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From Basic to Clinical: the Continuum of Research at UHN

A special issue

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The continuum of research—our ability to pursue fundamental research questions, devise treatments based on our observations and then test these treatments in patient volunteers—is a particular strength of UHN. Several factors contribute to this strength:

- Being part of a patient care environment leads to the development of clinically-relevant research questions: e.g., Why is chemotherapy not working in this case? How can we help treat this side effect?
- The proximity of basic researchers and clinician-scientists provides the full spectrum of expertise required to tackle human health problems
- Finally, as a hospital-based research institute, UHN provides a safe and regulated environment for conducting research with human samples and human volunteers—an advantage not available to researchers in universities and private sector R&D departments

“The interplay between research labs and patient care is a driver of innovation” says Dr. Christopher Paige, Vice President, Research. “You can think of this continuum as a 'time-to-patient-impact' chain. UHN researchers make important contributions along the entire length of the chain.”

Biomedical Research Types: The Overview



Basic research:

- Primarily conducted to understand normal and abnormal processes
- May appear to be only indirectly related to a specific disease, but the same basic research finding is often relevant to many diseases
- Many biological processes are conserved across species. e.g., the genes that control the cell cycle in yeast are the same as those that control the cell cycle in humans, so basic research into these processes can make use of animal and in vitro models

Examples of Basic Research

New Channel Associated With Immune Cancers

Cells live and die by regulating the movement of cellular chemicals (ions) across their membranes by using “tiny doors”, or channels, on their surface. Recently, Drs. [Lyanne Schlichter](#) and [Florence Tsui](#) (TWRI/TWH) discovered a new and unusual type of potassium channel that seems to be associated with cancers of the immune system. They have shown for the first time that the gene HERG is upregulated in leukemia cells but not in cells affected with immune disorders. Even more importantly, blocking the activity of the HERG channel slows cancer cell growth. The finding is significant in providing a new marker for, and a potential therapeutic target for, these types of cancers.

J Biol Chem 2002. May; 277:18528-18534

Originally published in Research Report 2003.

Cancer Genes Keep Genome in Check

Before scientists can develop a cure for a disease they must first understand how

cells divide and how they die, and the answer to this lies in our genes. UHN researchers Drs. [Angela Cheung](#) (TGRI/TGH), [Ming-Sound Tsao](#), [Jeremy Squire](#), [Robert Bristow](#) (OCI/PMH), [Razq Hakem](#), and [Tak Mak](#) (AMD/OCI/PMH) recently made progress on this front with their finding that the breast cancer susceptibility gene BRCA2 has an important role in repairing DNA damage in immune cells. They have shown that when this gene is mutated in mice, genetic material becomes unstable and prone to errors. When this mutation is coupled with a mutation in another cancer gene, p53, cell growth goes awry and tumours develop. Together, these findings constitute new insight into the mechanisms of cancer development.

Cancer Res 2002 Nov 1; 62(21):6194-204

Originally published in Net Results EXPRESS ([January, 2003](#))

Protein is Key for Zapping Infected Cells

The first explanation for why people with Wiscott-Aldrich syndrome (WAS) suffer from recurrent infections was recently reported by Dr. [Kathy Siminovitch](#) (TGRI/TGH). WAS, a disorder that affects four out of every 1M male children, is caused by a mutation in the WAS gene. Dr. Siminovitch's research shows that immune T cells require the WAS protein to successfully eradicate infected cells from the body—a process that goes awry in patients with this disease.

Immunity. 2003 Jan;18(1):141-54

Originally published in Research Report 2003.

Translational research:

- Validates if new knowledge obtained in basic research applies to human health and disease
- Conducted to better understand specific aspects of human health
- The first step in developing new or improved diagnostic tests, therapies or procedures
- Can include small-scale clinical research

Examples of Translational Research

Using Forces of Nature to Engineer Better Treatments

Research by Drs. [Ren-Ke Li](#), [Richard Weisel](#) and [Donald Mickle](#) (TGRI/TGH) shows that a mechanical stretch regimen can enhance the formation and strength of cell-engineered cardiac tissue. Growing heart cells on a 3-D biodegradable framework, the team used a computerized stretch machine to apply controlled forces to the cell seeded graft. The regimen improved the growth and organization of the cells, producing tissue grafts that were stronger than grafts engineered without the stretch regimen. This research will help build better cardiac grafts for the repair of heart defects, and may improve the long-term results of cardiac surgery.

Circulation. 2002 Sep 24;106(12 Suppl 1):1137-42

Originally published in Research Report 2003.

Scientists One Step Closer to Personalizing Cancer Care

Personalized cancer therapy has the goal of understanding the specific genetic mutations that produce an individual tumour and how that tumour will respond to treatment. A better understanding of this is the first step towards developing improved screening procedures and therapies for cancer patients. Recently, Drs. [Malcolm Moore](#) and Steve Gallinger (OCI/PMH) and Christine Ribic brought personalized cancer therapy for colon cancer patients one step closer to reality with the development of a simple genetic test designed to determine if chemotherapy will be an effective treatment for their cancer. Their research shows that 100% of patients who have a specific type of mutation in their tumour called “high-frequency microsatellite instability” do not benefit from chemotherapy.



New TWRI Tool Can Identify Idiopathic Disorder

Using the ATECO MRV technology developed at TWRI (auto-triggered elliptic-centric-ordered three-dimensional gadolinium-enhanced MR venography) together with a novel scoring system, Drs. [Karel terBrugge](#), [David Mikulis](#), [Robert Willinsky](#), [George Tomlinson](#), Richard Farb and Irene Vanek of TWRI/TWH and TGRI/TGH were able to diagnose patients with idiopathic intracranial hypertension (IIH) with 93% specificity. IIH is a condition of elevated cerebrospinal fluid pressure in the brain. It primarily affects women of child bearing age who suffer from obesity, and can cause headaches, vision loss and blindness. The disorder was identified by measuring the degree to which the veins in the sinuses were narrowed in 29 IIH patients and 59 control patients. This research is the first to provide a sensitive and specific imaging criterion for diagnosing this disease.

Neurology 2003 May 13;60(9):1418-24

Originally published in Net Results ([Summer, 2003](#))

Clinical research:

- Patient-oriented research that is directly related to the prevention, diagnosis, or treatment of disease
- The testing of specific products in human models such as drugs and treatments, psychological tools, models of disease spread
- Includes clinical trials, observational, epidemiological, intervention and prevention studies
- Findings often relevant to improving health in the short term

Examples of Clinical Research

Heart Disease Risk Greater in Women With SLE

The reason why women with systemic lupus erythematosus (SLE), or lupus, are at greater risk for developing coronary heart disease may be their higher levels of triglycerides and VLDL cholesterol, or “bad” cholesterol, reports Drs. [Murray Urowitz](#), [Dafna Gladman](#) (TWRI/TWH), and [George Steiner](#) (TGRI/TGH). Although many patients can reduce their risk using screening and intervention procedures, more research is needed to learn how to accurately predict the risk of heart disease in these women.

Arthritis Rheum. 2003. Nov;48(11):3159-67

Treating Sleep Disorder Reduces Stress on Tired Hearts

From 25 to 40% of people with heart failure also suffer from obstructive sleep apnea, a disorder in which the muscles of the throat relax during sleep, leading to temporary suffocation and stress on the heart. In a study of 24 patients, Drs. [Douglas Bradley](#) and [John Floras](#) (TGRI/TGH) recently showed that by using a simple device to force air into the lungs during sleep, they could reduce the number of sleep apnea episodes. More importantly, the treatment improved heart function by 35% and reduced daytime blood pressure.

Pioneering Prostate Cancer Treatment Promises Speed

One of the world's first trials of a new method of delivering radiation to treat prostate cancer—called hypofractionated intensity modulated radiation therapy (IMRT)— is currently being tested on 200 patients at OCI/PMH. The new therapy involves delivering larger daily doses of radiation over a shorter period of time, rather than smaller doses over a longer period of time. If the treatment proves effective, the overall treatment times for prostate cancer could be cut in half, doubling the capacity of hospitals to treat patients and improving patient access to care. *Originally published in Net Results EXPRESS ([November, 2003](#))*



At the top, the faces of UHN research include, from left to right: Drs. Igor Jurisica, Cheryl Arrowsmith, Ming-Sound Tsao, Tak Mak, Kevin Kain, Gary Rodin, Jenny Heathcote and Anthony Lang

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