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College of Dentistry scientist receives \$330,000 grant to study whether statin drugs may stop progression of Parkinson's

Kalipada Pahan, Ph.D., associate professor of biochemistry, oral biology and pharmacology at the University of Nebraska Medical Center College of Dentistry in Lincoln, has received a two-year, \$330,750 grant to study the effectiveness of statins in stopping the destruction of neurons in mouse models with Parkinson's disease.

Parkinson's disease is a progressive, incurable neurological disorder that results from degeneration of neurons in a region of the brain that controls movement. The cause is unknown. The degeneration creates a shortage of the brain-signaling chemical known as dopamine, causing the movement impairments that characterize the disease.

Dr. Pahan and his research team will look at if statins exert an anti-neuroinflammatory effect and prevent the loss of neurons in the Parkinson's disease process in laboratory mice models. Understanding how the disease works is important to developing effective drugs that protect the brain and stop the progression of Parkinson's disease stated Dr. Pahan.

Statins have been shown to inhibit the activation of Ras, a protein present naturally in the body that is involved in the production of different inflammatory molecules. Researchers have found when Parkinson's disease is present in animal models the inflammatory process markedly increases in the brain. "This may be an important reason for the loss of neurons in patients with Parkinson's disease," Dr. Pahan said.

While statins are known to lower cholesterol, it also inhibits the function of the Ras protein by lowering the concentration of farnesylpyrophosphate (FPP).

The drug levodopa has been the standard treatment for Parkinson's, but it is often associated with a number of side effects and unsatisfactory outcomes. "We hope that statins ultimately will be effective in people who have Parkinson's. We've already proven in the lab that statins inhibit Parkinson-related inflammatory effects in brain cells. Now we want to know if it works in mice models," Dr. Pahan said.

Professor Howard E. Gendelman, M.D., Chairman of the UNMC Department of Pharmacology and Experimental Neuroscience and Director of the Center for Neurovirology and Neurodegenerative Disorders (CNND) is a consultant on this grant.

"We are honored to collaborate with Dr. Gendelman on this important project," Pahan said. "If the study is successful, these widely-used FDA-approved drugs will go directly into clinical trials for Parkinson's disease."

In the United States, at least 500,000 people are believed to suffer from Parkinson's disease, and about

50,000 new cases are reported annually. These figures are expected to increase as the average age of the population increases. The disorder appears to be slightly more common in men than women.

Dr. Pahan and his colleagues are also investigating the anti-neuroinflammatory effect of NBD peptides in the inflammatory disease process of Parkinson's disease in mouse models. They are also involved in studying multiple sclerosis, another neurodegenerative disorder, and have published results of the effectiveness of a variety of drugs on multiple sclerosis in mouse models in the laboratory.