



March 2004

## New Research Breakthroughs at UHN

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
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## Protein Folding in Neurological Diseases: Harmful Aggregates May Share Similarities

Recent findings by Drs. [Avi Chakrabartty](#) and [Jim Lepock](#) (OCI/PMH) may yield new therapeutic targets for treating ALS (Lou Gehrig disease), a debilitating disease which causes paralysis and the loss of control of vital functions such as breathing, swallowing, and speech.

Drs. Chakrabartty and Lepock studied two different types of ALS (sporadic and familial) to learn more about the biological pathways involved. 

"In ALS, the motor neurons that transmit messages from the brain to the muscles may be destroyed when proteins clump together inside them," explains Dr. Chakrabartty. "Our research shows that there are definitely similarities in the way that proteins aggregate in the two forms of ALS, and there may be commonalities in other neurological diseases, like Alzheimer and Parkinson disease, that also have protein aggregation as a pathological feature. This tells us that we may be able to use similar strategies to treat this group of diseases in the future."

*J Bio Chem. 2004 Jan 20*

[\[PubMed abstract\]](#)

Institute: OCI/PMH

Division: Structural & Molecular Biology and Medical Physics

Priority Platform: Genes, Proteins & People

## Influx of Immune Cells Causes Heart Failure

High levels of the protein ET-1 in the heart lead to an increased risk of heart failure, and the findings of a recent study by Drs. [Mansoor Husain](#) and [Avrum Gotlieb](#) (TGRI/TGH) may tell us why.

Drs. Husain and Gotlieb compared heart function in normal mice to heart function in mice with high levels of ET-1.

"The heart tissue of mice with high amounts of ET-1 was full of immune cells," says Dr. Husain. "Since there was no real infection, the chemicals released by the immune cells were damaging the heart, causing heart failure."

When the researchers treated these mice in such a way that ET-1 was blocked, they were able to reduce the incidence of heart failure, proving that ET-1 was responsible for luring the immune cells to the heart. It also points to a potential new strategy for treating this condition.

*Circulation. 2004 Jan 20;109(2):255-61*


[\[PubMed abstract\]](#)

Institute: TGRI/TGH

Division: Cell & Molecular Biology

## Self Destructive B Cells May Hold Key to Lupus

Dr. [Joan Wither](#) (TWRI/TWH) has recently shown that "defective" immune B cells may contribute to the pathology of systemic lupus erythematosus (SLE [lupus]), a chronic autoimmune disease that can affect numerous organs in the body.

Normally, immune cells learn the difference between non-harmful and 

harmful proteins during their development. If this learning process fails, the immune cells may start attacking normal body tissues, resulting in autoimmune disease.

Dr. Wither compared the development of B cells in mice genetically predisposed to developing lupus, to B cell development in normal mice.

She says, "The B cells of lupus-prone mice fail the learning process because one of the mechanisms that should eliminate self-reactive cells from the B cell population is faulty. As a result, they survive and begin to produce antibodies that attack and damage normal body tissues, thus contributing to the pathology of lupus."

*J Immunol.* 2004 Feb 1;172(3):1553-60

[\[PubMed abstract\]](#)

Institute: TWRI/TWH

Division: Cell & Molecular Biology

Priority Platform: Genes, Proteins & People

## **“Survivin” Protein May be Target for Cancer Therapy**

Drs. [Tak Mak](#), Hitoshi Okada (AMDI/OCI/PMH) and [Robert Rottapel](#) (OCI/PMH) may have found a new target for killing cancer cells.

In more than 50% of human cancers, the brakes that control cell division and growth—better known as the p53 gene—are missing or rendered non-functional. Drs. Mak, Okada, and Rottapel may have found a way to stop these out-of-control cells, and stop cancer in its tracks, by targeting an unrelated protein called “survivin,” which they have found to be critical for T cell development and survival.

Says Dr. Mak, “Our research indicates that survivin is critical for the regulation of T cell death and proliferation, and it is completely independent of the p53 pathway. It may be possible, then, to target cancer cells by targeting survivin or pathways that lead to its activation, rather than trying to re-activate a mutant form of p53 in an effort to stop cancer growth.”

*J Exp Med.* 2004 Feb 2;199(3):399-410

[\[PubMed abstract\]](#)

Institute: AMDI/OCI/PMH and OCI/PMH

Division: Cell & Molecular Biology and Experimental Therapeutics

Priority Platform: Genes, Proteins & People

## **Breaking News from UHN Research**

### **UHN Researchers Win Over \$18M in CFI Funding**



UHN celebrated a record win in the Canada Foundation for Innovation awards announced March 8, 2004, as Drs. [David Jaffray](#), [Gary Levy](#), and [Tak Mak](#) led three successful proposals capturing \$18,165,133 in new infrastructure funding.

The funding will launch new research programs focusing on improved radiation therapy for cancer treatment; immune tolerance and transplantation research; and genomic instability and cancer cell survival.


## **Updates**

### **TWRI/TWH Appoints New Director**

UHN Research is pleased to announce the appointment of Dr. Peter St. George-Hyslop as the new Director of TWRI/TWH, effective April 1, 2004.

Dr. St. George-Hyslop's research is focused on determining the genetic and molecular processes that cause neurodegenerative diseases, particularly Alzheimer disease.

## Research Fact

Dr. [David Cassidy](#) (TWRI/TWH) recently published the results of a  six-year World Health Organization Task Force on mild brain injury (concussions). The Task Force conducted a review of the literature to determine optimal methods of preventing, diagnosing, and treating mild brain injuries. The study was published as a supplement of the *Journal of Rehabilitation Medicine*.

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