# New Research Breakthroughs at UHN

## Cardiology: Smoothing the Way for SMC

A key factor in the development of contractile smooth muscle cells, or SMCs—which form the walls of blood vessels and regulate circulation—has been identified at TGRI.

A team led by Dr. Mansoor Husain has used knock-out stem cells to create mature cells and tissues capable of cardiac-like beating, but not SMC contractions.

"We're excited by these findings because they are the first of their kind to show the distinctive role of c-myb in smooth muscle cell versus cardiac cell differentiation," says Dr. Husain. "Our studies also provide a tool for monitoring and understanding SMC behaviour in various conditions like those found in heart and circulatory diseases."

*Circ Res. 2008 Jan 10 [Epub ahead of print].* [Pubmed abstract]. *Research supported by the Canadian Institutes of Health Research and the Heart and Stroke Foundation of Ontario.*

## Prostate Cancer: Extending Knowledge of Survival

In attempts to better understand current treatment practices for men with hormone-refractory prostate cancer (HRPC)—patients who have become resistant to hormonal therapy—UHN scientists have revisited a 2004 study to report updated analysis of survival findings from patients administered docetaxel and prednisone, or mitoxantrone and prednisone, combination therapies.

UHN-lead Dr. Ian Tannock and colleagues approached investigators from the 2004 TAX 327 for follow-up information on over 1,000 patients across 24 countries. The patients were treated with docetaxel every 3 weeks, weekly or with mitoxantrone every 3 weeks.

"What we've found in our investigations re-confirms previous findings," notes Dr. Tannock. "Treating with docetaxel every 3 weeks remains the preferred treatment option for most patients with metastatic HRPC."

The median survival of patients on this regimen was the longest of the three treatment option at 19.3 months. Overall, the chances of prolonging survival with this treatment strategy was similar among those patients with higher and lower disease burden as indicated by PSA levels.

*J Clin Oncol. 2008 Jan 10;26(2):242-5.* [Pubmed abstract]. *Research supported by Sanofi-Aventis, Celgene, Centocor, Cytogen and Novartis.*

## Alzheimer's Disease: Krembil Triggers Stimulating

## Findings

Deep brain stimulation (DBS)—implanting battery-powered electrodes into the brain to deliver electrical signals to the brain—has been primarily used in Parkinson's patients and other movement disorders. However, recent findings from a Krembil researchers Drs. Andres Lozano, Mary Pat McAndrews and Colin Shapiro and Richard Wennberg reveal a new potential use for this technology.

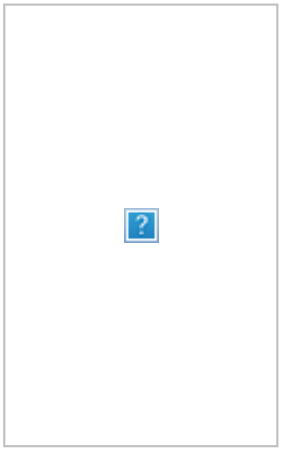
In the course of treating obesity in a patient by stimulating appetite suppressing sites in the hypothalamus, the team serendipitously discovered electrical stimulation triggered a deja vu sensation that consisted of the patient recalling perceptions of being in a park with friends some 30 years earlier. Increasing electrode stimulator intensity caused the memory to become more vivid and detailed.

"This was somewhat of a 'eureka' moment because we knew that unlocking these memories this was something quite unusual," said study lead Dr. Lozano.

Notes Dr. Lozano, "These findings demonstrate that it's possible to access and influence memory circuits and to to improve their function. This may lead to the development of new treatments for tens people with Alzheimer's disease and other memory problems."

*Ann Neurol, 2008; 63:119-123.* [Pubmed abstract].

## Neurology: Balancing Treatment in Rett Syndrome



A new finding from Krembil investigators holds promise for developing new treatment strategies for the genetic condition Rett syndrome, a devastating neurological condition primarily affecting young girls.

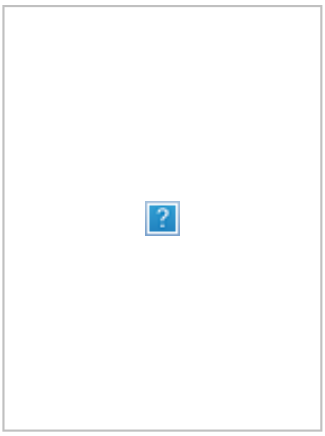
In an animal study, lead Dr. James Eubanks and colleagues replaced, or ‘rescued’, a malfunctioning form of the gene responsible for Rett syndrome with a working copy of the gene. Over a year of observing the behavior of these ‘rescued’ mice, the typical patterns of behavior such as diminished parenting, impaired mobility, and diminished locomotion were restored to normal.

“This is a really exciting finding because we've shown that reintroducing a gene in females could help improve some of the behavioral deficiencies we see in this syndrome,” says Dr. Eubanks. “With continued research, we’re excited to see if we can alleviate other symptoms as well.”

*Hum Mol Genet. 2008 Jan 25 [Epub ahead of print].* [Pubmed abstract].
*Research supported by the Canadian Institutes of Health Research.*

## Retinoblastoma: Finding the Cancer Tipping Point

Studies of a rare childhood eye tumor have provided important insight into the role of genetic disruption in cancer.



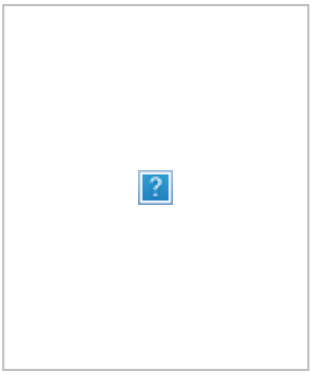
A team led by OCI Senior Scientist Dr. Brenda Gallie and involving Dr. Jeremy Squire and Dr. Helen Dimaras, then a PhD student, studied tissues of patients with cancerous retinoblastoma—and its benign precursor, retinoma—to show the effect of genomic instability, or changes in the number of gene copies in a tissue.

"We've been able to show that loss of the tumor suppressor gene RB1 and low level chromosome instability are insufficient for malignant change until a critical level of instability occurs. This instability likely involves key genes that tip the balance from control to one of uncontrolled cell growth in cancer," notes Dr. Gallie. "These molecular switches will constitute excellent targets for diagnosis, prevention and treatment for these children."

*Hum Mol Genet. 2008 Jan 22 [Epub ahead of print].* [Pubmed abstract]. *Research supported by the National Cancer Institute of Canada with funds from the Terry Fox Run and the Canadian Cancer Society, the Canadian Genetic Diseases Network, the Canadian Institutes for Health Research, the Keene Retinoblastoma Perennial Plant Sale, the Royal Arch Masons of Canada and the Canadian Retinoblastoma Society.*

## Lupus: Tackling Disease Management Early

Collaborative efforts by Krembil researchers Drs. Murray Urowitz, Dafna Gladman, Paul Fortin, and the Systemic Lupus International Collaborating Clinics group are providing additional evidence to support the fact that newly diagnosed patients with systemic lupus should be monitored carefully over time for coronary artery disease (CAD)—a condition where plaque builds-up in the arteries of the heart causing the openings to narrow.

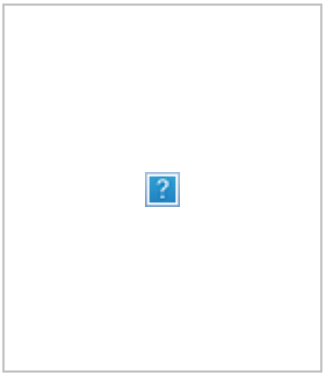


UHN study lead Dr. Urowitz and colleagues followed 278 patients from 27 centers across 11 countries for three years and found that over this period, all known CAD risk factors including hypertension and hypercholesteremia increased over the three year study period.

"What we've found is patients are continuing to accumulate risk factors over time," says Dr. Urowitz. "Although the risk profile was higher in men than in women from start to finish in this study, physicians should continue monitoring patients with known risk factors—such as smoking, diabetes, postmenopause and family history of CAD—to ensure proper disease management."

*Arthritis Rheum. 2008 Jan 31;59(2):176-180 [Epub ahead of print].* [Pubmed abstract]. *Research supported by the Canadian Institutes of Health Research, Lupus Foundation of Ontario, Lupus UK, Lupus Ontario, Conn Smythe Foundation, Tolfo Family, and the Lupus Foundation of America State Chapters of New Jersey, Long Island-Queens, Western New York, and Nashville.*

## Cancer: Coping Together



An OCI study led by Dr. Linda McLean and colleagues Drs. Jennifer Jones, Mary Jane Esplen, Camilla Zimmermann and Gary Rodin has, for the first time, identified the importance of couples intervention for patients facing advanced cancer and their spousal caregivers.

A total of 16 couples were recruited from PMH, enrolled in an Emotionally Focused Couple Therapy study and followed for 8-20 sessions and 3 months post-therapy. During this period, marital function improved significantly over time with 87.5% of the couples showing some improvement or significant improvement. There was a reduction in the mean scores of depression in both patients and spouse caregivers. Interestingly, this improvement was greatest for patients and not the caregiver.

“Although this is a small sample size, we saw a significant improvement in symptoms of depression in subjects over time and the majority of couples felt some benefit from the intervention,” says Dr. McLean. “Couples felt the therapeutic setting was a safe place to express their feelings and future studies will help us better understand how couples can cope during a time of stress.”

*Psychooncology. 2008 Jan 22 [Epub ahead of print].* [Pubmed abstract].
*Research supported by University Health Network (UHN) Allied Health.*

# Breaking News from UHN Research

## Director Lauded with MERIT

UHN congratulates OCI Director and Senior Scientist Dr. Benjamin Neel on the renewal of his MERIT award from the National Institutes of Health.

The MERIT award is presented to experienced researchers who have demonstrated a long-term commitment to and success in research. Awardees are recognized as leaders in their respective fields. Dr. Neel is the only researcher in Canada to hold this honour, and one of only 4 outside the US

## Royal College Recognizes OCI Scientist

The Royal College of Physicians and Surgeons of Canada recently awarded OCI Scientist Dr. Aaron Schimmer the 2008 Royal College Medal in Medicine in recognition of his original work as a clinician-scientist. Dr. Schimmer is recognized for his manuscript “Critical role for Fas-associated death domain-like interleukin-1-converting enzyme-like inhibitory protein in anoikis resistance and distant tumor formation”.

The medal recognizes research contributions by

clinicians who have completed training within the past ten years.

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