

Protein Pathway Involved In Parkinson Disease Development

Scientists have found a novel signaling pathway in cells that is altered by genetic mutations recently identified in Parkinson disease development. These new findings show how the mutations affect cellular function and could provide a target for drug therapies to treat the disease. The research by a team of Emory University scientists will be published June 18 in the Public Library of Science Biology (PLoS Biology) journal.

Parkinson disease is a degenerative disorder of the central nervous system resulting from the loss of neurons in the brain that produce dopamine. This lowering of dopamine leads to decreased stimulation of the brain's motor cortex. Although scientists have not known the exact cause of the loss of these dopamine-producing neurons, they believe it is related to dysfunctional mitochondria and oxidative stress. Mitochondria are the cell's "power plants," which metabolize oxygen and generate energy. Oxidative stress is the damage caused to cells by reactive oxygen produced during oxygen metabolism.

Although cells have mechanisms in place to protect against oxidative damage, this system can break down in the face of environmental challenges or genetic mutations.

The Emory researchers found that the mitochondrial protein PINK1 normally protects cells from oxidative stress and promotes cell survival by regulating function of the protein TRAP1. When PINK1 is mutated, however, the protective TRAP1 pathway is disrupted, leading to mitochondrial damage.

Other scientists recently have linked early onset Parkinson disease to mutations in both copies of the PINK1 gene (one from each parent). They also have evidence that single-copy mutations in PINK1 are a significant risk factor for the development of later-onset Parkinson disease.

"We now know much more about the effect of PINK1 mutations on the mitochondria and how this novel signaling pathway is disrupted in the development of Parkinson disease," says Lian Li, PhD, associate professor of pharmacology in Emory University School of Medicine and research team leader. "We believe the PINK1 and TRAP1 pathway may be a future target for therapeutic intervention."

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Other authors of the PLoS paper were Julia W. Pridgeon, PhD, James A. Olzmann, PhD and Lih-Shen Chin, PhD.

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