**Welcome Messages**

**Robert S. Bell, MDCM, MSc, FACE, FRSC, President & CEO, 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.

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

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 (TASHN) 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 (TGR) and Toronto Western Research Institute (TWR)—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.

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**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.**
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 Endowments award in support of UHN’s ATRP. This award—the largest single research award in UHN’s history—including $9.2M 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, Drug Discovery & Development, and Immunity in Health & Disease. 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

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FOUNdATIONAL THEMES

• High-throughput screening
• Partnerships with industry
•  Process chemistry, toxicology, production (GMP) stem cell & biomaterials
•  Functional analysis in pre-clinical models, Clinical trials, Functional or clinical improvement

SCIenCEThEMES

• Efficacy
•  Process chemistry, toxicology, production (GMP) stem cell & biomaterials
•  Functional analysis in pre-clinical models, Clinical trials, Functional or clinical improvement

The remaining three themes are classified 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.
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.
BLOOD CANCER: EXCITING NEW MODEL

JUVENILE MYELOMONOCYTIC leukemia (JML)—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 JML, 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 JML 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(8): 4414-24. This work was supported by the National Institutes of Health.

STROKE: POTENTIAL NEW DRUGS FOR BRAIN PROTECTION

DESPITE ITS ENORMOUS socioeconomic implications, stroke has not yet been significantly impacted by neuroprotectants—drugs that prevent or dramatically slow the deterioration of brain cells. An exciting series of studies conducted by Dr. Michael Tymianski and colleagues at TWR, the University of Western Ontario, the Hospital for Sick Children, the University of PSI 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 signalling 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).

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 TWR 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 TGI 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.

CANCER IMAGING: BUILDING NEW TREATMENT DOSE PRACTICES

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 cancer. 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.

BREAST CANCER: ASSESSING RISK EARLY IN LIFE

AN OCT 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 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(s): S69-80. This work was supported by the Canadian Breast Cancer Research Alliance.

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 aneurysms, 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 defects 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): 637-34.
MALARIA: UNCOVERING DIAGNOSTIC TOOLS

Dr. Kevin Kain

IN A WORLD FIRST FINDING, TGRM 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): e912. 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

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.

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—indeed, of the 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 Princess Margaret Hospital Foundation, Genome Canada through the Ontario Genome Institute, IBM, and fellowships from the ProCan Foundation and the Canadian Institutes of Health Research’s Excellence in Radiation Research for the 21st Century Strategic Training Initiative in Health Research Program.

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THYROID CANCER: IDENTIFYING MARKERS OF DISEASE

OCI’S DR. SYLVIA ASA AND Shereen Ezat, 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 Banchi 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 its advantage—such is the case with poxviruses.

“Mice who do not have CCR5 expression in T cells or orally and has been shown to 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.”

ENDOMETRIAL CANCER: ASSESSING TREATMENT FEASIBILITY

BETWEEN 36 AND 87 PERCENT of endometrial cancer patients oversupply 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 or amplifications 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): 4379-35. This work was supported by the Natural Sciences and Engineering Research Council of Canada and the Canadian Institutes of Health Research.

J Urol. 2009 Mar; 83(5): 2226-36. 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

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 radiotherapy (SBRT)—which involves delivering high doses of radiation precisely to tumour sites within the body—OCCI’s Dr. Laura Dawson and colleagues Drs. James Brierley, Rebecca Wong, Bernard Cummings, Jolee Ringash and Jennifer Knox recruited 66 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 69%.

“We’ve seen in this study that 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 of 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 favored strategies that improved quality of life but reduced survival time.

“Our findings show that when presented with these options, 55% of patients chose oral inotropes, preferring a significantly shorter life with fewer symptoms,” says Dr. Ross. “Alternatively, 43% 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, 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.).

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.

“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

TGRF’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.

“In contrast to existing treatment strategies, 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 fluclo.

Dr. Laura Dawson

Dr. Paul Fortin

Dr. Sharon Walmsley
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.

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.

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 TGR 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.

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

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.
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. 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.”

“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.

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—in mature 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.

“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.”

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LUNG TRANSPLANTATION: INCREASING THE DONOR POOL

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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. “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.”

ORGAN TRANSPLANTATION: IMPORTANT MOLECULE FOR PREVENTING REJECTION

DR. GARY LEVY AND colleagues at TGR 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.

TRANSPLANT REJECTION: UNMASKING THE ROLE OF SPECIAL IMMUNE CELLS

REGULATORY T CELLS ARE specific 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 1 diabetes. How these cells are involved with this action, however, is largely unknown. “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,” says Dr. Levy.

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 inflammation and immune disorders.”

“Recent studies from the laboratories of Dr. Li Zhang and colleagues at TGR 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.”

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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 TWR’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 impulsive 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.” 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 (Q2)—that could induce death in human and mouse cancer cells.

More importantly, it was found that Q2 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.

“Q2 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 Jan; 13(6): 748-55. This work was supported by the Canadian Institutes of Health Research.
The Research Pipeline at the UHN Board of Trustees Retreat

Transforming Discovery to Impact Health

TRANFORMATION 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.

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.”

UHN has a longstanding history of driving discoveries to improve patient outcomes.
### OCI BY THE NUMBERS

**Research Space**
373,000 sq ft

**Publications**
373,000

**Total External Funding**
$112,878,000

### STAFF & STUDENTS

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### RESEARCH COUNCIL ON ONCOLOGY (RCO)

- **Director, Ontario Cancer Institute and Chair, RCO**: Benjamin Nadel
- **Division Head, Applied Molecular Oncology**: Andrew Rudin
- **Division Head, Biophysics & Bioimaging**: Brian Wison
- **Division Head, Cancer Genomics & Proteomics**: Linda Penn
- **Division Head, Psychosocial**: Gary Robinson
- **Division Head, Signaling Biology**: Mitsuhiro Iwakura
- **Division Head, Stem Cell & Developmental Biology**: Howard Rutter

### Clinical Representatives

- **Clinical Representative, Radiation Oncology**: Mary Gospodarowicz
- **Clinical Representative, Surgical Oncology**: Jonathan Crawford
- **Clinical Representative, Medical Oncology**: Michelle Olson
- **Clinical Representative, Pathology**: Sylvia Aas

### Where researchers have more than one affiliation, only one is listed. See www.uhnresearch.ca for more information on affiliations.
Appointments as of June 30, 2009. Research space figure is approximate due to ongoing construction.

Total External Funding $73,193,000

Toronto General Research Institute

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Toronto General Research Institute
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

Brain, Imaging & Behaviour - Systems Neuroscience
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Brichta, Jonathan
Chen, Robert
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Jungst, Jan
Mills, Linda
Sichteln, Lyanne
Stankel, Ellis
Talier, Charles
Tsi, Florence
Wilner, Joanne

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Division Head, Health Care & Outcomes Research
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Division Head, Clinical Research
Jenny Heathcote

Division Head, Visual Science
Martin Steinbach

Clinical Representative, Krembil Neuroscience Program
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Nizar Mahomed

Clinical Representative, Musculoskeletal Health & Arthritis Program
Robert Immen

Representative, CRADT
Frances Skinner

Site Leader, TWRI
Kathy Sobo

Representative, Research Operations
Peggy McGill

Director, TWRI and Chair, TWRI Research Council
Pete St George-Hyper

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

Toronto Western Research Institute

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

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 THM. The only NIH clinical centre in Canada to be funded, it will support a clinical therapeutic trial and infrastructure to enhance UHN’s drug development capacity in the 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.

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 neuroscience extending into arthritis, cardiology, transplantation.

APRIL 2009: LAUDING UHN INVENTORS
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 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.

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

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JULY 2009: ENGAGING INTERNATIONAL INDUSTRY IN LOCAL RESEARCH PARTNERSHIPS

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. Bradley 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, Brady 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

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

Honour Roll
UHN Investigators Recognized for Their Contributions to Biomedical Research

Dr. Claire Bombardier
- Canada Research Chair in Knowledge Transfer for Manual Osteopathic Care (Tier I)
- Bailey K. Ashford Medal, American Society of Tropical Medicine and Hygiene
- Inducted into the Canadian Medical Hall of Fame

Dr. Peter Chung
- Canada Research Chair in Chromatin Regulation (Tier II)
- Ministries of Research and Innovation

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

Dr. John Dick
- E. Donnell 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 Pathology (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, American Society of Tropical Medicine and Hygiene

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

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

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Dr. Murray Hime
- Evelyn F. Price, MD, MACF Medical Research Council Award Foundation of America

Dr. Alan Yakubov
- Canada Research Chair in Diabetes (Tier II)

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

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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.”
**Arthritis & Autoimmunity Research Centre Foundation**

**Highlight: Power of Movement**

One phone call and one caring listener at UHN’s Arthritis & Autoimmunity Research Centre (AARC) Foundation 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 Dr. 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’s strength lies in its ability to connect with young people.”

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

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Participants perform the Crescent Moon posture at the 2009 Power of Movement event.
Princess Margaret Hospital Foundation

Highlight: Weekend to End Breast Cancer

“Everyone who walks ‘becomes’ something or someone different after experiencing The Weekend.”

-Paul Alofs, President & CEO of PMHF

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.”

-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 centers 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.

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Toronto General & Western Hospital Foundation

Highlight: Grand Cru Culinary Wine Festival

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

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 $1M in support of the i3 Centre and the Festival, which raised $5.5M. Located at the Toronto General Hospital, the i3 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 i3 and the feast included wines from world-class vintners, international chefs, notable vintners, and some of Toronto’s most distinguished homes. 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 Lazaro 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.

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.

Dr. Levy, a TGRI senior scientist and Founding Director of the Institute, 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.”

University of Toronto Transplantation Institute

Fostering Scientific Partnerships

• 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 THG had become the first person to ever receive reconditioned lungs using the Toronto Xvivo Lung Perfusion system. TOH Senior Scientists Dr. Shaf Keshavjee, the inventor of this system, conducted external-to-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 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.

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 Otsava and Toshih Tamita.
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 23,000 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.

These figures have been validated through the UHN Research Financial Services and Research Grant and Contract Services. These figures may not be due to rounding.

All figures represent the 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). These figures may not include all programs and services.
External Agencies Funding UHN Research

Top Sources of External Funding (in thousands)

<table>
<thead>
<tr>
<th>Source of Funding</th>
<th>Amount</th>
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<tbody>
<tr>
<td>Canadian Institutes of Health Research</td>
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Abbott Laboratories
Abbott Vascular
Actelion Pharmaceuticals
Actelion
Advanced Cardiovascular Systems
Advanced Neuromodulation Systems
Aegera Therapeutics
AGA Medical
American Health Assistance Foundation
American Glaucoma Research
Alba Therapeutics
Alcon Canada
Alcon Therapeutics
Alinka Pharmaceuticals
Alzheimer Society of Canada
American Association for the Study of Liver Diseases

American Association of Neurosurgical Surgeons
American Association of Physicians in Medicine
Amgen Canada
Amofax Life Sciences
Amyotrophic Lateral Sclerosis Association
Andhera Pharmaceuticals
AOSpine North America
Ardex Biosciences
Arixus Research
Arthritis Society
Astellas Pharma Canada
AstraZeneca Canada
Avestis Pasteur
Aviva Canada
Banting and Best Diabetes Centre
Bayer
Beckman Coulter
Bill & Melinda Gates Foundation
BioDiscovery Toronto
Biogen Idec
Bioniche Therapeutics
BioThyrx
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
Colón Cancer Canada
Council of Ontario Universities
Craig H. Neilson Foundation
CSL
Cyclocel
DaVita
Den Haag Trust
DermaPort
Dystonia Medical Research Foundation
Eastman Kodak Company
Elekta Instrument
Elekta Oncology Systems
El Lilly Canada
Ethicon
European Hematology Association
Exelixis
Expression Diagnostics
Eye Research Institute of Canada
Fight for Sight
The Foundation Fighting Blindness - Canada
Gambr BCT
Gemini 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
Innovative 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 BioGen
Medical Council of Canada
Medicare
Medpace
Medtronic MinMed
Medtronic Neurological
Medtronic of Canada
Merck Frosst
MethylGene
MGI Pharma
Millennium
Mizutani Foundation for Glycoscience
Momenta Pharmaceuticals
Montreal General Hospital
Research Institute
Mount Sinai Hospital
Multiple Myeloma Research Foundation
Multiple Sclerosis Society of Canada