New Research Breakthroughs at UHN

Gene Bars Rod Development in the Retina

A team headed by UHN researcher Dr. Rod Bremner found that the gene Chx10 directly controls retinal cell development by discouraging cells from becoming 'rods'—a type of photoreceptor cell.

Rods and cones are the two types of retinal cells that capture and process light, helping us to see. A number of eye diseases are caused by the loss of rod cells, including retinitispigmentosa, a progressive degenerative eye disease affecting one in 4000 people.

By manipulating Chx10 expression in the retina, the researchers discovered that the gene 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.

"In the early stage of retinal development, Chx10 is required for retinal cells to multiply. We found that later on, retinal cells multiply even without Chx10. However, at this stage Chx10 is required to control what type of cells are produced. Thus Chx10 changed jobs in mid-career," explains Dr. Bremner, a member of UHN's Vision Science Research Program. "Our findings could help in discovering new treatments for eye disease, such as using stem cells to produce new rods."

PNAS. 2006 Mar 17; [Epub ahead of print]. [PubMed Abstract] Research supported by Canadian Institutes of Health Research.

Drug Pressures Tumours to Respond to Therapy

A drug that disrupts blood vessels in tumours may improve the effectiveness of anti-cancer drugs according to a recent study by UHN researchers Drs. Richard Hill, Alex Vitkin and Michael Milosevic. The team investigated how the fluid pressure level in a tumour—known as the interstitial fluid pressure (IFP) level-was impacted by a blood vessel disrupting drug in *in vivo* studies.

Tumours with high IFP levels have been linked to poor prognosis for cancer patients, perhaps because high pressure hinders therapeutic drugs from penetrating the tumour. The research team showed that a blood vessel disrupting drug, ZD6126 reduces the IFP and kills almost all the tumour cells in the centre of the tumour but its efficacy depends on the IFP level.

"Our research gave the surprising result that even drugs which disrupt blood vessels within tumours have reduced efficacy when the tumour has an high IFP level. The results suggest that careful scheduling of the use of such drugs in conjunction with other anti-cancer drugs will be needed to obtain the maximum benefit in the treatment of cancer patients," says Dr. Hill.

Cancer Res. 2006 Feb 15;66(4):2074-80. [PubMed Abstract] Research supported by the National Cancer Institute and the Terry Fox Foundation.

Discovery Stresses New Direction for Repairing Blood Vessels

A recent finding from the laboratory of UHN's Dr. Lowell Langille sheds light

on blood vessel disorders, including the narrowing of blood vessels that occurs with coronary artery disease and when therapies to correct this disease fail.

Cells that line the interior of blood vessels are able to change their shape in response to the shear stress of blood flowing over their surfaces. As these cells—vascular endothelial cells—stretch and flatten in response to shear stress, the cell's internal machinery becomes organized in a single direction—a phenomenon called planar cell polarity. Blood vessel repair is influenced by the direction in which the cells are polarized. The team found that a molecule, GSK-3ß, is critical to this process.

“By manipulating the activity of GSK-3ß we have, for the first time, shown that a single cell type can reverse the direction of its polarity,” says Dr. Langille, “This capacity to manipulate cellular machinery that is important in repair processes may lead to improvements in the treatment of blood vessel diseases, and other disorders, by enhancing the cell's own repair mechanisms.”

Circ Res. 2006 Mar 9; [Epub ahead of print] [PubMed Abstract]
Research supported by the Canadian Institutes of Health Research and the Canadian Hypertension Society.

New Faces in UHN Research

Rudi von Harsdorf
Scientist, Division of Experimental Therapeutics, TGRI/TGH

There is no other organ where tumour growth is prevented as well as it is in the heart. Clinician-scientist Dr. Rudi von Harsdorf, a recent recruit to TGRI/ TGH, believes that this may be due to the fact that heart muscle cells do not replicate like other cells do in the body; after birth, they no longer divide.

“Recently, we discovered that factors that regulate the cell cycle are involved in maladaptive growth—scar tissue that happens as a result of damage to the heart,” says Dr. von Harsdorf. “If we can determine how to block these factors we can attenuate the scarring of the heart after it is damaged.”

Dr. von Harsdorf, Robert R. McEwen Chair in Cardiac Regenerative Medicine, was recruited to TGRI from Germany and he is excited about the attractive research prospects here in Canada.

Brian Raught
Scientist, Division of Genomics and Proteomics,OCI/PMH

Dr. Brian Raught, OCI/PMH’s recent recruit, will be using a highly precise technique called mass spectrometry (MS) to shed light on biological molecules.

Dr. Raught, who is appointed at the McLaughlin Centre for Molecular Medicine, has been successful in developing the first MS-based methods of characterizing molecules used to shuttle other molecules around cells.

“At UHN I have already been able to brainstorm with bioinformaticians about our ‘data-crunching' methods and I am looking forward to new innovations based on these productive meetings,” says Dr. Raught.

Breaking News from UHN Research

Biotechnology Focus Explores Microarray Centre

Bioscienceworld featured UHN's Microarray Centre in an in-depth article in the March 2006 issue of their monthly magazine, *Biotechnology Focus*. The article describes the impact of this state-of-the-art facility on genomics research in Toronto and worldwide.

Dr. Peter Liu Appointed CIHR Scientific Director

UHN Research congratulates TGRI's Dr. Peter Liu on his appointment as incoming Scientific Director of the Canadian Institutes of Health Research (CIHR)'s Institute of Circulatory and Respiratory Health.

Each of CIHR's thirteen Institutes is led by a Scientific Director, a position which helps direct Canada's biomedical research priorities. Dr. Liu is renowned for his substantial contributions to cardiovascular disease research and he is the author or co-author of over 250 peer-reviewed publications.

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Upcoming Events

Symposium Celebrates OCI/PMH Stem Cell Pioneer

Dr. E.A. McCulloch's 50-year scientific career and his dedication to the science and methods of stem cell research will be honoured by a symposium on April 26, 2006 at Princess Margaret Hospital. Invited speakers include Dr. Irv Weissman, Director, Institute of Stem Cell Biology and Regenerative Medicine, Stanford University School of Medicine, and Dr. Alan Bernstein, President, Canadian Institutes of Health Research.

The event is being organized by Drs. Hans Messner, Norman Iscove, Mark Minden and Tak Mak.

Research Fact

Did you know that many of Canada's current research leaders were once based at the Ontario Cancer Institute and significantly developed their careers here? A short list of such luminaries includes:

- Dr. Alan Bernstein, President, Canadian Institutes of Health Research (CIHR)
- Dr. Philip Branton, the current Scientific Director for the CIHR Institute of Cancer Research
- Dr. Victor Ling, Vice President, Research for the British Columbia Cancer Agency
- Dr. Robert Phillips, former President, National Cancer Institute of Canada and head, Ontario Cancer Research Network
- Dr. Lou Siminovitch, former head of the Samuel Lunenfeld Research

Institute at Mount Sinai Hospital and founder of the University of Toronto Department of Molecular and Medical Genetics

Future issues of *Net Results Express* will look at research leaders who once called TGRI and Krembil “home”.

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