# Genetic mutation linked to Parkinson's disease

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Researchers have discovered a new gene mutation they say causes Parkinson's disease. The mutation was identified in a large Swiss family with Parkinson's disease, using advanced DNA sequencing technology.

The study, published today in the American Journal of Human Genetics, was led by neuroscientists at the Mayo Clinic campus in Florida and included collaborators from the U.S., Canada, Europe, United Kingdom, Asia and the Middle East.

"This finding provides an exciting new direction for Parkinson's disease research," says co-author Zbigniew Wszolek, M.D., a Mayo Clinic neuroscientist. "Every new gene we discover for Parkinson's disease opens up new ways to understand this complex disease, as well as potential ways of clinically managing it."

The team found that mutations in VPS35, a protein responsible for recycling other proteins within cells, caused Parkinson's disease in the Swiss family. Mutated VPS35 may impair the ability of a cell to recycle proteins as needed, which could lead to the kind of errant buildup of protein seen in some Parkinson's disease brains and in other diseases like Alzheimer's disease says co-author Owen Ross, Ph.D., a neuroscientist at Mayo Clinic in Florida. "In fact, expression of this gene has been shown to be reduced in Alzheimer's disease, and faulty recycling of proteins within cells has been linked to other neurodegenerative diseases," he says.

So far, mutations in six genes have been linked to familial forms of Parkinson's disease, with many mutations identified as a direct result of Mayo Clinic's collaborative research efforts. Dr. Wszolek has built a worldwide network of Parkinson's disease investigators, many of whom have conducted research at Mayo Clinic. The study's first author, Carles Vilariño-Güell, Ph.D., and the senior investigator, Matthew Farrer, Ph.D., worked on this study while at Mayo Clinic in 2010; they have since moved to the University of British Columbia in Vancouver. The joint first author, neurologist Christian Wilder, M.D., first identified the Swiss Parkinson's disease family and continued to study them while he was a research fellow at Mayo Clinic; he has now returned to Centre Hospitalier Universitaire Vaudois in Lausanne, Switzerland.

Investigators used a new genetic sequencing technique to find the VPS35 mutation, according to Dr. Ross. They used 'exome' sequencing to look for shared variations in a pair of first cousins within a large Swiss family affected by Parkinson's disease. Collectively, exons, which provide the genetic blueprint used in the production of proteins, make up only 1 percent of the entire genome and so it is much easier to look for novel variations, causing changes in the protein sequence, that would represent possible disease-causing mutations, he says. "Cousins only share about 10 percent of their genome, whereas parents and children or siblings share much more. This narrowed the field of novel variations for us," says Dr. Wszolek, with VPS35 emerging as the latest Parkinson's disease gene.

"There is much more we need to know about this gene," Dr. Ross says. "Although it appears to be a rare cause of Parkinson's disease, it seems to be very important from a mechanistic viewpoint for this disease and possibly other neurodegenerative disorders.

Provided by Mayo Clinic