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Researchers identify role of FOXO1 gene in Parkinson's disease

June 29 2012

A recent study led by researchers at Boston University School of Medicine (BUSM) revealed that the FOXO1 gene may play an important role in the pathological mechanisms of Parkinson's disease. These findings are published online in *PLoS Genetics*, a peer-reviewed open-access journal published by the Public Library of Science.

The study was led by Alexandra Dumitriu, PhD, a postdoctoral associate in the department of neurology at BUSM. Richard Myers, PhD, professor of neurology at BUSM, is the study's senior author.

According to the Parkinson's Disease Foundation, 60,000 Americans are diagnosed with Parkinson's disease each year and approximately one million Americans are currently living with the disease.

Parkinson's disease is a complex neurodegenerative disorder characterized by a buildup of proteins in nerve cells that lead to their inability to communicate with one another, causing motor function issues, including tremors and slowness in movement, as well as dementia. The substantia nigra is an area of the midbrain that helps control movement, and previous research has shown that this area of the brain loses neurons as Parkinson's disease progresses.

The researchers analyzed gene expression differences in brain tissue between 27 samples with known Parkinson's disease and 26 samples from neurologically healthy controls. This data set represents the largest number of brain samples used in a whole-genome expression study of

Parkinson's disease to date. The novel aspect of this study is represented by the researchers' emphasis on removing possible sources of variation by minimizing the differences among samples. They used only male brain tissue samples that showed no significant marks of Alzheimer's disease pathology, one of the frequently co-occurring neurological diseases in Parkinson's disease patients. The samples also had similar tissue quality and were from the brain's prefrontal cortex, one of the less studied areas for the disease. The prefrontal cortex does not show neuronal death to the same extent as the substantia nigra, although it displays molecular and pathological modifications during the disease process, while also being responsible for the dementia present in a large proportion of Parkinson's disease patients.

Results of the expression experiment showed that the gene FOXO1 had increased expression in the brain tissue samples with known Parkinson's disease. FOXO1 is a transcriptional regulator that can modify the expression of other genes. Further examination of the FOXO1 gene showed that two single-nucleotide polymorphisms (SNPs), or DNA sequence variations, were significantly associated with age at onset of Parkinson's disease.

"Our hypothesis is that FOXO1 acts in a protective manner by activating genes and pathways that fight the neurodegeneration processes," said Dumitriu. "If this is correct, there could be potential to explore FOXO1 as a therapeutic drug target for Parkinson's disease."

Provided by Boston University Medical Center