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New Research Breakthroughs at UHN

Defect in Cell's Disposal System a Cause of Parkinson Disease

Malfunctions in the parkin gene are a major cause of Parkinson disease, and new research by TWRI/TWH's Dr. Andres Lozano, student Suneil Kalia, and post-doctoral fellow Sang Lee reveals another way in which the parkin gene can be compromised. The finding may lead to new drugs for treating the disease.

Part of the cell's "garbage disposal system", parkin tags damaged proteins in the cell for destruction. If prevented from doing this, damaged proteins clump together forming aggregates—a lethal consequence occurring in many neurodegenerative diseases. The researchers found that a protein called BAG5 prevents parkin from doing its job. It also inhibited parkin's helper-protein, Hsp70.

"High levels of BAG5 inhibited the actions of parkin and Hsp70 resulting in enhanced neuronal cell death," says Dr. Lozano. "Our results propose a mechanism for the cause of neurodegeneration in Parkinson disease and other diseases, and points to BAG5 as a potential therapeutic target."
Neuron 2004 Dec 16;44(6):931-45.
[Read Press Release]

Institute: TWRI/TWH
Division: Applied & Interventional Research

Fabry Disease Treatment Successfully Tested

There is good news for sufferers of Fabry disease, a hereditary disorder caused by a faulty gene. People with the disease are missing the activity of the alpha-Gal-A enzyme, and as a result, fats accumulate in their blood vessels damaging the kidneys, heart, and other organs.

Fortunately, OCI/PMH's Dr. Jeffrey Medin and colleagues have discovered a way to stop the disease. Using gene therapy tools, they gave the alpha-Gal-A enzyme to 1-2 day old Fabry mice. The treatment proved successful: alpha-Gal-A levels increased, and the levels of accumulated fats dropped. Moreover, the effects were long-lasting.

"The problem with current treatments is that they are given to patients after the damage is done and they aren't long-term solutions," says Dr. Medin. "We needed to find a way to treat Fabry patients sooner, to avert the irreversible damage before it happened and also provide sustained therapy."

Further testing is required before the therapy can be used in humans.
PNAS USA 2004 Nov 30;101(48):16909-14.
[PubMed abstract]

Institute: OCI/PMH
Division: Experimental Therapeutics

Anxiety Under-Treated in Heart Patients

A recent study by Drs. Donna Stewart, Sherry Grace, Susan Abbey and Jane Irvine (TGRI/TGH) reveals that anxiety symptoms are under-recognized and under-treated in heart patients—something which may negatively impact their recovery and health.

Using surveys, the research team assessed anxiety in 913 heart patients over one year of recovery. Over one-third of patients suffered from anxiety at the time of their coronary event, and approximately 50% of them continued to report it at six months and one year post-event.

"Surprisingly, we found that only 38% of patients with anxiety were asked about anxiety symptoms by their healthcare providers during the course of the year," says Dr. Grace. "This tells us that anxiety symptoms are likely under-recognized and under-treated in heart patients, and that anxiety-reducing interventions are needed to improve quality of life."
Psychother Psychosom. 2004 Nov-Dec;73(6):344-52.
[PubMed abstract]

Institute: TGRI/TGH
Division: Behavioural Sciences & Health

Finding May Lead to New Treatments for Heart Disease

In collaboration with TGRI/TGH's Drs. Ren-Ke Li, Richard Weisel, and Donald Mickle, Dr. Rama Khokha (OCI/PMH), surgical resident Paul Fedak, and fellows Zamaneh Kassiri and David Smookler have found that a protein called TIMP-3 is essential for healthy heart function.

The research team compared heart function in two groups of aging mice: those lacking TIMP-3, and those with the TIMP-3 gene intact.

The heart cells of mice missing TIMP-3 were enlarged and proteins critical for maintaining the heart's structural matrix were disrupted. The overall result in these mice was an enlargement of the left ventricle and general heart dysfunction (which occurred with aging).

"Our study provides proof that lack of TIMP-3 contributes to incorrect cardiac function,"says Dr. Khokha. "Knowing this, we are one step closer to developing novel therapies for heart disease."
Circulation. 2004 Oct 19;110(16):2401-9.
[PubMed abstract]

Institutes: OCI/PMH and TGRI/TGH
Division: Experimental Therapeutics

Updates

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Happy Holidays & Season's Greetings!

The editors of *Net Results* *EXPRESS* wish you a safe and happy holiday season!

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