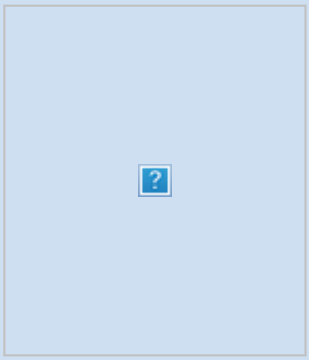
March 2010

Lupus: Understanding the Benefits of Antimalarial Treatment

Recent study findings from a TWRI-led study confirm that administration of the antimalarial drug hydroxychloroquine to patients with systemic lupus erythematosus (SLE)—an autoimmune disorder causing acute or chronic inflammation of multiple organs—reduces the risk of thrombovascular events (TEs) by 68%.



Led by Dr. Paul Fortin, with Drs. Dafna Gladman and Murray Urowitz, the team took a closer look at patients diagnosed with SLE between 1970 and 2004 and matched patients according to year of diagnosis and severity of disease. This approach helped to clarify whether exposure to antimalarial drugs was associated with a decrease in TEs and not a product of changing patterns of medication usage. Overall, the use of antimalarials reduced the risk of arterial and venous TEs by 66% and 74% respectively.

"For patients with SLE, we have identified older age, being older than 50 years of age and ever having hypertension as being associated with an increased risk of TEs," says Dr. Fortin. "Our data support the wide and prolonged use of hydroxychloroquine for the treatment of patients with SLE who do not have any contraindication to treatment with antimalarials. Future studies will help determine what the maximum duration of treatment with antimalarial drugs should be, as well as the side effects of prolonged use."

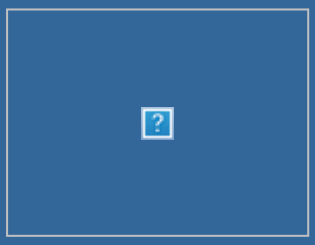
Jung H, Bobba R, Su J, Shariati-Sarabi Z, Gladman DD, Urowitz M, Lou W, Fortin PR. Arthritis Rheum. 2010 Jan 7;62(3):863-868. [Epub ahead of print]. [Pubmed abstract]. *Research supported by the Arthritis Society, the Canadian Institutes of Health Research, Lupus Canada, Lupus Ontario, the Lupus Foundation of Ontario, BC Lupus, and the Arthritis and Autoimmune Research Centre Foundation, the Smythe Foundation, Dance for the Cure, and Flare for Fashion.*

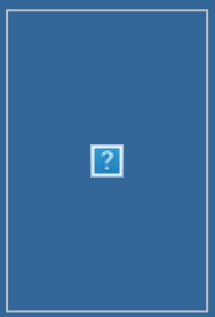
Head and Neck Cancer: Global Screen Identifies Future Therapy Targets

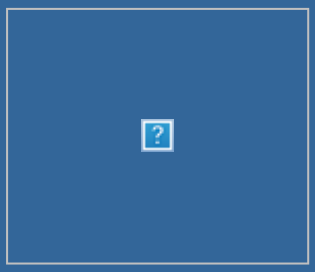
TWRI Breaks Ground on Krembil

Thursday March 4, 2010 marked the beginning of a new era in research and innovation at TWRI with the official groundbreaking ceremony of the highly anticipated Krembil Discovery Centre (KDC).

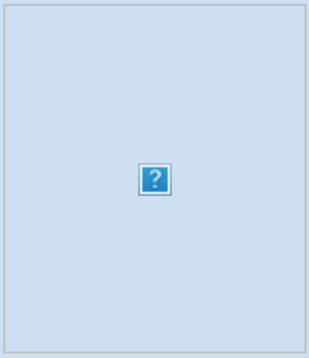
Watch this historic event unfold as told through the photos below.







For patients with head and neck cancer (HNSCC), there is a need to develop predictive molecular signatures; recent findings out of the laboratory of OCI's Dr. Fei-Fei Liu will contribute to this aim.



Comments Dr. Liu, "Patients with locally advanced HNSCC have a 30% 5-year overall survival rate which translates into a major opportunity to treat patients based on the molecular abnormalities of their disease. Specifically, with the development of predictive tests, health care teams could significantly improve patient selection for appropriate treatment, and guide the development and evaluation of new therapies."

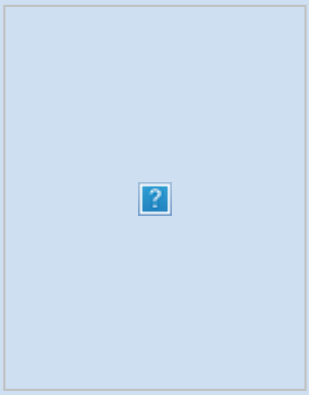
With Drs. Bayardo Perez-Ordonez, Igor Jurisica, Brian O'Sullivan, John Waldron and Bernard Cummings, Dr. Liu's team, led by Dr. Angela Hui, conducted a series of molecular tests to survey the global expression of microRNAs (miRNAs)—important molecules involved in the regulation of gene expression—in HNSCC versus normal or non-cancerous tissue. In total, 38 of the 117 detected miRNAs (33%) were significantly differentially expressed in malignant tissues.

"We have identified a group of differentially expressed miRNAs in HNSCC," says Dr. Liu. "Specifically, our studies have found that low levels of miR-375 and high levels of miR-106b-25 might play cancer-promoting roles in HNSCC. Our future studies will look to further dissect the complex molecular activities that underlie this disease in an effort to develop a molecular disease signature, and ultimately, help to design future treatment strategies."

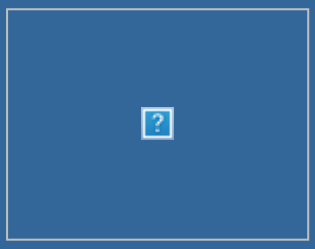
Hui AB, Lenarduzzi M, Krushel T, Waldron L, Pintilie M, Shi W, Perez-Ordonez B, Jurisica I, O'Sullivan B, Waldron J, Gullane P, Cummings B, Liu FF. Clin Cancer Res. 2010 Feb 15;16(4):1129-39. Epub 2010 Feb 9. [Pubmed abstract]. *Research supported by the Ontario Institute for Cancer Research, the Canadian Institutes of Health Research, Dr. Mariano Elia Chair in Head and Neck Cancer Research, the Wharton family, Joe's Team, Gordon Tozer, the Canada Research Chairs Program, the Canada Foundation for Innovation, IBM, the Campbell Family Cancer Research Institute, and the Ministry of Health and Long-Term Planning.*

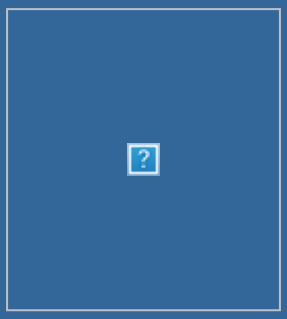
Lung Injury: Getting to the Bottom of Injury Promotion and Prevention

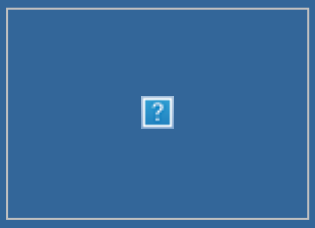
According to recent findings from a TGRI study, vascular endothelial growth factor (VEGF)-A (VEGF)—a protein involved in regulating vascular permeability, angiogenesis and promoting lung cell survival—helps protect lung cells from programmed cell death during times of acute lung injury (ALI).

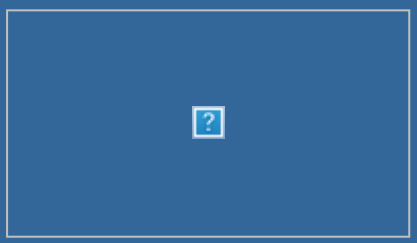


Led by Dr. Mingyao Liu and collaborators Drs. David Hwang, Thomas Waddell, Shaf Keshavjee, and Dr. Matthew Binnie at Mount Sinai Hospital, the team used an animal model to show that lung development was not significantly affected in mice without VEGF. However, in older mice, emphysema-like evidence was detected which indicates that VEGF may be critical to maintaining lung structure, especially in older adults.









"Our studies provide strong evidence supporting the fact that VEGF is important to maintain alveolar structure in adulthood," explains Dr. Liu. "In terms of ALI, VEGF is helpful and a hindrance depending on the situation. Specifically, VEGF contributes to acute inflammation and pulmonary edema but also has protective properties for alveolar epithelial barriers as well. Ultimately, caution should be exercised when considering VEGF as a therapeutic target for ALI until further research is conducted."

Mura M, Binnie M, Han B, Li C, Andrade CF, Shiozaki A, Zhang Y, Ferrara N, Hwang D, Waddell TK, Keshavjee S, Liu M. Am J Pathol. 2010 Feb 18. [Epub ahead of print]. [Pubmed abstract]. *Research supported by the Canadian Institutes of Health Research.*

Neurology: Establishing a Circulation and Brain Landscape Relationship

TWRI researchers have determined that patients with narrowed blood vessels supplying the brain can have an unusual physiological condition where one part of the brain "steals" blood from another part. The part of the brain experiencing the reduced blood was shown by the researchers to have thinning of the brain's gray matter (the cortex).

Study lead Dr. David Mikulis, with Drs. Jorn Fierstra, Frank Silver and Michael Tymianski reviewed 250 imaging studies and identified 17 patients with severe one-sided exhausted brain blood flow areas demonstrating this "steal" physiology but with normal appearing cortex landscapes on MRI. Using advanced imaging tools, the team then made electronic brain 'maps' of the areas with steal physiology in order to measure cortex thickness and found an 8% thinner cortex than corresponding healthy areas.

"For the first time we have evidence showing a relationship between impaired autoregulation in the brain with steal physiology and cortical thinning," explains Dr. Mikulis. "The important point here is that severely narrowed blood vessels can still produce brain injury even if a sudden stroke has not yet happened. In effect we have discovered a previously unrecognized disease process. Now that we more clearly understand this condition, future studies will work towards determining if there is a relationship between gray matter thinning due to steal physiology and brain function."

Fierstra J, Poublanc J, Han JS, Silver F, Tymianski M, Crawley AP, Fisher JA, Mikulis DJ. J Neurol Neurosurg Psychiatry. 2010 Mar;81(3):290-3. [Pubmed abstract]. *Research supported by the Ontario Research Fund Brain Consortium.*