NET RESULTS
REPORT ON RESEARCH AT UNIVERSITY HEALTH NETWORK
EXPRESS
December 2012

Welcome to the Year in Review Issue of Net Results EXPRESS

Net Results EXPRESS (NRx) is an award-winning, monthly e-newsletter highlighting medical and scientific breakthroughs, major grants and honours awarded, and other research-related events at UHN. In this special issue, you can read about selected research accomplishments and milestones of the past year of our five research institutes, the Ontario Cancer Institute (OCI), the Toronto General Research Institute (TGRI), the Toronto Western Research Institute (TWRI), the Toronto Rehabilitation Institute (TRI) and the Techna Institute for the Advancement of Technology for Health (Techna).

We hope you will find this newsletter informative and helpful and we wish you a festive holiday season. If you have feedback or questions, please contact www@uhnresearch.ca.

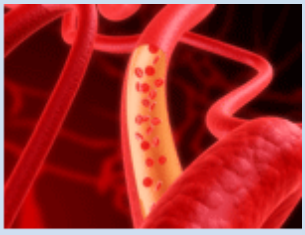
Christopher J. Paige, PhD, FCAHS
Vice President, Research
UHN

2012 Research Breakthroughs

January

Ovarian Cancer: Drug Delays Disease Progression

An international ovarian cancer clinical trial, co-led by OCI's Dr. Amit Oza, found that bevacizumab (Avastin®) held off disease recurrence for two months and delayed disease progression. For women with the highest disease risk, the delay was five to six months. It is the first time in 15 years that a new drug for ovarian cancer has demonstrated improved outcomes. [Abstract]



Avastin® blocks the formation of blood vessels in a growing tumour, depriving it of nutrients.

Hormone Therapy: Bone Density Monitoring in Prostate Cancer Patients

Androgen deprivation therapy (ADT) is often prescribed for patients with prostate cancer. However, one of the side effects of ADT is an increased risk of bone fractures that occurs as a result of decreased bone density. Low bone density can be easily measured and monitored using bone mineral tests (BMT). TGRI and TRI's Dr. Shabbir Alibhai found that although the rate at which physicians ordered BMTs increased between 1998 and 2008, it still remained low, suggesting that there should be more education on the use of BMTs when monitoring and treating patients

Honour Roll

A selection of honours conferred this past year

OCI Researchers Honoured

UHN congratulates all of the OCI researchers who were recognized over the past year. Some of the scientists honoured this year include:

Dr. Mary Gospodarowicz was elected President of the Union for International Cancer Control at an international conference held in Montreal. Not only is Dr. Gospodarowicz the first Canadian to be given the prestigious position, she is the first woman to hold the post.

Dr. Benjamin Neel was elected to the American Association for Cancer Research (AACR) Board of Directors. Dr. Neel also served as the Chairperson of the 2012 AACR Annual Meeting which brings together scientists from all areas of cancer research.

Prostate Cancer Canada honoured Dr. Robert Bristow with the *John Ferguson Memorial Award for Prostate Cancer*. The award is given to individuals whose "outstanding impact in the fight against pancreatic cancer is an inspiration to others".

Dr. Fei-Fei Liu was named the Health Sciences Honouree for the 2012 Israel Cancer Research Fund's *Women of Action Award* in acknowledgment of her outstanding achievements in the field of cancer research.

on ADT. [Abstract]

February

Structural Biology: Insights on the Mechanics of Calcium Release

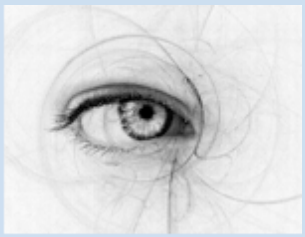
Calcium release is critical for biological processes and is regulated by specialized channels that act as calcium 'gates' or receptors. It is unclear exactly how these gates function, however, a study by OCI's Dr. Mitsuhiko Ikura which compared the structures of two different types of calcium receptors found that they have comparable structures that orient in a similar manner to allow calcium release. These findings increase our understanding of how calcium release is controlled at the cellular level and will be useful in determining how calcium regulates biological responses. [Abstract]

Development: Imprinting in the Mouse Genome

There are two copies of each chromosome in the genome, one from each parent. For a number of genes, one parental copy is shut off by a phenomenon known as 'imprinting'. Imprinting errors can lead to developmental and chronic diseases. TWRI's Drs. Cathy Barr and James Eubanks carried out a systematic survey of the mouse genome, and identified 23 new—and unknown—imprinted regions. They also found a pattern in the genetic code that predisposes genes to imprinting, which may help guide the development of treatments that correct imprinting errors involved in disease. [Abstract]

Neurology: Controlling the Growth of Neurons

A small number of factors in careful balance control the formation of connections between cells in the nervous system. TWRI's Dr. Philippe Monnier found that one protein involved in this process—repulsive guidance molecule (RGMa)—is cut into seven smaller forms. Six of these forms were able to block nerve cell growth by interacting with another protein. If the other proteins that guide the formation of connections can also be split into multiple functional forms, there may be more diversity in the cues that guide neural growth and development than previously thought. [Abstract]



RGMa is key to the proper development of the central nervous system, including the retinal ganglion in the eye.

March

Stroke: Development of a New Neuroprotective Drug

During a stroke, regions of the brain are deprived of blood and oxygen, leading to neurological impairment or death. TWRI's Dr. Michael Tymianski has demonstrated the neuroprotective effects of a drug, a postsynaptic density (PSD95) inhibitor, which prevents the neurotoxic reactions that occur in tissue deprived of oxygen. The treatment reduced the neurological damage associated with stroke even after the time when conventional therapies no longer have an effect. [Abstract]

April

Spinal Cord Injury: Reducing Inflammation with a Smart Material

Dr. Gary Rodin received the Canadian Association of Psychosocial Oncology *Life Time Achievement Award* in tribute to his distinguished career in the field of psychosocial oncology which has focused on studying the psychosocial challenges that patients and their families endure when they are faced with advanced or terminal cancer.

Drs. Frances Shepherd and Michael Baker were awarded the *Queen Elizabeth II Diamond Jubilee Medal*, created to celebrate The Queen's 60 year reign and given to Canadians in honour of their contributions to society.

Dr. Alex Vitkin was elected as a Fellow of the Optical Society of America in recognition of his contributions to the field of biophotonics and biomedical optics.

Techna Researcher Honoured

Dr. Joseph Cafazzo received the World Congress mHealth Innovation Congress People's Choice Award on behalf of the Centre for Global eHealth Innovation for the bant diabetes app which was created to help patients manage their diabetes

TGRI Researchers Honoured

UHN congratulates all of the TGRI researchers who were recognized over the past year. Some of the scientists honoured this year include:

Dr. Daniel Winer received the *Benjamin Castleman Award* from the Massachusetts General Hospital and the United States and Canadian Academy of Pathology.

Dr. Brain Hodges was recognized by the Canadian Association for Medical Education with the *2012 Ian Hart Award for Distinguished Contribution to Medical Education*.

Dr. Eleanor Fish was awarded the Canadian Society for Immunology *2012 Investigator Award*.

Drs. I George Fantus and Gary Lewis and UHN's Dr. Eleftherios Diamandis are among 53 new Fellows inducted into the Canadian Academy of Health Sciences.

Dr. Angela Cheung received the *2012 Dr. David Sackett Senior Investigator Award* from the Canadian Society of Internal

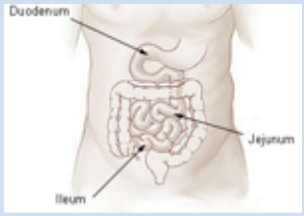
Following a spinal cord injury, some patients will experience a condition called post-traumatic syringomyelia (PTS), severe inflammation in the tissue surrounding the spinal cord associated with chronic pain or paralysis. TWRI's Dr. Michael Fehlings examined the use of a specific 'smart material'—a gel that holds a therapeutic agent in place near the injury and slowly releases it over time—in an experimental model of PTS. When the gel was injected into the tissue surrounding the injured spinal cord, the extent of inflammation and scarring was significantly reduced. [Abstract]

PTS is associated with progressive weakness and stiffness in the limbs and chronic, severe pain.

May

Diabetes: Regulation of Glucose by the Intestine

Gastrointestinal bypass surgery decreases the risk of diabetes in obese patients by reducing blood glucose levels; however, the mechanism by which it does so is unknown. A study by TGRI's Dr. Tony Lam found that when nutrients are redirected from the stomach into a part of the intestine known as the jejunum, there is a decrease in blood glucose levels that occurs without any change in insulin levels. This suggests that the jejunum can sense and control glucose levels. Understanding how this occurs may be useful in developing new treatments for diabetes. [Abstract]



The intestine is believed to interact with the brain to regulate blood glucose levels.

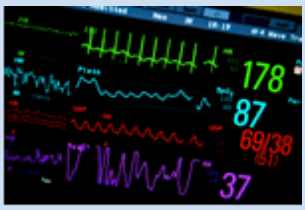
Hypertension: Efficacy of Home Blood Pressure Telemonitoring

Techna's Drs. Joseph Cafazzo, Peter Rossos and Anthony Easty reported on the effectiveness of a home telemonitoring system that helps patients monitor their blood pressure and sends them messages that alert them if it is too high. The home telemonitoring system was found to be effective at reducing patients' blood pressure without the use of medications or visits to physicians. [Abstract]

June

Patient Care: Model Predicts Risk of Mortality After Heart Failure

TGRI's Dr. Douglas Lee and his team developed and validated a model to predict acute heart failure mortality, known as the Emergency Care Heart Failure Mortality Risk Grade system (EHMRG). The system was developed to predict the risk of mortality by using variables that are routinely collected in the clinic including blood pressure, hemoglobin concentration and transportation by emergency medical services. EHMRG will be a useful tool for physicians when making the decision on whether or not to hospitalize or discharge coronary heart patients. [Abstract]



Approximately 50,000 Canadians are newly diagnosed with heart failure each year.

Pancreatitis: How Alcohol Damages the Pancreas

Chronic alcohol abuse causes a number of negative health effects, including pancreatitis—an inflammation of the pancreas. TWRI's Dr.

Medicine for research excellence by a general internist.

TRI Researchers Honoured

UHN congratulates all of the TRI researchers who were recognized over the past year. Some of the scientists honoured this year include:

Drs. Geoff Fernie, Catriona Steele and Dina Brooks were awarded the *Queen Elizabeth II Diamond Jubilee Medal*.

Dr. Fernie was recognized for his work in developing solutions for problems commonly encountered by people with disabilities

Dr. Steele was awarded this medal for her contributions to gerontology through her research into the causes and treatments of swallowing disorders.

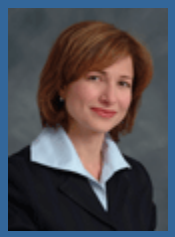
Dr. Brooks was honoured for her research into new methods of rehabilitation for patients with chronic lung disease.

TWRI Researchers Honoured

UHN congratulates all of the TWRI researchers who were recognized over the past year. Some of the scientists honoured this year include:

Dr. Charles Tator received the *2012 Council Award* from the College of Physicians and Surgeons of Ontario in recognition of his achievements in neurosurgery research, education, teaching and advocacy.

Drs. Tator and Michael Fehlings were awarded the *Reeve-Irvine Research Medal* for Spinal Cord Injury Research from the Reeve-Irvine Research Center at the University of California for their contributions to spinal cord repair.



Dr. Rosemary Martino was elected a Fellow of the American Speech-Language-Hearing Association (ASHA), one of the highest forms of recognition given by ASHA.

Dr. Murray Urowitz was awarded a *Queen Elizabeth II Diamond Jubilee Medal* in recognition of his longstanding contributions to lupus research and his work in the field of rheumatology.

Herbert Gaisano explains, "It's not alcohol itself that is toxic, but rather its metabolites, the byproducts of its breakdown by the body." His research team exposed pancreatic cells to different alcohol metabolites and found that the metabolites caused a decreased ability to secrete digestive enzymes critical for the breakdown of food. [Abstract]

July

Leukemia: An Experimental Model for AML Provides New Insights

Mutations in the gene for isocitrate dehydrogenase 1 and 2 (IDH1/2) are frequent in acute myeloid leukemia (AML). OCI's Dr. Tak Mak and colleagues recently investigated the most common IDH1 mutation in an experimental model, showing that it caused enlarged spleens and decreased blood-producing cells in bone marrow, characteristics of AML. The mutation also affected the epigenome—a non-genetic mechanism that controls gene expression without altering the genetic sequence—shedding light on the mechanism linking the mutation to the disease. [Abstract]

August

Medical Care: Effects of Social Pressure on Surgical Performance

A study led by TGRI's Dr. Carol-anne Moulton found that appropriate surgical behaviour requires surgeons to be decisive and confident and is strongly influenced by surgical culture. This leads to performance that may impact surgical judgment and decision making. Observations from the study suggest that by identifying social pressures that influence their surgical identity, surgeons can better manage their responses to social pressure which could help prevent surgical errors. [Abstract]

As the responsibilities of a surgeon increase, so do the demands placed on them to show confidence and certainty.

September

Osteoporosis: Inaccurate Assessment of Fracture Risk

Physicians will use extra care when treating patients that have an increased risk of developing fractures. TRI's Dr. Susan Jaglal sought to determine how accurate fracture risk assessments are in Ontario's non-urban areas. The research team re-evaluated assessments from 48 patients, and showed that over 50% of the reports underestimated the risk of future fractures. Osteoporosis Canada has already updated their fracture risk assessment guidelines to remedy this gap. [Abstract]

Fracture risk assessments use bone mineral density to determine a patient's risk of developing fractures.

October

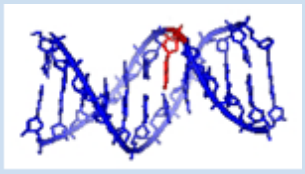
Cancer: A Single DNA Nucleotide Difference Regulates Breast Cancer Cell Growth

In 2012 Dr. Andres Lozano received a number of awards and accolades. He received the *Pioneer in Medicine Award* from the Society of Brain Mapping and Therapeutics and the *2012 Olivecrona Medal* from the Karolinska Institutet, both awarded in recognition of his research in deep brain stimulation. He was also named one of 53 new Fellows inducted into the Canadian Academy of Health Sciences for 2012.

UHN Inventor of the Year

Dr. Aaron Schimmer was presented with UHN's *2012 Inventor of the Year Award* which is given annually to an exemplary researcher whose innovations have made a major impact to the field of biomedical research. Dr. Schimmer received the award for his research in drug development in which he studies known drugs to determine if they may be efficacious in treating diseases other than those they are normally used for.

A specific type of variation in DNA—known as a single nucleotide polymorphism (SNP)—can alter gene expression and potentially increase the risk of developing breast cancer. OCI's Dr. Mathieu Lupien used a novel computational method to show that breast cancer risk-associated SNPs preferentially target the elements that regulate gene expression instead of directly targeting genes to promote cancer growth as previously thought. [Abstract]



Thousands of DNA variants are associated with human traits and disease, however the mechanism by which they promote disease risk has remained elusive.

Heart Disease: Effect of Depression on Coronary Heart Disease

A study by TRI and TGRI's Dr. Sherry Grace examined the results of 22 different studies to determine the effects that depression may have on coronary heart disease (CHD) outcomes. This analysis found that patients that suffered from depression either before or after CHD diagnosis were more likely to have adverse cardiac events or die from CHD. These observations underscore the need to investigate therapeutic interventions that may improve the moods of CHD patients. [Abstract]

Treatment of depression in patients with heart disease can improve quality of life and may reduce cardiac morbidity.

November

Heart Disease: Improving Outcomes with Surgery

Diabetic and heart disease patients with narrow or blocked arteries often undergo one of two procedures to restore blood flow. These are coronary-artery bypass grafting (CABG), where healthy blood vessels are transplanted to bypass the blocked artery, or percutaneous coronary intervention (PCI), in which a balloon is used to inflate the blocked artery and a tube is placed to keep the artery open. TGRI's Dr. Michael Farkouh led a clinical trial comparing the two surgeries and found that CABG was more effective at reducing rates of death and heart attacks in patients with diabetes and heart disease albeit with an increased risk of stroke. [Abstract]

Diabetes is a leading risk factor for heart disease or stroke in Canada.

Cancer: Palliative Care Referral Practices in Oncology

Specialized palliative care (SPC) services can help lessen physical and psychosocial symptoms in patients with advanced cancers through a holistic approach. OCI's Dr. Camilla Zimmermann surveyed oncologists across Canada regarding their SPC referral practices. Oncologists with access to more comprehensive services or to services that accepted patients still receiving chemotherapy tended to refer patients to SPC earlier. One third would refer to SPC earlier if it was renamed 'supportive care', indicating that there may be biases associated with the term 'palliative care'. [Abstract]

Highlights: Research Growth & New Initiatives

Dr. Kevin Kain Awarded International Funding

TGRI's Dr. Kevin Kain received a four-year, $1.25M award from the Preventing Preterm Birth (PPB) initiative—a Grand Challenge in Global Health administered by the Global Alliance to Prevent Prematurity and Stillbirth, an initiative of Seattle Children's. PPB funding will be used towards Dr. Kain's research into the discovery of new biological signatures and interventions to prevent preterm birth and stillbirth associated with placental malaria.

UHN Researchers Awarded with FedDev Ontario Funding

In June, the Government of Canada, through the Federal Economic Development Agency for Southern Ontario (FedDev Ontario), announced an investment of nearly $11M towards accelerating the commercialization of neurotechnologies, in partnership with the Ontario Brain Institute, universities and private sector companies. UHN's Drs. Geoff Fernie, Andres Lozano and Kieran Murphy will lead three of the 14 funded projects focused on the prevention, early diagnosis and treatment of brain disease.

UHN Researchers Capture New Funding from Canadian Cancer Society

OCI's Dr. Senthil Muthuswamy and TGRI's Dr. Andrea McCart were both awarded with Innovation Grants from the Canadian Cancer Society. These grants support unconventional concepts, approaches or methodologies to address problems in cancer research. This funding will enable Dr. Muthuswamy to use a three-dimensional biological model he created to unravel the mystery of how pancreatic cancer develops, and will support Dr. McCart's research into viruses engineered to target cancer cells.

OCI Researcher Awarded a Canada Research Chair

OCI's Dr. Thomas Kislinger successfully renewed his Tier II Canada Research Chair (CRC) in Proteomics in Cancer Research this past March. Dr. Kislinger's CRC will provide funding over the next five years to support his research program, which is aimed at using proteomics to identify biomarkers and molecular mechanisms of epithelial ovarian cancer and will help develop tools to improve the diagnosis of this cancer.

Dr. Fish Receives Early Researcher Award

TGRI's Dr. Jason Fish received an Early Researcher Award (ERA) from the Ontario Ministry of Economic Development and Innovation. The ERA program helps promising, recently appointed Ontario researchers build their research programs. The award will support Dr. Fish's research into the molecular mechanisms that govern blood vessel pathology. His lab will seek to develop innovative therapeutic strategies that block blood vessel inflammation by manipulating the expression of microRNAs.

TRI Start-up Wins Business Venture Award

Simple Systems Inc.—founded by TRI's Dr. Milos Popovic and members of the Neural Engineering and Therapeutics Team—won the *2012 TiEQuest Business Venture Competition*. The company is in the process of commercializing RECLAIM, a rehabilitation therapy that helps patients paralyzed by stroke, spinal cord injury or traumatic brain injury restore voluntary movements using electrical stimulation. Simple Systems was also awarded the *TiEQuest 2012 Best Intellectual Property Award*.

UHN Patient Diagnostic Simulation Software a Success

This year UHN's Perioperative Interactive Education (PIE) team in the Department of Anesthesia and Pain Management at the Toronto General Hospital distributed the Virtual Interactive Case (VIC) software designed by TGRI Scientific Associate Dr. Gordon Tait and Tabby Lulham, a member of the PIE team. VIC software helps health providers gain clinical experience by allowing them to develop and practice their diagnostic skills. The software is now being used by the University of Toronto's Faculty of Medicine, Toronto General Hospital, Mount Sinai Hospital, St. Michael's Hospital, Hypertension Canada, George Brown College School of Nursing, Sunnybrook Health Sciences Centre and the Centre for Addiction and Mental Health. It was also awarded first prize in the Canadian Health Care Education Commons Virtual Patient Challenge.

Final Construction Beam Hoisted for Krembil Discovery Tower

The final structural beam of the Krembil Discovery Tower was hoisted to the top of the building on August 22nd. The Tower will be a state-of-the-art facility to house research teams exploring new treatments across a spectrum of diseases, which include stroke, brain cancer, depression, spinal cord injuries, Parkinson's disease, epilepsy, Alzheimer's disease, arthritis, vision research and a range of neurodegenerative and neuromuscular conditions. The contributions of philanthropists Robert and Linda Krembil, the Canada Foundation for Innovation, the Toronto General & Western Hospital Foundation and generous donors have helped create this important research endeavour.

2012 Annual Research Report

To read more about research over the past year, UHN's 2012 Research Report is available. This 52-page report features top UHN research from 2012, including top research events, prestigious awards, UHN's Foundations, as well as feature articles on the Techna Institute for the Advancement of Technology for Health, TRI's cutting edge iDAPT facility and marketplace innovation at UHN.

Feedback

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