

Scientists uncover potential drug target to block cell death in Parkinson's disease

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Oxidative stress is a primary villain in a host of diseases that range from cancer and heart failure to Alzheimer's disease, Amyotrophic Lateral Sclerosis and Parkinson's disease. Now, scientists from the Florida campus of The Scripps Research Institute (TSRI) have found that blocking the interaction of a critical enzyme may counteract the destruction of neurons associated with these neurodegenerative diseases, suggesting a potential new target for drug development.

These findings appear in the January 11, 2013 edition of The [Journal of Biological Chemistry](#).

During periods of cellular stress, such as exposure to UV radiation, the number of highly reactive oxygen-containing molecules can increase in cells, resulting in serious damage. However, relatively little is known about the role played in this process by a number of stress-related enzymes.

In the new study, the TSRI team led by Professor Philip LoGrasso focused on an enzyme known as c-jun-N-terminal kinase (JNK). Under stress, JNK migrates to the mitochondria, the part of the cell that generates chemical energy and is involved in cell growth and death. That migration, coupled with JNK activation, is associated with a number of serious health issues, including mitochondrial dysfunction, which has long been known to contribute to neuronal death in Parkinson's disease.

The new study showed for the first time that the interaction of JNK with

a protein known as Sab is responsible for the initial JNK localization to the mitochondria in neurons. The scientists also found blocking JNK mitochondrial signaling by inhibiting JNK interaction with Sab can protect against neuronal damage in both cell culture and in the brain.

In addition, by treating JNK with a peptide inhibitor derived from a mitochondrial membrane protein, the team was able to induce a two-fold level of protection of neurons in the substantia nigra pars compacta, the brain region devastated by Parkinson's disease.

The study noted that this inhibition leaves all other cell signaling intact, which could mean potentially fewer side effects in any future therapies.

"This may be a novel way to prevent neuron degeneration," said LoGrasso. "Now we can try to make compounds that block that translocation and see if they're therapeutically viable."

More information: "Blocking c-jun-N-terminal Kinase (JNK) Translocation to the Mitochondria Prevents 6-hydroxydopamine-induced Toxicity in vitro and in vivo" [www.jbc.org/content/early/2012 ... M112.421354.full.pdf](http://www.jbc.org/content/early/2012/01/10/jbc.M112.421354.full.pdf)

Provided by Scripps Research Institute

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