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Therapeutic avenues for Parkinson's investigated at UH

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Scientists at the University of Houston (UH) have discovered what may possibly be a key ingredient in the fight against Parkinson's disease.

Affecting more than 500,000 people in the U.S., Parkinson's disease is a degenerative disorder of the central nervous system marked by a loss of certain nerve cells in the brain, causing a lack of dopamine. These dopamine-producing neurons are in a section of the midbrain that regulates body control and movement. In a study recently published in the Proceedings of the National Academy of Sciences (PNAS), researchers from the UH Center for Nuclear Receptors and Cell Signaling (CNRCS) demonstrated that the nuclear receptor liver X receptor beta (LXRbeta) may play a role in the prevention and treatment of this progressive neurodegenerative disease.

"LXRbeta performs an important function in the development of the central nervous system, and our work indicates that the presence of LXRbeta promotes the survival of dopaminergic neurons, which are the main source of dopamine in the central nervous system," said CNRCS director and professor Jan-Åke Gustafsson, whose lab discovered LXRbeta in 1995. "The receptor continues to show promise as a potential therapeutic target for this disease, as well as other neurological disorders."

To better understand the relationship between LXRbeta and Parkinson's disease, the team worked with a potent neurotoxin, called MPTP, a contaminant found in street drugs that caused Parkinson's in people who

consumed these drugs. In lab settings, MPTP is used in murine models to simulate the disease and to study its pathology and possible treatments.

The researchers found that the absence of LXRbeta increased the harmful effects of MPTP on dopamine-producing neurons. Additionally, they found that using a drug that activates LXRbeta receptors prevented the destructive effects of MPTP and, therefore, may offer protection against the neurodegeneration of the midbrain.

"LXRbeta is not expressed in the dopamine-producing neurons, but instead in the microglia surrounding the neurons," Gustafsson said. "Microglia are the police of the brain, keeping things in order. In Parkinson's disease the microglia are overactive and begin to destroy the healthy neurons in the neighborhood of those neurons damaged by MPTP. LXRbeta calms down the microglia and prevents collateral damage. Thus, we have discovered a novel therapeutic target for treatment of Parkinson's disease."

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