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New Research Breakthroughs at UHN

Cancer: Understanding the Importance of Cell Structure

A recent finding from UHN researchers Dr. Mitsuhiko Ikura and colleagues provides insight into how cell structure deviations can contribute to metastasis—the spreading of cancer.

The study found that CLIP170 and p150Glued microtubule proteins—protein tubes lining a cell that are involved in cell movement—are very similar in their three dimensional structures. As a result, they compete to attach to the growing end of a microtubule.

“Competition between these proteins alters the cells' foundation, causing changes in cellular organization,” explains Dr. Ikura. “These findings help us work towards understanding cell adhesion and developing therapies against the spread of cancer.”

Nat Struct Mol Biol. 2007 Sep 9; [Epub ahead of print]. [Pubmed abstract].
Research supported by the National Cancer Institute of Canada.

Lung Cancer: Targeting Growth Controls

Non-small cell lung cancer patients may benefit from a future therapeutic strategy that targets tumor growth by controlling tumor cell microenviroment, as recently highlighted by findings from an OCI research team.

UHN Drs. Ming Tsao, Linda Penn and Igor Jurisica used molecular and computational biology tools to show that the integrin protein alpha11—a protein involved in controlling physical interactions between tumor cells and tissue that surrounds them—markedly enhanced tumor growth in mice when present in lung cancer cells. This tumor growth promoting activity is mediated by induced growth factors. This is a collaborative work with Dr. Gullberg at the University of Bergen, Norway.

“These findings are important from a patient therapy perspective because we now know that this protein has an important role in malignant growth of lung cancer cells,” said Dr. Tsao. “Knowing where control lies, we can look at ways of preventing growth right at the start.”

Proc Natl Acad Sci U S A. 2007 Jul 10;104(28):11754-9. [Pubmed abstract].
Research supported by the Canadian Cancer Society, Helse Vest, Research Council of Norway Grant and the Swedish Research Council Grant.

Cardiology: Age Makes a Difference

The effectiveness of stem cell therapy in heart attack patients may depend on age, according to a recent study by TGRI scientists.

Using an animal model, UHN researchers Drs. Ren-Ke Li and Richard Weisel compared the growth of muscle stem cells after being implanted into the hearts of young and mature rats.

After four weeks, older rats experienced heart failure more frequently, blood vessel density was reduced, and survival of implanted stem cells was reduced.

“Our study is unique in that we are able to show that recipient age is clearly a factor in how well the therapy works,” notes Dr. Li. “As one ages, the regenerative capacity is decreased. New therapies are required not only to treat the occluded artery after a heart attack, but also to enhance the cells injected into the heart to improve its function and to improve the ability of the body to repair the injured heart. Future clinical treatments may include rejuvenation of the body’s response to injury.”

J Am Coll Cardiol. 2007 Sep 11;50(11):1086-92. Epub 2007 Aug 24. [Pubmed abstract]. *Research supported by the Heart and Stroke Foundation of Ontario..*

Memory: Mapping Out the Memory Network

Research into brain imaging has moved from merely locating and characterizing the extent of damage to providing functional information on the effects of damage, thanks to recent investigations by Krembil neuroscientists.

The most recent of these experiments provides important information on the memory network in left temporal lobe epilepsy (LTLE) patients and how memory information is transferred.

Autobiographical memory (AM) refers to one’s own memories of one’s life experiences and UHN researcher Dr. Mary Pat McAndrews and former doctoral student Dr. Donna Addis compared 11 people with LTLE and significant hippocampal damage to individuals without LTLE or damage. Using interviews and imaging technologies, her team showed that the area of the brain--called the hippocampus--acts as a hub for the collection and processing of memories during AM retrieval.

“Memory networks are complex and interconnected and when damage occurs in the hippocampus. It is evident that important connections are changed,” says Dr. McAndrews. “This study provides solid evidence towards the key role of the hippocampus in the formation and recollection of memories which is important to our understanding of how a damaged brain recovers its function.”

Brain. 2007 Sep;130(Pt 9):2327-42. Epub 2007 Aug 6 [Pubmed abstract]. *Research supported by the Physicians’ Services Inc. and James S. McDonnell Foundations, and the Canadian Institutes of Health Research.*

Type 1 Diabetes: Harnessing the Immune System

UHN researchers Dr. Li Zhang, Sylvia Asa and Pamela Ohashi have targeted a new route of therapy for autoimmune type-1 diabetes (T1D) that uses a protein to activate a class of immune T cells.

T1D results from destruction of insulin-producing pancreatic cells by rogue T cells. Double negative (DN) T cells are known to counterattack the rogues, suppressing their harmful effects.

Using an animal model of T1D, the team was able to activate the animal's DN cells by injecting a novel type of protein. More importantly, they were able to prevent diabetes by injecting prediabetic animals with activated DN cells.

"This is very exciting because for the first time we've been able to show that protein activation of DN T cells can prevent the development of autoimmune T1D," according to Dr. Zhang. "These cells are now a starting point for the development of future potential cellular therapy for this chronic illness."

Eur J Immunol. 2007 Jun 19; [Epub ahead of print] [Pubmed abstract]. *Research was supported by the Canadian Institutes of health Research and National Cancer Institutes of Canada.*

Respiratory Diseases: Using Stem Cells for Regeneration

Cell replacement therapy may be a new possibility for patients with lung injuries or diseases like cystic fibrosis after a recent report from TGRI scientists showing that adult stem cells can successfully engraft and grow into specific lung cell types.

In the new therapy, recently tested in an animal model, lungs are subjected to a mild chemical which prepares the area for engraftment.

Following this, adult bone marrow stem cells are injected directly into the site. Stem cells developed into the appropriate bronchial epithelial cells and future studies will determine if these approaches are able to promote recovery and improve lung function.

"Cell replacement therapy allows treatment for areas using selective, mild acute destruction followed by carefully timed, targeted cell delivery directly to the tissue," says Dr. Thomas Waddell. "The findings from this study lend solid evidence for this kind of therapy to be used as a future novel treatment for other types of lung diseases."

Am J Physiol Lung Cell Mol Physiol. 2007 Jul 6; [Epub ahead of print] [Pubmed abstract]. *Research was supported by the Canadian Cystic Fibrosis Foundation, Canadian Institutes of Health Research and the R. Fraser Elliott Chair in Transplantation Research.*

Osteoporosis: The Factors Causing Fractures

New osteoporosis research findings from a UHN team suggest that age and delays in starting medication for this disease are predictors of fracture and/or bone break risk.

Osteoporosis, which affects millions of Canadians, is an age-related chronic illness and is characterized by decreased bone mass and increased susceptibility to fractures.

TGRI scientists Drs. Angela Cheung, Olga Gajic-Veljanoski (doctoral student in clinical epidemiology), Aileen Davis, David Trichler and George Tomlinson collaborated with scientists at CANDOO (Canadian Database for Osteoporosis and Osteoporotic Fractures) to evaluate 1,145 men and women. They found that the risk of first fracture increases 3% each year. Conversely, starting medication decreases fracture risk by 58% over 2.5 years. Low physical activity and high body mass index may also contribute to these risks.

"With the rapidly growing elderly population, this study provides key evidence that early medication and an active lifestyle will greatly decrease the risk of bone fractures," says senior author Dr. Cheung. "We recommend starting treatment early to help reduce the burden of osteoporosis in our society."

Osteoporos Int. 2007 Aug;18(8):1091-100. Epub 2007 Feb 24. [Pubmed abstract]. *Research supported by the Canadian Institute of Health Research, the Ontario Women's Health Council and a Premier's Research Excellence Award.*

Breaking News from UHN Research

2007 Awardees Announced in Joint UHN Funding Initiative

The UHN office of Technology Development & Commercialization (TDC), together with Johnson & Johnson's Corporate Office of Science and Technology (COSAT), is pleased to announce the recipients of the 2007 J&J-UHN Development Acceleration Awards.

The award recipients (in no particular order) are:

Dr. David Jaffray for "Imaging-enabled liposome platform to adaptively modulate the micro-distribution of targeted therapeutics".

Dr. Lothar Lilge for "Low cost and high patient acceptance device for transillumination spectroscopy based breast cancer risk assessment".

Dr. Li Zhang for "Evaluation of human GMP-grade DNT cells as a novel

cancer immunotherapy by in vivo imaging".

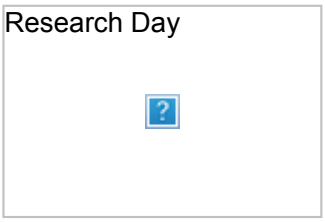
Dr. Gang Zheng for "HDL-like peptide-phospholipid scaffold as a novel nanocarrier for targeted delivery of cancer imaging and therapeutic agents".

The 2007 awards will fund early-stage development of new product opportunities emerging from UHN Research, with specific emphasis on the development of imaging technologies in the context of neoplastic, cardiovascular, autoimmune, infectious, and/or neurological disease.

Upcoming Events

UHN Research Day 2007

Mark October 29th on your calendar for Research Day 2007. This event brings the research community from all three institutes (TGRI, Krembil and OCI) together to recognize and celebrate the breadth and depth of research at UHN. This year's Research Day will be held at 89 Chestnut Street.



Organized by the Centre for Research Education & Training (CREdiT), the agenda will feature oral and poster sessions, a plenary address, a Research Institutes update and networking opportunities.