The following research breakthroughs are a selection of the achievements made by UHN researchers this year. For more research stories see Net Results and Net Results EXPRESS archives.

January

A family of enzymes called the disintegrin metalloproteases were found to be associated with structural changes in the heart tissues of congestive heart failure patients, according to Toronto General Research Institute (TGRI) researchers Drs. Ren-Ke Li and Richard Weisel. Congestive heart failure is usually associated with weakened heart muscle and reduced ability of the heart to pump blood. [Pubmed abstract]

February

A research team led by Dr. Sylvia Asa at Ontario Cancer Institute (OCI) has discovered that mice lacking Ikaros, a gene implicated in immune system cell development, suffer from stunted growth. This research shows for the first time that Ikaros plays a role in brain development by directing higher centres in the brain that control the hormonal production of growth signals. [Pubmed abstract]

March

Blood vessel repair is influenced by the direction in which the cells are polarized. A team of TGRI researchers led by Dr. Lowell Langille has discovered that manipulating the activity of the molecule GSK-3ß can reverse the direction of a cell's polarity. These findings may lead to improvements in the treatment of vascular diseases. [Pubmed abstract]

Research conducted by Dr. Rod Bremner of Toronto Western Research Institute (TWRI) has shown that manipulating the expression of a gene called Chx10 in the retina promotes progenitor cells to become bipolar neuron cells—the first in a series of nerve cells that transmit visual information to the brain—diverting them from becoming rods. These findings may help in discovering new treatments for eye diseases.[Pubmed abstract]

Adult brain stem cells transplanted into the sites of spinal cord injuries in rats multiply and replace missing spinal cord cells, partially regrow the missing myelin sheath, and help restore mobility, according to a study led by TWRI's Dr. Michael Fehlings. [Pubmed abstract]

April

TWRI's Dr. Peter St George-Hyslop and his research team have discovered the molecule, TMP21, that produces the toxic compound amyloid beta. Amyloid beta is the toxin that accumulates around nerve cells in the brain, causing them to die and the brain to degenerate. This discovery might have profound implications for the treatment of Alzheimer's disease. [Pubmed abstract]

May

New TGRI research could contribute to development of new treatments for blood vessel disorders such as atherosclerosis, restenosis and hypertension. A research team led by Dr. Mansoor Husain has discovered that a specific calcium-sensitive protein complex called cyclin E/CDK2 triggers the switch between different vascular smooth muscle cells growth cycle stages, important for the development of new tissues and structures. [Pubmed abstract]

June

A new finding stresses the need for alternative therapies for people with anorexia. A recent study conducted by Dr. Allan S. Kaplan of TGRI, in collaboration with and Columbia University's Dr. B. Timothy Walsh, found that the commonly prescribed antidepressant fluoxetine does not reduce the risk of relapse for patients with anorexia nervosa, highlighting the need for development of additional options including psychotherapy and innovative medications. [Pubmed abstract]

AML1-ETO, generated by translocation between chromosomes 8 and 21, occurs in up to 15% of acute myeloid leukemias (AML). Researchers at the OCI laboratory of Dr. Mitsu Ikura have revealed the three-dimensional solution structure of an AML1-ETO fusion domain critical for E protein interaction (TAFH domain) using NMR spectroscopy. These results provide a deeper insight into leukemia and may one day contribute to the design of therapeutic chemical inhibitors. [Pubmed abstract]

July

UHN regenerative medicine researchers led by Dr. Ren-Ke Li have identified the SOS distress signal that mobilizes a subset of bone marrow cells, expressing the cell surface molecule c-kit, to the heart after a heart attack. This signal helps stimulate the growth of new blood vessels in the heart after damage. [Pubmed abstract]

September

A research study following 109 survivors of acute respiratory distress syndrome (ARDS) has established that patients experience reduced health-related quality of life two years after being discharged from an intensive care facility. The findings of this study, conducted by TGRI's Drs. Margaret Herridge, Angela Cheung and their colleagues, suggest that investigating early intensive rehabilitation programs could be worthwhile for improving long-term outcomes for ARDS survivors. [Pubmed abstract]

October

OCI/TGRI's Dr. John Dick and his team, reported that a monoclonal antibody directed to the adhesion molecule CD44 decreased cancer stem cells in a type of leukemia. The emerging “cancer stem cell model”, first proposed by Dr. Dick and colleagues, suggests that cancers arise from stem cells that could be targeted for therapy. This study, using a mouse model, may offer new strategies for treating acute myeloid leukemia, for which existing therapies offer only a 30% long-term survival rate. [Pubmed abstract unavailable]

Improved patient understanding leads to a willingness to consider joint replacement surgery as a treatment option for debilitating arthritis of the hip and knee. Results of a recent prospective study, led by TWRI’sDr. Elizabeth Badley, of 2,103 individuals with disabling hip and/or knee arthritis show that willingness to consider

surgery was the strongest predictor of the time to first total joint arthroplasty. These findings highlight the importance of patient education. [Pubmed abstract unavailable]

November

Establishing factors that determine the fate of hematopoietic stem cells (HSC) is critical for the development of regenerative medicine. Currently there is little known about how an HSC's fate is decided. Using a sophisticated method to track human blood cells transplanted into mice, Dr. John Dick and his colleagues discovered that there was a wide variation in the cell division and renewal properties of the blood cells that were transplanted, and that the fate of HSCs is unpredictable before they enter more rigid 'downstream' developmental programs. [Pubmed abstract]

December

TWRI's Drs. Mark Erwin and Robert Inman have discovered that notochord cells—which are primary cells that organize the developing embryo—release a factor called connective tissue growth factor (CTGF) that may be responsible for providing certain strains of dogs with their remarkable resistance to degenerative disc disease. This research will likely provide the groundwork to regenerate disc cartilage for patient treatment in the future. [Pubmed abstract]

Breaking News from UHN Research

UHN Researchers Capture Record Share of CFI Funding

Announced in Waterloo November 27, UHN researchers have won up to $28M from Canada Foundation for Innovation (CFI) to support five research projects led by Drs. Richard Weisel, Kathy Siminovitch, John Dick, Igor Jurisica and Pamela Catton.

In a record round for UHN, CFI is awarding UHN researchers with $21,494,110 for infrastructure and up to $6,448,233 for operating funding to be allocated at a later date, adding up to the largest amount ever awarded by CFI to UHN in a single round. UHN's project success rate was 50% (national average 18%) and its funding success rate was 72% (national average 23%).

The research projects cover a wide scope of research areas: regenerative medicine (Dr. Weisel - $7,200,000), proteomics and genomics (Dr. Siminovitch - $4,800,000), cancer stem cells (Dr. Dick - $4,293,069), computational cancer profiling and modelling (Dr. Jurisica - $4,001,041) and interdisciplinary cancer survivorship (Dr. Catton - $1,200,000). Infrastructure will include animal facilities, sophisticated imaging equipment and computer technologies, among others.

"Our three hospitals are home to some of the most innovative and successful medical researchers in the world and they are fully committed to finding solutions to the pressing medical challenges facing us today," says Dr. Christopher J. Paige, VP UHN Research. "Today's announcement is a major boost that will support

collaboration, discovery and impact."

Overall CFI funded 86 projects across Canada with a maximum CFI investment of $325,000,000.

Congratulations to all the project leaders, their PI teams and their staff who participated in this CFI round as well as to the Research Facilities and Research Communications teams and other members of Research Support Services who supported the work in many ways.

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