the paradigm of health care for Canadians and the world.

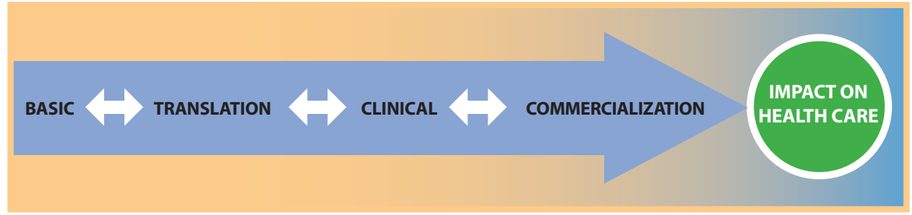
UHN has a longstanding history of driving discoveries to improve patient outcomes. Throughout each stage of the research pipeline, UHN has strategically partnered with key local, national, and international collaborators to bring a range of expertise and disciplines to address some of our most challenging health problems.

UHN has a longstanding history of driving discoveries to improve patient outcomes.

This year, the spotlight was on UHN Research at the annual Board of Trustees Retreat. After welcoming remarks by UHN President & CEO Dr. Bob Bell and VP of Research Dr. Christopher Paige, external speakers—Minister John Wilkinson (Ministry of Research and Innovation, Ontario) and Dr. Alain Beaudet (President, Canadian Institutes of Health Research)—provided key insights into the health research landscape. Sessions that focused on the pipeline stages were led by Drs. Benjamin Neel (Basic Research), Eleanor Fish (Translational Research), Lillian Siu (Clinical Research), and Brian Barber (Commercialization). Session speakers—including leading scientists Drs. John Dick, Tak Mak, Peter St George-Hyslop, Shaf Keshavjee, John Floras and David Jaffray—discussed new and current highlights underway at UHN in each stage of the pipeline.

Dr. Brian Barber, Director of UHN's Technology Development & Commercialization Office, also presented the Inventor of the Year Award to Drs. Ming-Sound Tsao, Frances Shepherd and Igor Jurisica. This team of investigators was acknowledged for having made the greatest contribution to the advancement of human health by means of a patentable invention at UHN in 2009: the development of a groundbreaking prognostic genomic analysis tool for early stage non-small cell lung cancer.

"UHN is a vibrant and exciting place," comments Dr. Paige. "The accomplishments of our dedicated research teams are remarkable. Our researchers have firmly established UHN as an internationally recognized, leading Research Hospital."



Ontario Cancer Institute

OCI

OCI BY THE NUMBERS

Research Space
373,000 sq ft

Publications
735

Total External Funding
$112,878,000

STAFF & STUDENTS

Senior Scientists	53
Scientists	19
Affiliate Scientists	9
CRU Members	167
TOTAL RESEARCHERS	248
Fellows	211
Graduate Students	214
TOTAL TRAINEES	425
TOTAL STAFF	622

Appointments as of June 30, 2009. Research space figure is approximate due to ongoing construction.

Applied Molecular Oncology

Senior Scientists
Asa, Sylvia
Bristow, Robert
Ezzat, Shereen
Gallie, Brenda
Hedley, David
Hill, Richard
Liu, Fei-Fei
Moore, Malcolm
Tannock, Ian
Tsao, Ming-Sound
Kamel-Reid, Suzanne
Scientists
Done, Susan
Liu, Geoffrey
Trudel, Suzanne
Affiliate Scientists
Martin, Lisa
Reedijk, Michael
Johnston, Michael
Bradley, Grace
Leong, Wey-Liang

Biophysics & Bioimaging

Senior Scientists
Chakrabartty, Avijit
Hunt, John
Jaffray, David
Sherar, Michael
Siewerdsen, Jeff
Vitkin, Alex
Wilson, Brian
Zheng, Gang
Scientists
Lilge, Lothar
Brock, Kristy

Cancer Genomics & Proteomics

Senior Scientists
Arrowsmith, Cheryl
Gariépy, Jean
Pai, Emil
Penn, Linda
Privé, Gilbert
Rose, David
Scientists
Kislinger, Thomas
Raught, Brian
Schimmer, Aaron
Tillier, Elizabeth
Affiliate Scientists
Gauthier, Mona

Prevention

Senior Scientists
Boyd, Norman
Minkin, Salomon
Till, James
Trichler, David
Affiliate Scientist
Ritvo, Paul

Psychosocial Oncology & Palliative Care

Senior Scientists
Devins, Gerry
Gagliese, Lucia
Rodin, Gary
Scientists
Edelstein, Kim
Howell, Doris
Zimmermann, Camilla
Affiliate Scientists
Esplen, Mary Jane
Stewart, Donna

Signaling Biology

Senior Scientists
Hakem, Razqallah
Ikura, Mitsuhiko
Jurisica, Igor
Khokha, Rama
Manoukian, Armen
Ohashi, Pamela
Wouters, Bradly
Scientists
Cheung, Peter
Koch, Anne
Okada, Hitoshi
Stambolic, Vuk
Vaziri, Homayoun

Stem Cell & Developmental Biology

Senior Scientists
Barber, Dwayne
Dick, John
Iscove, Norman
Keller, Gordon
Mak, Tak
McCulloch, Ernest
Medin, Jeffrey
Messner, Hans
Minden, Mark
Muthuswamy, Senthil
Neel, Benjamin
Paige, Christopher
Rottapel, Robert
Schuh, Andre
Scientists
Moghal, Nadeem
Ailles, Laurie

Clinical Research Unit (CRU)

Members
Amato, Dominic
Anglin, Peter
Baker, Michael
Barth, David
Bayley, Andrew
Bell, Robert
Bernardini, Marcus
Bernstein, Lori
Bernstein, Mark
Bezjak, Andrea
Blackstein, Martin
Boerner, Scott
Brade, Anthony
Brandwein, Joseph
Brien, William
Brierley, James
Brown, Dale
Burkes, Ronald
Catton, Charles
Catton, Pamela
Chan, Kelvin
Chang, Hong
Chen, Christine
Chen, Eric
Chetty, Runjan
Cheung, Carol
Cho, John
Chung, Peter
Cil, Tulin
Clarke, Blaise
Cleary, Sean
Clemons, Mark
Crook, Juanita
Croul, Sidney
Crump, R. Michael
Cserti, Christine
Cummings, Bernard
Czarnota, Gregory
D'Agostino, Norma
Darling, Gail
Dawson, Laura
de Perrot, Marc
Deheshi, Ben
Dinniwell, Robert
Dodge, Jason
Easson, Alexandra
Elantholiparameswaran, Saibishkumar
Elliott, Mary
Elser, Christine
Escallon, Jaime
Evans, Andrew
Feld, Ronald
Ferguson, Peter
Ferguson, Sarah
Finelli, Antonio
Fleshner, Neil
Freeman, Jeremy
Fyles, Anthony
Galal, Ahmed
Gallinger, Steven
Geddie, William
Ghazarian, Danny
Gilbert, Ralph
Gladdy, Rebecca
Goldstein, David
Goodwin, Pamela
Gospodarowicz, Mary
Grant, David
Greig, Paul
Gryfe, Robert
Guha, Ab
Gullane, Pat
Gupta, Abha
Gupta, Vikas
Hales, Sarah
Hodgson, David
Hofer, Stefan
Hogg, David
Hope, Andrew
Irish, Jonathan Crawford
Jewett, Michael
Joshua, Anthony
Keating, Armand
Kennedy, Erin
Keshavjee, Shaf
Kiehl, Tim-Rasmus
Kim, John
Knox, Jennifer
Krzyzanowska, Monika
Kukreti, Vishal
Kuruvilla, John
Laframboise, Stefan
Laperriere, Normand
Leighl, Natasha
Levin, Wilfred
Li, Madeline
Lipton, Jeffrey
Mackay, Helen
Manchul, Lee
Martens, Chandra
Mason, Warren
Matthew, Andrew
McCart, Andrea
McCready, David
McGilvray, Ian
McLean, Linda
McLean, Michael
McLeod, Anne
McLeod, Robin
Ménard, Cynthia
Millar, Barbara-Ann
Miller, Naomi
Milosevic, Michael
Moulton, Carol-Anne
Murphy, Joan
O'Brien, Catherine
Olivieri, Nancy
O'Sullivan, Brian
Oza, Amit
Paul, Narinder
Payne, David
Pendergrast, Jacob
Perez-Ordonez, Bayardo
Pierre, Andrew
Rasty, Golnar
Reece, Donna
Reznick, Richard
Ringash, Jolie
Rosen, Barry
Rotstein, Lorne
Rouzbahman, Marjan
Sahgal, Arjun
Santos, Gilda
Shaw, Patricia
Shepherd, Frances
Simpson, Rand
Siu, Lillian
Sridhar, Srikala
Strevel, Elizabeth
Sun, Alexander
Sutherland, Robert
Swallow, Carol
Sweet, Joan
Taylor, Bryce
Tkachuk, Douglas
Trachtenberg, John
Tsang, Richard
Tsao, May
Van Der Kwast, Theodorus
Waddell, Thomas
Waldron, John
Wang, Jean
Warde, Padraig
Warr, David
Wei, Alice
Weinreb, Ilan
Wells, Woody
Witterick, Ian
Wong, Rebecca
Wood, Bob
Wunder, Jay
Yasufuku, Kazuhiro
Yee, Karen
Yeo, Erik
Youngson, Bruce
Zhong, Toni
Zlotta, Alexandre

Where researchers have more than one affiliation within each institute, only one is indicated. See www.uhnresearch.ca for more information on affiliations.

RESEARCH COUNCIL ON ONCOLOGY (RCO)

Director, Ontario Cancer Institute and Chair, RCO
Benjamin Neel

Division Head, Applied Molecular Oncology
Fei-Fei Liu

Division Head, Biophysics & Bioimaging
Brian Wilson

Division Head, Cancer Genomics & Proteomics
Linda Penn

Division Head, Psychosocial Oncology
Gary Rodin

Division Head, Signaling Biology
Mitsuhiko Ikura

Division Head, Stem Cell & Developmental Biology
Robert Rottapel

Director, Campbell Family Institute for Breast Cancer Research
Tak Mak

Clinical Representative, Medical Oncology and Hematology
Malcolm Moore

Clinical Representative, Pathology
Sylvia Asa

Clinical Representative, Radiation Oncology
Mary Gospodarowicz

Clinical Representative, Surgical Oncology
Jonathan Crawford Irish

Site Leader, PMH
Sarah Downey

Executive Director, Research Operations
Lisa Alcia

Vice President, Research
Christopher Paige

Toronto General Research Institute

TGRI BY THE NUMBERS

Research Space
257,000 sq ft

Publications
637

Total External Funding
$73,193,000

STAFF & STUDENTS

Senior Scientists	58
Scientists	17
Affiliate Scientists	50
CSRC Members	59
TOTAL RESEARCHERS	184
Fellows	133
Graduate Students	98
TOTAL TRAINEES	231
TOTAL STAFF	342

Appointments as of June 30, 2009. Research space figure is approximate due to ongoing construction.

Behavioural Sciences & Health

Senior Scientists
Flint, Alastair
Kaplan, Allan
Olmsted, Marion
Regehr, Glenn
Rodin, Gary
Stewart, Donna

Scientists
Carter, Jacqueline
Esplen, Mary Jane
Grace, Sherry
Jones, Jennifer

Affiliate Scientists
Baker, Brian
Colton, Patricia
Davis, Caroline
Gucciardi, Enza
Hall, Peter
Heslegrave, Ronald
Hodges, Brian
Irvine, Jane
Katz, Joel
McVey, Gail
Nolan, Robert
Styra, Rima
Woodside, Blake

Cell & Molecular Biology

Senior Scientists
Backx, Peter
Berger, Stuart
Cardella, Carl
Cattral, Mark
Cybulsky, Myron
Dick, John
Fantus, George
Fish, Eleanor
Gorczynski, Reginald
Gotlieb, Avrum
Grant, David
Husain, Mansoor
Levy, Gary
Liles, W. Conrad
Liu, Mingyao
Rubin, Barry
Waddell, Thomas
Zacksenhaus, Eldad
Zhang, Li

Scientists
Dunn, Shannon
Irwin, David
Jin, Tianru
Kotra, Lakshmi
Lam, Tony
Lee, Douglas
Volchuk, Allen

Affiliate Scientists
Belsham, Denise
Branch, Donald
Chang, Hong
Clark, David
Cole, Edward
Drucker, Daniel
Feld, Jordan
Ghanekar, Anand
Gramolini, Anthony
Lee, Ping
Phillips, James
Rocheleau, Jonathan

Clinical Decision-Making & Health Care

Senior Scientists
Bombardier, Claire
Cheung, Angela
Daar, Abdallah
Eysenbach, Gunther
Jadad, Alex
Krahn, Murray
Naglie, Gary
Singer, Peter

Scientists
Alibhai, Shabbir
Urbach, David

Affiliate Scientists
Gagliardi, Anna
Kennedy, Erin
Lok, Charmaine
Tomlinson, George
Wei, Alice

Clinical Studies Resource Centre (CSRC) Members
Daly, Paul
Jewett, Michael
Kapral, Moira
Singer, Lianne

Clinical Investigation & Human Physiology

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

Affiliate Scientists
Easty, Anthony
Gianfelice, David
Herzenberg, Andrew
Perkins, Bruce
Raboud, Janet
Reilly, Raymond
Sawka, Anna
Wong, Florence

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

Experimental Therapeutics

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

Scientists
de Perrot, Marc
Nanthakumar, Kumaraswamy
Yau, Terrence

Affiliate Scientists
Fremes, Stephen
Hwang, David
McCart, Andrea
McGilvray, Ian
Medin, Jeffrey
Radisic, Milica
Ross, Heather
Sefton, Michael

Genomic Medicine

Senior Scientists
Cole, David
Kain, Kevin
MacDonald, Kelly
Pei, York
Siminovitch, Katherine

Scientists
Kaul, Rupert

Affiliate Scientists
Boright, Andrew
Denomme, Gregory
Downey, Gregory
Osborne, Lucy

Clinical Studies Resource Centre (CSRC)

Members
Bargman, Joanne
Beattie, Scott
Brister, Stephanie
Colman, Jack
David, Tirone
Dzavik, Vladimir
Fenton, Stanley
Gardam, Michael
Girgrah, Nigel
Gold, Wayne
Goldszmidt, Eric
Granton, John
Grigoriadis, Sophie
Kachura, John
Kennedy, Sidney
Keystone, Edward
Lilly, Leslie
Loke, Julian
Neary, Mary Ann
O'Malley, Martin
Rajan, Dheeraj
Rakowski, Harry
Ralph-Edwards, Anthony
Reznick, Richard
Richardson, Robert
Roberts, Heidi
Ross, John
Straus, Sharon
Sutton, David
Sweet, Joan
Wolman, Stephen
Yeo, Erik

Where researchers have more than one affiliation within each institute, only one is indicated. See www.uhnresearch.ca for more information on affiliations.

TGRI RESEARCH COUNCIL

Director, Toronto General Research Institute and Chair, TGRI Research Council
Richard Weisel

Division Head, Behavioural Sciences & Health
Gary Rodin

Division Head, Cell & Molecular Biology
Eleanor Fish

Division Head, Clinical Decision-Making & Health Care
Claire Bombardier

Division Head (Interim), Clinical Investigation & Human Physiology
Richard Weisel

Division Head (Interim), Experimental Therapeutics
Richard Weisel

Division Head, Genomic Medicine
Katherine Siminovitch

Clinical Representative, Heart and Circulation/ Physician in Chief
John D. Parker

Clinical Representative, Medical and Community Care
W. Conrad Liles

Clinical Representative, Surgical and Critical Care
Shaf Keshavjee

Clinical Representative, Transplant Unit, Platform Leader
Gary Levy/Ian McGilvray

Site Director, CREdiT
Mingyao Liu

Standing Guests
Reg Gorczynski
Shaf Keshavjee
Tony Lam
Ren-Ke Li
Vivek Rao
Thomas Waddell
Li Zhang

Site Leader, TGH
Marnie Escaf

Executive Director, Research Operations
Lisa Alcia

Vice President, Research
Christopher Paige

Toronto Western Research Institute

TWRI BY THE NUMBERS

Research Space
105,000 sq ft

Publications
494

Total External Funding
$27,410,000

STAFF & STUDENTS

Senior Scientists	43
Scientists	9
Affiliate Scientists	16
CSRC Members	58
TOTAL RESEARCHERS	126
Fellows	55
Graduate Students	78
TOTAL TRAINEES	133
TOTAL STAFF	203

Appointments as of June 30, 2009. Research space figure is approximate due to ongoing construction.

Brain, Imaging & Behaviour - Systems Neuroscience

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

Scientist
Kucharczyk, Walter

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

Fundamental Neurobiology

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

Scientist
Sugita, Shuzo

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

Genetics & Development

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

Scientist
Monnier, Philippe

Health Care & Outcomes Research

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

Scientist
Côté, Pierre

Affiliate Scientists
Cott, Cheryl
Lineker, Sydney
Martino, Rosemary

Patient Based Clinical Research

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

Scientists
Bernstein, Mark
Ferguson, Niall
Tarlo, Susan

Affiliate Scientist
Stephens, Robyn

Visual Science

Senior Scientists
Flanagan, John
Steinbach, Martin
Trope, Graham

Scientists
Hudson, Chris
Wong, Agnes

Affiliate Scientists
Eizenman, Moshe
Ethier, C. Ross
Gallie, Brenda
Irving, Elizabeth
Wilkinson, Frances

Clinical Studies Resource Centre (CSRC)

Members
Anastakis, Dimitrios
Bookman, Arthur
Buys, Yvonne
Chan, Vincent
Chapman, Kenneth
Chung, Frances
Davey, Roderick
del Campo, Jose Martin
Devenyi, Robert
Epstein, Trina
Escallon, Jaime
Etlin, David
Evans, Michael
Farb, Richard
Fung, Ken
Gentili, Fred
Graham, Brent
Hawa, Raed
Iwanochko, Mark
Lam, Wai-Ching
Lam, Robert
Manninen, Pirjo
Massicotte, Eric
McGuire, Glenn
McIntyre, Roger
Melvin, Kenneth
Miyasaki, Janis
Moro, Elena
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
Shaw, James
Silver, Frank
Simons, Martin
Singer, Shaun
Slomovic, Allan
St George-Hyslop, Peter
Stanbrook, Matthew
Stubbs, Barbara
Syed, Khalid
Terbrugge, Karel
Tu, Karen
Tumber, Paul
von Schroeder, Herbert
Wherrett, John
Willinsky, Robert
Wong, Jean
Wong, David
Yu, Eric

Where researchers have more than one affiliation within each institute, only one is indicated. See www.uhnresearch.ca for more information on affiliations.

TWRI RESEARCH COUNCIL

Director, TWRI and Chair, TWRI Research Council
Peter St George-Hyslop

Division Head, Brain, Imaging & Behaviour – Systems Neuroscience
Karen Davis

Division Head, Fundamental Neurobiology
Peter Carlen

Division Head, Genetics & Development
Rod Bremner

Division Head, Health Care & Outcomes Research
Elizabeth Badley

Division Head, Patient Based Clinical Research
Jenny Heathcote

Division Head, Visual Science
Martin Steinbach

Clinical Representative, Krembil Neuroscience Program
Michael Fehlings

Clinical Representative, Musculoskeletal Program
Nizar Mahomed

Clinical Representative, Musculoskeletal Health & Arthritis Program
Robert Inman

Representative, CREdiT
Frances Skinner

Site Leader, TWH
Kathy Sabo

Representative, Research Operations
Peggy McGill

Vice President, Research
Christopher Paige

YEAR IN REVIEW 2008–2009

JUNE 2008: DONATION SPARKS CREATION OF NEW INSTITUTE

The Campbell family announced a long-term gift of $37.5M towards the creation of the Campbell Family Cancer Research Institute (CFCRI), housed at the Ontario Cancer Institute (OCI). Funding for the new institute will support a high content tumour bank; a state-of-the-art Advanced Molecular Profiling Lab (AMPL); and cancer research in tumour metabolism, cancer stem cells, cancer genomics, proteomics, informatics and guided therapeutics. This brings the total support provided to UHN by the Campbell family to $67.5M, the largest cumulative private gift to cancer research in Canada. Dr. Benjamin Neel, Director of OCI, will also serve as the inaugural Director of the CFCRI.

AUGUST 2008: LANDMARK FUNDING FOR UHN ANNOUNCED

The results of the Canada Foundation for Innovation's 2007 Research Hospital Fund (RHF) competition were publicly announced: UHN's Advanced Therapeutics Research Platform was awarded $119.9M, the largest grant in UHN's history. This award will be put towards construction projects and equipment across UHN and will support research in major diseases of relevance to the Canadian population, including cancer, cardiovascular diseases, diabetes mellitus, obesity, rheumatology and neurodegenerative disorders.

(L-R) UHN's Drs. Brenda Gallie, Christopher Paige, Gordon Keller, Richard Weisel, Bob Bell and Benjamin Neel attend the RHF announcement.

The UHN Pathology Tissue bank is located at TGRI and will form the backbone of the core facility.

SEPTEMBER 2008: NEW RESEARCH DISCOVERY CENTRE LAUNCHED

The Biomarker Discovery Centre was launched with facilities located across the UHN campus. The new Centre will help to standardize procedures and establish facilities to collect, process and bank cells for subsequent biomarker analysis. This initiative will allow for greater emphasis to be placed on preventative medicine, individualized therapies and earlier treatment options that may ease disease progression and provide targets for new drug development.

OCTOBER 2008: $2M BOOST TO TWRI HEPATITIS PROGRAM

A multidisciplinary team of investigators, led by TWRI's Dr. Jenny Heathcote, was awarded $2M in National Institutes of Health (NIH) funding towards establishing a Clinical Centre for Chronic Hepatitis B at TWH. The only NIH clinical centre in Canada to be funded, it will support a clinical therapeutic trial and infrastructure examining dual antiviral therapy.

FEBRUARY 2009: NEUROSCIENCE DRUG DISCOVERY TAKES OFF

UHN welcomed Dr. Barry Greenberg to TWRI as Director of Neuroscience Drug Discovery and Development. In his new role, Dr. Greenberg will use his experience from the pharmaceutical and biotechnology sectors to enhance UHN's drug development capacity in the areas of neuroscience—extending into arthritis, cardiology, transplantation, infectious diseases and diabetes—by developing an integrated platform across the research institutes and clinical programs to promote the discovery and development of novel therapeutic compounds. He will work collaboratively with UHN's Technology Development and Commercialization Office to develop all private sector contractual relationships.

Dr. Barry Greenberg, TWRI Director of Neuroscience Drug Discovery and Development

APRIL 2009: LAUDING UHN INVENTORS

(L-R) TDC's Dr. Brian Barber presents OCI's Drs. Igor Jurisica, Ming-Sound Tsao and Frances Shepherd with the 2009 Inventor of the Year Award.

On April 15, 2009, UHN's Technology Development and Commercialization (TDC) Office presented the Inventor of the Year Award to Drs. Ming-Sound Tsao, Frances Shepherd and Igor Jurisica—recognizing the team of inventors that had made the greatest contribution to the advancement of human health by means of a patentable invention at UHN in the past year. The team is responsible for developing a groundbreaking prognostic genomic analysis tool for early stage non-small cell lung cancer.

JUNE 2009: MINISTRY RECOGNIZES INNOVATIVE CANCER RESEARCH

OCI's Drs. Ming-Sound Tsao and Igor Jurisica were awarded funding in Round 3 of the Ministry of Research and Innovation's Ontario Research Fund - Research Excellence program. The project will receive upwards of $4.6M to develop unique, patient-derived xenograft models of lung cancer. It will also develop a robust informatics platform to comprehensively define the molecular genetic abnormalities and critical pathways of this disease. It is anticipated that this innovative project will help overcome current challenges in developing effective therapies for non-small cell lung cancer.

JULY 2009: ENGAGING INTERNATIONAL INDUSTRY IN LOCAL RESEARCH PARTNERSHIPS

UHN President & CEO Dr. Bob Bell (right) speaks with OICR President Dr. Thomas Hudson (left) following the announcement of a new partnership between UHN, Pfizer Inc. and OICR. (Image courtesy of Ministry of Research and Innovation)

Pfizer Inc. and the Ministry of Research and Innovation announced a new partnership with UHN and the Ontario Institute for Cancer Research (OICR) that will provide $6.9M in funding towards finding abnormalities in the genetic makeup of colon cancer cells and developing drugs to target these aberrations. The project, led by OCI's Dr. Bradly Wouters, could lead to new treatments for colon cancer patients that have a poor chance of recovery. This project will also aim to develop tests to determine tumour type and whether a patient is likely to benefit from a particular treatment strategy. Drs. John Dick and Catherine O'Brien—also involved with this project—are establishing new experimental models of cancer directly from cancer stem cells.

JULY 2009: NEW FRONTIERS FOR UHN RESEARCH

The Terry Fox Foundation announced $12.5M in operating and equipment support to UHN's Drs. Christopher Paige, Bradly Wouters and Robert Bristow under the New Frontiers Program Project Grant competition. These grants are awarded to groups of investigators and support new frontiers in Canadian cancer research—breakthrough and transformative biomedical, clinical and translational research which may form the basis for innovative cancer prevention, diagnosis and/or treatment.

SEPTEMBER 2009: CELEBRATING SCIENCE AT THE McEWEN CENTRE

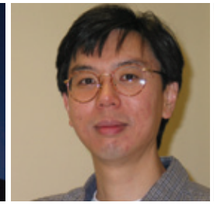
Michael J. Fox speaks to members of the media at the launch of Fox's foundation as a registered Canadian charity.

The McEwen Centre for Regenerative Medicine and TWH joined efforts with The Michael J. Fox Foundation for Parkinson's Research on September 24, 2009, to celebrate the cutting-edge research conducted at UHN. The event celebrated the formal launch of Fox's foundation as a registered Canadian charity and included a research roundtable discussion open to the public featuring clinicians and researchers from UHN, including Drs. Anthony Lang, Connie Marras and Michael J. Fox Foundation advisory board member Andres Lozano.

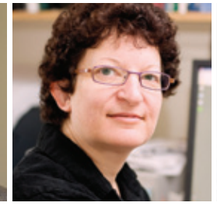
Honour Roll

UHN Investigators Recognized for Their Contributions to Biomedical Research

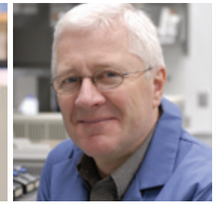
Dr. Claire Bombardier
- Canada Research Chair in Knowledge Transfer for Musculoskeletal Care (Tier I)



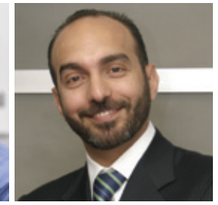
Dr. Peter Cheung
- Canada Research Chair in Chromatin Regulation (Tier II)
- Early Researcher Award, Ministry of Research and Innovation



Dr. Karen Davis
- Inducted into the Johns Hopkins Society of Scholars



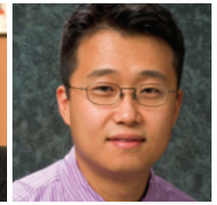
Dr. John Dick
- E. Donnall Thomas Lecture and Prize, American Society of Haematology



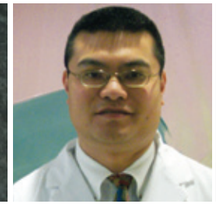
Dr. Alejandro Jadad
- Canada Research Chair in eHealth Innovation (Tier I)

Dr. Kevin Kain
- Canada Research Chair in Molecular Parasitology (Tier I)
- Bailey K. Ashford Medal, American Society of Tropical Medicine and Hygiene

Dr. Tony Lam
- Early Researcher Award, Ministry of Research and Innovation



Dr. Douglas Lee
- Early Researcher Award, Ministry of Research and Innovation



Dr. Geoffrey Liu
- William E. Rawls Prize, National Cancer Institute of Canada

Dr. Andres Lozano
- Jonas Salk Award, Ontario March of Dimes

Dr. Tak Mak
- Named to Order of Ontario
- Canada Research Chair in Inflammation Responses and Traumatic Injury (Tier I)
- Inducted into the Canadian Medical Hall of Fame

Dr. Benjamin Neel
- Premier's Summit Award, Ministry of Research and Innovation

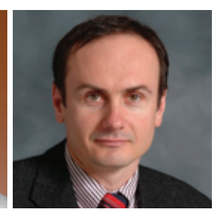
Dr. Pamela Ohashi
- Canada Research Chair in Autoimmunity and Tumour Immunity (Tier I)

Dr. Lyanne Schlichter
- Rick Gallop Award, Heart and Stroke Foundation of Ontario

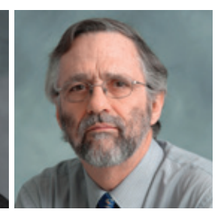
Dr. Frances Shepherd
- Named to Order of Ontario

Dr. Charles Tator
- Inducted into the Canadian Medical Hall of Fame

Dr. Murray Urowitz
- Evelyn V. Hess, M.D., MACP, MACR Award, Lupus Foundation of America



Dr. Allen Volchuk
- Canada Research Chair in Diabetes (Tier II)



Dr. Brian Wilson
- Robert L. Noble Prize, Canadian Cancer Society

Building the Krembil Discovery Centre

Ushering in a New Era of Discovery

THE TORONTO WESTERN RESEARCH INSTITUTE (TWRI) IS SETTING ITS SIGHTS ON 2012 when the doors to the new Krembil Discovery Centre (KDC) are slated to open. The $165M facility will create a research centre along Nassau and Leonard Streets that will rival the most modern research facilities worldwide.

The building received initial funding with a $30M lead gift from Robert Krembil and an additional $30M through the Toronto General & Western Hospital Foundation. In 2007, further KDC funding was awarded through the Canada Foundation for Innovation's Research Hospital Fund Large-Scale Institutional Endeavours competition. Construction on the nine-story, 400,000 square foot building is set to begin in December 2009 and will be spearheaded by a project team that includes Prism Partners, Stantec in partnership with NXL Architects, SNC Lavalin, Merrick Canada ULC and ABE (AMEC, Black and McDonald, and Ellis Don).

Five and a half floors of dedicated research space will house state-of-the-art biomedical research facilities, and KDC will be home to some of the country's leading research programs in arthritis and rheumatism, autoimmune diseases such as lupus and fibromyalgia, spinal cord injury, stroke, Parkinson's disease, epilepsy, Alzheimer's disease, brain tumours and aneurysms, pain disorders, Tourette syndrome, eye diseases (macular degeneration, diabetic retinopathy, retinal disease, glaucoma, corneal disease) and orthopedics such as bone and joint disorders.

The KDC research areas will provide open, flexible wet lab environments that will include tissue culture, electrophysiology, imaging, molecular biology, biochemistry and flow cytometry. Dry lab environments will include space for data analysis and write-up, seminar rooms and occupational health. Unique to the new facility is the 'Sky Lobby', a series of two-floor glass enclosures built into the corner of the structure designed to promote collaboration between research groups.

The development of KDC provides an opportunity for 50,000 square feet of purpose-renovated space within TWH for clinical research teams currently located at TWRI. KDC will also include two and a half floors that will be dedicated to Rehabilitation Solutions—a successful UHN enterprise that provides innovative solutions for health and disability management. Revenues will assist in financing and building operational costs.

Currently, TWRI is home to over 120 researchers and more than 130 trainees from around the globe, and in 2008/09, it attracted over $27M in external funding. As explained by UHN's VP of Research Dr. Christopher Paige, "There was no question that TWRI was in need of better research space to house its top flight research programs. The KDC will allow us to attract and retain the top medical researchers which will ensure continued advancement."

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Arthritis & Autoimmunity Research Centre Foundation

Highlight: Power of Movement

Participants perform the Crescent Moon posture at the 2009 Power of Movement event.

"Power of Movement's strength lies in its ability to connect with young people."

-Erin Moraghan, Senior Development Officer, AARC Foundation, and Founder, Power of Movement

ONE PHONE CALL AND ONE CARING listener at UHN's Arthritis & Autoimmunity Research Centre (AARC) Foundation: these were the roots of Power of Movement, the world's largest public hot yoga class.

Yoga teacher Dorna Chee called the AARC Foundation in 2005 with the idea of using yoga to help people manage autoimmune illness, as she had done during her own long recovery from near kidney failure associated with lupus. Erin Moraghan, Senior Development Officer at the Foundation, was deeply moved by her story and desire to help others, so she developed the idea to create a large-scale yoga fundraiser—the Power of Movement challenge—which harnesses the power of yoga to improve the lives of those with arthritis and autoimmune illness and to raise awareness and funds for new research in these areas.

Launched initially in Toronto in 2007, Power of Movement held its third annual event on February 22, 2009. Over 1,500 participants—led by notables such as world-renowned Moksha Yoga co-founders Ted Grand and Jessica Robertson—gathered together to practice yoga in 10 cities from coast-to-coast to raise more than $250,000 for the AARC Foundation. "Net proceeds from Power of Movement are directed to the Foundation's annual grant of $1,000,000, which supports three main disciplines representative of the range of science undertaken at AARC: cellular and molecular biology, clinical therapeutics and outcomes, as well as population health," explains Gerri Grant, Executive Director of the AARC Foundation.

"Based on feedback from the inaugural event, key AARC scientists have become increasingly involved in the annual challenge," notes Moraghan, also Founder of the event. Participants in the 2009 Power of Movement event included TWRI investigators Drs. Mark Erwin and Barry O'Shea, who examine disc degeneration and ankylosing spondylitis, respectively. Along with representatives from Moksha Yoga, Dr. O'Shea hosted an informative Q & A session on the Power of Movement and good musculoskeletal health.

Moraghan sees great potential for Power of Movement as it continues to evolve. In 2008, she traveled to India to complete her yoga training and is now a certified Moksha Yoga instructor. This will enable her to achieve one of her goals: informing the younger generations about the impact of arthritis-related conditions for people of all ages.

Power of Movement is creating a deep and lasting impact on people from all walks of life. One example is Kelly Tipler, a volunteer who was diagnosed with Wegener's Granulomatosis, a form of vasculitis, while in her early 20s. "In a matter of months, I had gone from being a triathlete to barely being able to climb the stairs without getting winded," explains Tipler. "I always knew that I had to raise awareness for Wegener's, but the question was, how?" Since learning about the AARC Foundation's Power of Movement, I have been a top fundraiser and have joined the planning committee to help make a difference. This is my way of raising awareness about vasculitis and to help AARC researchers work toward finding cures for the many autoimmune diseases that exist today."

As Moraghan notes, "Power of Movement's strength lies in its ability to connect with young people—and to help them see that progress in arthritis research is changing patients' lives."

Princess Margaret Hospital Foundation

Highlight: Weekend to End Breast Cancer

Participants start off the Weekend to End Breast Cancer at the Princes' Gates in Toronto.

"Everyone who walks 'becomes' something or someone different after experiencing The Weekend."

-Paul Alofs, President & CEO of PMHF

THE ROAD TO VICTORY OVER BREAST cancer is being shortened thanks to the thousands of participants and volunteers in the Weekend to End Breast Cancer (WEBC)—the largest single-event breast cancer fundraiser held in Toronto and organized by the Princess Margaret Hospital Foundation (PMHF).

The sixth annual WEBC was held in Toronto on September 5-7, 2008 with the participation of 4,757 women and men whose lives have been touched by breast cancer. Over a two-day period, the participants walked a 60-kilometer circuit within the city in an effort that raised over $13M for breast cancer research at UHN. As Paul Alofs, President and CEO of PMHF, states, "This event celebrates survivors, remembers those who have lost their battle and helps us continue building awareness and raising funds that will make a significant difference for survivors today and for future generations."

"The Weekend to End Breast Cancer is our major fundraiser for breast cancer research at The Princess Margaret Hospital," explains Dr. Benjamin Neel, Director of the Campbell Family Cancer Research Institute and the Ontario Cancer Institute. "Over the last ten years, there has been much advancement in our understanding of breast cancer progression and these findings have begun to translate into the clinic. For the first time, breast cancer death rates are actually falling. But there is still much to do, and support will help scientists at one of the world's top five cancer research centres make further progress against this major killer of our mothers, wives, daughters and friends."

Funds raised from the WEBC are directed to leading research programs at UHN as well as to clinical enhancements and a survivorship program at the Princess Margaret Hospital. Examples of research receiving support from the WEBC include Drs. Tak Mak and Hal Berman's studies on the link between breast cancer and ovarian cancer, Dr. Pamela Ohashi's research into T cell activation and tumour immunity, and Dr. Norman Boyd's work on breast cancer prevention with a focus on understanding mammographic density as a risk factor.

Other examples of programs supported by WEBC funds include Dr. David McCready's Breast Cancer Rapid Diagnosis program—a pilot program designed to provide same-day testing, diagnosis and treatment planning for breast cancer—as well as Dr. Pamela Catton's unique Survivorship Program at the Princess Margaret Hospital, which also provides reconstructive breast surgery for women who have had breast cancer. PMHF stakeholders are updated on the use of WEBC funds at a public symposium held in March of each year at the Ontario Cancer Institute.

Future walks will incorporate several exciting changes. As Christine Anderson, Business Development Manager at PMHF explains, "The event has expanded to support gynecologic cancers and will be renamed in 2010 as 'The Weekend to End Women's Cancers'. In addition, to better accommodate participant schedules and physical abilities, a one day 30-kilometer 'Weekend Lite' option is now offered along with the ability to check-in online. These enhancements will encourage first-time walkers and make the event more inclusive and convenient for all participants."

"Everyone who walks 'becomes' something or someone different after experiencing The Weekend to End Breast Cancer," notes Alofs. "You become part of a group that has done a courageous thing. You become an advocate for breast cancer research, treatment and survivorship. You become more than a participant in a fundraising event; you become someone who steps up and steps forward instead of stepping back and stepping away. As my dear late Mom would remind us, 'Becoming is Superior to Being.'"

Toronto General & Western Hospital Foundation

Highlight: Grand Cru Culinary Wine Festival

Over the past year, TG&WHF has raised $55.7M

At Grand Cru 2008, guests of Clayton Ruby and Madame Justice Harriet Sachs—including Dr. Gary Lewis (far right), Senior Scientist at the Toronto General Research Institute—enjoyed a dinner prepared by Chefs Ryo Ozawa and Toshio Tomita.

THE PAST YEAR AT UHN RESEARCH has been filled with significant discoveries—many of which are world firsts—and would not have been possible without the significant support from the Toronto General & Western Hospital Foundation (TG&WHF), which is responsible for supporting the priority needs of the Toronto General and Toronto Western Research Institutes. Over the past year, TG&WHF has raised $55.7M in net funding for research, education and the enhancement of patient care.

Specifically, TG&WHF supports 13 campaigns year round, which range in focus from heart disease, organ failure, diabetes, Parkinson's disease, stroke and arthritis through the coordination of a variety of events throughout the city. Events have included charity golf tournaments, A Night to Celebrate, The 8 Ball, Moto Amore, International Pub Night and an evening at the races with Horse and Boogie.

One of the grandest events organized by the Foundation this year was the Grand Cru Culinary Wine Festival, which raised $1M in support of the I^3 Centre and brought the total amount raised by Grand Cru events over the past four years to $5.5M. Located at the Toronto General Hospital, the I^3 Centre is a new cardiovascular imaging facility that merges highly specialized and talented cardiologists with the latest in imaging, intervention and innovation in cardiovascular diagnosis and treatments. Event proceeds went towards supporting research programs at I^3 and will contribute to further strengthening the Toronto General Hospital's role as a global leader in cardiac research and care.

The Festival provided an opportunity for Toronto's elite corporate community, wine connoisseurs, prominent local and international chefs, notable vintners, and UHN scientists—including Drs. Tirone David, Gordon Keller, Andres Lozano and Gary Lewis—to meet. Also included in the Festival was an exclusive wine tasting followed by 19 dinner parties hosted at some of Toronto's most distinguished homes. The feast included wines from world-class vintners matched with gourmet cuisine specially prepared by renowned chefs.

In 2009, the Grand Cru Culinary Wine Festival will hold its third live auction and half of the proceeds will support the McEwen Centre for Regenerative Medicine, while the remaining funds will support research at the Toronto General and Toronto Western Hospitals.

University of Toronto Transplantation Institute

Fostering Scientific Partnerships

UHN celebrated the establishment of the University of Toronto Transplantation Institute at a gala dinner. Attendees included (front row, L-R) Dr. Christopher Paige, Gillian Howard, Marnie Escaf, Dr. Bryce Taylor, (back row, L-R) Dr. Richard Reznick, Dr. John Parker, Dr. Bob Bell, Dr. Charles Chan and Dr. Gary Levy, Founding Director of the Institute.

ON MAY 4, 2009, THE MULTI-ORGAN Transplant (MOT) Program at the University of Toronto officially announced the creation of the University of Toronto Transplantation Institute. The announcement serves as no surprise for a program that has emerged as Canada's leading hub of clinical transplant excellence and that has achieved international fame for its research contributions to the fields of transplantation and regenerative medicine.

Explains UHN President & CEO Dr. Bob Bell, "University Health Network is honoured to partner with the new University of Toronto Transplantation Institute. We have a remarkable group of people supporting our Multi-Organ Transplant Program under the direction of Dr. Gary Levy."

Dr. Levy, a TGRI Senior Scientist and Medical Director of the MOT, has been responsible for merging transplant programs in kidney, lung, heart and liver at four Toronto teaching hospitals—Toronto General Hospital, Toronto Western Hospital, St. Michael's Hospital and the Hospital for Sick Children. Home to some of the world's best transplant investigators and clinician-scientists, the MOT program has contributed significantly to life-changing advances in transplantation techniques, care and research, including:

- North America's first islet cell transplant into a patient with Type 1 diabetes;
- The first successful kidney transplant program in Canada;
- The first successful single and double lung transplants in the world;
- Highly successful living-related liver and kidney transplant programs;
- The largest program for lab-based and clinical research in solid organ transplantation in Canada;
- Over $5.2M per year in peer-reviewed research funding from the National Institutes of Health and the Canadian Institutes of Health Research awarded to investigators affiliated with the MOT Program, and;
- $20M of funding from the Canada Foundation for Innovation that established research programs in tolerance induction and genomics/proteomics in 2003.

"With innovation and the highest clinical and academic quality for patient care in mind, the Transplant program performs approximately 250 transplants annually, provides follow-up care to over 2,500 transplant recipients, and serves as a model for many other transplant centres around the world," explains Dr. Levy.

In the winter of 2008, the internationally respected program with a history of innovative findings that impact patient care announced that a patient at TGH had become the first person to ever receive reconditioned lungs using the Toronto XVIVO Lung Perfusion system. TGRI Senior Scientist Dr. Shaf Keshavjee, the inventor of this system, conducted external-to-the-body repairs to injured donor lungs, rendering them acceptable for transplant. The technique is expected to significantly expand the donor organ pool and improve patient outcomes.

The Transplantation Institute will be led by Dr. Levy in its inaugural year, with additional governance from a 12-member Advisory Board of stakeholders from across the University of Toronto and its affiliated hospitals, as well as from the government, the business community and the public. The Board will be chaired by the Vice-Provost, Relations with Health Care Institutions and will provide advice and recommendations to the Institute with respect to strategic planning, operations and growth.

Over $35M of New Funding to Advance UHN Priorities

Supporting Areas of Strategic Importance

2008/09 MARKED ANOTHER REMARKABLE YEAR FOR UHN IN THE CANADA FOUNDATION for Innovation (CFI) competitions. The most recent round of New Initiative and Leading Edge Fund competitions resulted in three research teams receiving a collective total of $15.4M in new infrastructure funding and $4.6M in operating funding. Later in the year, these projects were collectively awarded an additional $15.4M through the Ontario Research Fund (ORF) Research Infrastructure program, resulting in a funding total of over $35M.

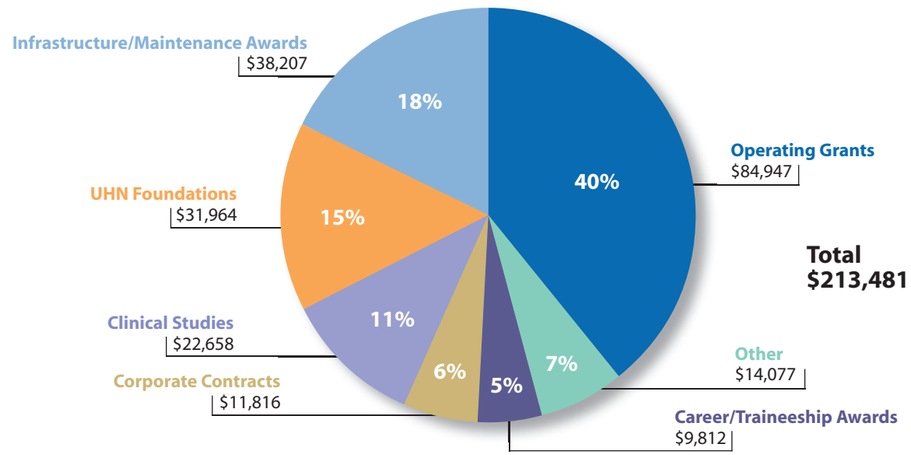
The "Ontario Regional Center for Cell and Vector Production," led by Dr. Armand Keating, will serve as a core facility for the preparation of clinical grade cell and vector products for six collaborating institutions across the province: Ottawa Health Research Institute, McMaster University, University of Western Ontario, St. Michael's Hospital, Sunnybrook Hospital and UHN. With approximately $7.4M in CFI funding, this 25,000 square foot facility, located at UHN, will service a full spectrum of therapeutic cell and gene research, including regenerative medicine, cancer and immune dysregulation.

Dr. David Jaffray's "Robotic Positioning for Image-Guided Surgery and Radiation Therapy" project will establish two state-of-the-art facilities at UHN that integrate imaging technology and robotics in the therapeutic suite. These two translational research environments, which secured over $5.5M in CFI funding, will allow clinician scientists to develop and apply minimally invasive MR-imaging, radiation, surgery and robotics technologies to patients at an accelerated rate, leading to rapid advances in the delivery of cancer and neurological health care.

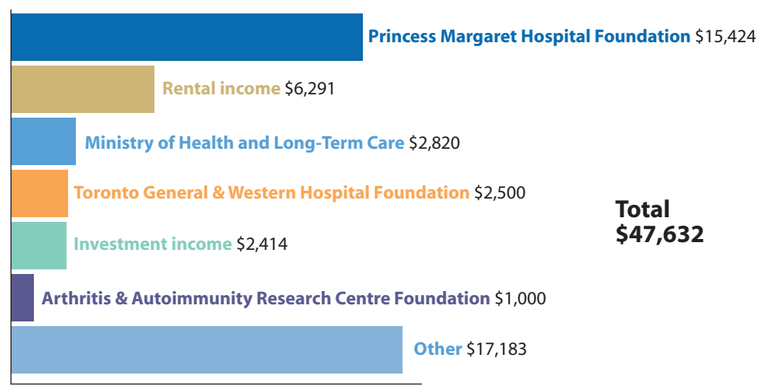
"NanoMed Fab: A Nanofabrication Centre for Personalized Medicine," led by Dr. Gang Zheng, was awarded approximately $2.5M in CFI funding to establish a Centre for the creation of nanoparticles and associated therapies, and to move these new therapies from the laboratory towards studies in patients. The goal is to create novel tools for improving tumour visualization, which will help with earlier detection and more effective treatment strategies for cancer patients. Nanoparticles will also be used to create more targeted therapies for the treatment of cancer and cardiovascular disease.

FUNDING

Total Project Funding Awarded by Type
(in thousands)



UHN Research Core/TMDT Operating Funding
(in thousands)



All figures represent fiscal year 2008/09 and include Ontario Cancer Institute (Princess Margaret Hospital); Toronto General Research Institute (Toronto General Hospital); and Toronto Western Research Institute (Toronto Western Hospital). Figures may not sum due to rounding.

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.

External Agencies Funding UHN Research

Top Sources of External Funding (in thousands)	
Canadian Institutes of Health Research	$40,733
Canada Foundation for Innovation/Ontario Research Fund (Ministry of Research and Innovation)	$34,718
Ontario Institute for Cancer Research	$8,352
National Institutes of Health	$7,815
National Cancer Institute of Canada	$5,891
Heart and Stroke Foundation	$3,884
Canada Research Chairs Program	$3,733
Ontario Genomics Institute	$2,451

Abbott Laboratories
Abbott Vascular
Actelion Pharmaceuticals
ActiViews
Advanced Cardiovascular Systems
Advanced Neuromodulation Systems
Aegera Therapeutics
AGA Medical
American Health Assistance Foundation: National Glaucoma Research
Alba Therapeutics
Alcon Canada
Allon Therapeutics
Alnylam Pharmaceuticals
Alzheimer Society of Canada
American Association for the Study of Liver Diseases
American Association of Neurosurgical Surgeons
American Association of Physicists in Medicine
Amgen Canada
Amorfix Life Sciences
Amyotrophic Lateral Sclerosis Association
Anthera Pharmaceuticals
AOSpine North America
Ardea Biosciences
Arius Research
Arthritis Society
Astellas Pharma Canada
AstraZeneca Canada
Aventis Pasteur
Aviva Canada
Banting and Best Diabetes Centre
Bayer
Beckman Coulter
Bill & Melinda Gates Foundation
BioDiscovery Toronto
Biogen Idec
Bioniche Therapeutics
BioTheryx
Boehringer Ingelheim
Brain Tumour Foundation of Canada
Bristol-Myers Squibb
Canada Foundation for Innovation
Canada Research Chairs Program
Canadian Anesthesiologists' Society
Canadian Arthritis Network
Canadian Association for the Study of the Liver
Canadian Association of Radiation Oncologists
Canadian Breast Cancer Foundation
Canadian Breast Cancer Research Alliance
Canadian Chiropractic Protective Association
Canadian Cystic Fibrosis Foundation
Canadian Dermatology Foundation
Canadian Diabetes Association
Canadian Foundation for AIDS Research
Canadian Institutes of Health Research
Canadian Liver Foundation
Canadian Lung Transplant Study Group
Canadian Patient Safety Institute
Canadian Stroke Network
Canadian Urologic Oncology Group
Cancer Care Ontario
Cancer Research Institute
Cancer Research Society
Cardiokine Biopharma
Celgene
Centocor
Centre for Addiction and Mental Health
Cephalon
Cervical Spine Research Society
ChemGenex Pharmaceuticals
Chiron
Christopher Reeve Paralysis Foundation
CHUM - Centre Hospitalier de l'Université de Montréal
Colon Cancer Canada
Council of Ontario Universities
Craig H. Neilsen Foundation
CSL
Cyclacel
DaVita
Den Haag Trust
DermaPort
Dystonia Medical Research Foundation
Eastman Kodak Company
Elekta Instrument
Elekta Oncology Systems
Eli Lilly Canada
Ethicon
European Hematology Association
Exelixis
Expression Diagnostics
Eye Research Institute of Canada
Fight for Sight
The Foundation Fighting Blindness - Canada
Gambro BCT
Gemin X Biotechnologies
Genentech
Genome Canada
Genzyme
Gilead Sciences
Glaucoma Research Society of Canada
GlaxoSmithKline
Government of Ontario
Hamilton Health Sciences
Hana Biosciences
Heart and Stroke Foundation
Hoffman-La Roche
Hospital for Sick Children
Howard Hughes Medical Institute
Human Genome Sciences
Innovive Pharmaceuticals
Intercept Pharmaceuticals
International Institute for Research in Paraplegia
International Society for Heart & Lung Transplantation
Janssen-Ortho
Johnson and Johnson
Juvenile Diabetes Research Foundation International
Juvenile Diabetes Research Foundation Canada
Keryx Biopharmaceuticals
Kidney Foundation of Canada
KuDOS Pharmaceuticals
Kyphon
Lawson Health Research Institute
Leukemia & Lymphoma Society
Ontario Lung Association - Ontario Thoracic Society
Lupus Clinical Trials Consortium
Lupus Ontario
Lymphoma Foundation Canada
Mayo Clinic
McMaster University
Med BioGene
Medical Council of Canada
Medicure
Medpace
Medtronic MiniMed
Medtronic Neurological
Medtronic of Canada
Merck Frosst
MethylGene
MGI Pharma
The Michael J. Fox Foundation for Parkinson's Research
Microvention
Miikana Therapeutics
Millenium
Ministry of Health and Long-Term Care
Ministry of Research and Innovation
Mizutani Foundation for Glycoscience
Momenta Pharmaceuticals
Montreal General Hospital Research Institute
Mount Sinai Hospital
Multiple Myeloma Research Foundation
Multiple Sclerosis Society of Canada

National Alliance for Research on Schizophrenia and Depression
National Blood Foundation
National Cancer Institute of Canada
National Institutes of Health
Kidney Foundation of Canada
National Postdoctoral Association
National Sanitarium Association
Natural Sciences and Engineering Research Council of Canada
Networks of Centres of Excellence
NCE: Canadian Arthritis Network
NCE: Canadian Network for Improved Outcomes in SLE
NCE: PrioNet
NCE: Stem Cell Network
Neuroprotection
Neuroscience Institute
Neurosurgery Research and Education Foundation
NoNO
Novalung
Novartis
Novo Nordisk Canada
NPS Pharmaceuticals
Nuvelo
Nycomed Amersham
Ontario Centres of Excellence: Centre of Excellence for Photonics
Ontario Council on Graduate Studies
Ontario Genomics Institute
Ontario HIV Treatment Network
Ontario Institute for Cancer Research
Ontario Mental Health Foundation
Ontario Neurotrauma Foundation
Ontario Rett Syndrome Association
Ortho Biotech
Osiris Therapeutics
Paracor Medical
Parkinson Society Canada
Pfizer Canada
Philips Electronics North America
Photopharmacia
Physicians' Services Inc. Foundation
Physiotherapy Foundation of Canada
Princess Margaret Hospital Foundation
Prostate Cancer Research Foundation of Canada
Proteolix
Quintiles
RaySearch Medical
ResMed Foundation
Respironics Sleep and Respiratory Research Foundation
Rheuminations
Royal College of Physicians and Surgeons of Canada
SAIC Frederick
Sangamo Biosciences
Sanofi-Aventis
Schering Canada
Schering-Plough Research Institute
Servier Canada
Shire Human Genetic Therapies
Siemens Medical Solutions Germany
Society for Progressive Supranuclear Palsy
Society of American Gastrointestinal and Endoscopic Surgeons
SuperGen
Susan G. Komen Breast Cancer Foundation
Synthes Spine Company
Teva Neuroscience
Thallion Pharmaceuticals
Thoratec
Toronto General & Western Hospital Foundation
Trillium Therapeutics
U.S. Army Medical Research Acquisition Activity
University of British Columbia
University of Pennsylvania
University of Toronto
Ventana Medical Systems
Vertex Pharmaceuticals
ViroPharma
VistaGen Therapeutics
Workplace Safety and Insurance Board
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