

Researchers find drug that stops progression of Parkinson's disease in mice

March 8 2011

In a major breakthrough in the battle against Parkinson's disease, researchers at the University of Colorado School of Medicine have discovered a drug that stops the progression of the degenerative illness in mice and is now being tested in humans.

"Drugs currently used to treat Parkinson's disease just treat symptoms; they do not stop the disease from getting worse," said senior author Curt Freed, MD, who heads the division of [Clinical Pharmacology](#) and Toxicology at the CU School of Medicine. "We've now discovered that we can prevent the progression of the disease by turning on a protective gene in the brain."

The results have been published online in the [Journal of Biological Chemistry](#).

Lead author Wenbo Zhou, PhD, Assistant Professor of Medicine, and Freed, a national pioneer in Parkinson's research, have found that the drug phenylbutyrate turns on a gene that can protect dopamine neurons in Parkinson's disease. The gene, called DJ-1, can increase production of antioxidants like [glutathione](#) to reduce the debilitating effects of excess oxygen in brain cells. In addition, activating DJ-1 helps cells eliminate abnormal proteins that otherwise accumulate and kill brain cells. Dopamine neurons are particularly susceptible to too much oxygen and [abnormal protein](#) deposits. Parkinson's disease is caused by dying midbrain dopamine neurons.

Zhou and Freed have studied the DJ-1 gene since 2003 when a European group discovered that mutations in DJ-1 could cause Parkinson's disease. The Colorado scientists immediately started work to see why the gene was so important and have published a series of papers on the subject since 2005. But to convert their findings into a practical treatment for Parkinson's disease, they needed to find a drug to turn on the DJ-1 gene.

"We know some drugs can turn on genes. For example, steroids like testosterone act on genes in muscle cells to create muscle bulk," said Freed.

After testing many drugs, the team found that phenylbutyrate could activate DJ-1 and keep [dopamine neurons](#) from dying. Next, they put the drug in the drinking water of mice genetically programmed to get Parkinson's disease as they aged.

Aging mice receiving the drug were able to move normally, had no decline in mental function, and their brains did not accumulate the protein that causes Parkinson's. By contrast, older animals that did not get the drug saw a steady decline in their ability to move as their brains were damaged by abnormal proteins.

The researchers began giving phenylbutyrate to people in 2009, to test the safety of the drug in Parkinson patients.

Zhou and Freed will publish the human results in the coming months.

"We look forward to a future when Parkinson patients will be able to take a pill that will turn on the DJ-1 gene and stop the progressive disability associated with the illness," Freed said. "Right now, when you get the diagnosis of Parkinson's, you can expect to have a steady decline in the ability to move. While drugs like L-DOPA are very important for generating dopamine in the brain and making movement possible, these

drugs have little impact on the ongoing deterioration of the patients' own [brain cells](#)."

Over one million people in the United State have the disease which usually strikes those in their 50s and 60s. Patients have a decline in their ability to walk, talk, and write because of slow movement and rigid muscles. They develop tremors and reflexes slow down. The current treatment of Parkinson's is based on drugs that increase dopamine production in the brain.

Freed is a national leader in transplanting dopamine cells into the human brain to relieve symptoms. He and his neurosurgical colleague Robert Breeze, MD, have done the operation in 61 patients, more than any other group in the world. The procedure can replace the need for drugs but even cell transplants do not prevent the progression of the disease.

Freed and Zhou are now looking for other drugs that might turn on the DJ-1 gene. One drawback of phenylbutyrate is that patients must take very large doses, 16 grams per day or 32 large tablets taken at frequent intervals. While the drug is approved by the FDA for treating a rare genetic disease in infants, whether it can stop Parkinson's in people remains to be seen.

But Zhou and Freed believe the discovery offers new hope for those suffering from [Parkinson's disease](#).

"If we can say to someone that as of today we can stop your disease from getting worse, that would be a truly significant achievement," Freed said.

More information:

<http://www.jbc.org/content/early/2011/03/03/jbc.M110.211029.full.pdf+html>

Provided by University of Colorado Denver

Citation: Researchers find drug that stops progression of Parkinson's disease in mice (2011, March 8) retrieved 23 March 2023 from <https://phys.org/news/2011-03-drug-parkinson-disease-mice.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.