# New Research Breakthroughs at UHN

## Lung Transplantation: New Test Will Increase Pool of Donor Organs

The pattern of gene expression of several key biochemical mediators of inflammation—called cytokines—in donor lungs may help predict their suitability for lung recipients.

Recent work by UHN researchers Drs. Shaf Keshavjee, Mingyao Liu, Thomas Waddell and their colleagues opens the door to using biological markers to quickly profile donor lungs before implantation. Currently donor lungs are conservatively selected according to a list of clinical factors—such as age and smoking history—of which only 20% of the available pool of donor lungs meet the criteria for transplantation.

"Rapid biological profiling could increase the number of available donor lungs by reliably assessing organs from donors who would not meet the normal criteria for transplantation," says Dr. Keshavjee. "By looking at the levels of cytokines in lung biopsies, we were able to develop and validate one of the first biological predictors of donor lung survival."

*American Journal of Transplantation*. 2006; 6: 544-551. [PubMed Abstract] Research supported by the Canadian Institutes of Health Research.

## Alzheimer's Disease: Finding Offers New Therapeutic Targets

The discovery that a molecule—TMP21—is involved in the accumulation of a toxin in the brain could have a profound impact on the treatment of Alzheimer's disease (AD). AD is the most common cause of dementia in older people and an estimated 290,000 Canadians currently have the condition.

UHN's Dr. Peter St George-Hyslop led a research team that determined TMP21 is a key molecule in the biological processes that produce a toxic compound called amyloid beta. This toxin accumulates around nerve cells in the brain, causing them to die and the brain to degenerate.

*Nature*. 2006 Apr 27;440(7088):1208-12. [PubMed Abstract] Research supported by the Canadian Institutes of Health Research, the Howard Hughes Medical Institute, Canadian Institutes of Health Research-Japan Science and Technology Trust, the Alzheimer's Society of Ontario, the Ontario Research & Development Challenge Fund and the Canada Foundation for Innovation.

## Cancer: New UHN Software Finds Partner "Suspects"

UHN's Dr. Elisabeth Tillier and her colleagues have developed a groundbreaking new method to predict interacting protein partners based on evolutionary history.

Since interacting proteins would likely evolve similarly, the researchers developed an algorithm that seeks out similar sequence patterns between proteins. Finding out which proteins interact is crucial for understanding what a protein suspected to be involved with cancer does biologically.

"Our method has been developed into a computer program, Codep, that is freely available to academic users," says Dr. Tillier. "Codep will help researchers discover protein targets that could lead to new anti-cancer treatments."

Access Codep on The Tillier Group's webpage.

*Proteins* . 2006 Apr 21; [Epub ahead of print]. [PubMed Abstract] Research supported by the Canadian Institutes of Health Research and University of Toronto Life Science.

### Better Liver Transplants: Answer's in the Genes

The recent anonymous living liver transplant at TGH—and the thousands of other liver transplants that occur annually around the world—may be improved by the recent identification at UHN of a set of genes involved in acute liver injury.

A donated liver undergoes many stresses during transplantation and if it becomes injured, the likelihood increases of the transplanted organ failing or being rejected.

UHN researchers, led by Dr. Ian McGilvray, used microarrays to compare liver gene activity during and after transplantation with gene activity in chronic liver conditions—such as hepatitis B or C infections.

"We identified 25 genes that were uniquely active in acute liver stress—such as during transplantation—but not active in chronic liver diseases," says Dr. McGilvray. "Many of these genes have never before been linked to acute liver injury. These results could aid researchers in understanding the molecular processes behind acute liver damage and lead to better outcomes for liver transplants."

*Am J Transplant*. 2006 Apr;6(4):806-24. [PubMed Abstract] Research supported by Fujisawa Canada and the Physicians Services Incorporated Foundation.

## New Faces in UHN Research

### Hitoshi Okada, MD, PhD

Scientist, Division of Signaling Biology, Ontario Cancer Institute

Dr. Hitoshi Okada plays basketball as a hobby, but spends most of his time bouncing ideas around as one of OCI/PMH's newest recruits.

As a member of The Campbell Family Institute for Breast Cancer Research, he uses genetic screening methods to identify genes that in combination with a molecule often found in high levels in many cancer cells—aurora kinase—lead to cell death or cancer.

By breeding fruit flies that have aurora kinase mutations with other mutants, Dr. Okada studies which genes, when missing, affect the most commonly observed characteristic of aurora kinase mutations—a small eye. He will then carry out experiments to confirm the involvement of these other genes with aurora kinase and to investigate them further as potential targets for cancer therapy.

Says Dr.Okada, "Working as a post-doc with Dr. Tak Mak, I found the

environment here provides many opportunities to interact with other new investigators. This really drew me to become part of the team at OCI/PMH."

# Breaking News from UHN Research

## Cardiac Regeneration and Proteomics Boosted with New UHN Chairs

UHN Research congratulates Drs. Ren-Ke Li, TGRI, and Brian Raught, OCI, on their recent appointments as Canada Research Chairs (CRC).

Dr. Li was appointed to a senior Tier I CRC in Cardiac Regeneration with an award of $1.4M and Dr. Raught was awarded a Tier II CRC in Proteomics and Molecular Medicine worth $0.5M.

The CRC program was designed to attract researchers to Canadian universities and to strengthen Canada's status as a world leader in research.

## Microbiologist Elected American Academy Fellow

Dr. Eleanor Fish, Senior Scientist, TGRI and Director of the Arthritis and Autoimmunity Research Centre, was recently elected as a Fellow of the American Academy of Microbiologists. Fellows are elected on the basis of their contributions and achievements that have advanced the science of microbiology. UHN congratulates Dr. Fish on receiving this outstanding honour.

## Cystic Fibrosis Researcher Honoured

Dr. Gregory Downey's research on lung inflammation and how it injures the lungs of patients with cystic fibrosis was recognized by this year's Zellers Senior Scientist Award from the Canadian Cystic Fibrosis Foundation. This prestigious award acknowledges the contributions of Dr. Downey (Senior Scientist, TGRI) to the field of cystic fibrosis research.

# Upcoming Event

## Mark Your Calendar For UHN Research Day 2006

This year UHN Research Day will be held on November 20th at a new location: the MaRS building. This annual event invites the entire UHN research community to present their own research and attend poster sessions and talks by their colleagues across all research institutes.

---