MedicalXpress

Researchers Identify Gene Mutations Underlying Risk for Most Common Form of Parkinson's Disease

November 17 2009

(PhysOrg.com) -- Two genes containing mutations known to cause rare familial forms of parkinsonism are also associated with the more common, sporadic form of the disease where there is no family history, researchers have found.

The finding came in the largest genome-wide association study (GWAS) reported to date involving Parkinson's disease. GWAS studies look in the DNA on all of the chromosomes in a specific population of individuals for common genetic associations with a disease. To date, such studies have been done on relatively small numbers of samples and have not been able to identify genetic variations of smaller effect in Parkinson's disease. But now, GWAS studies in very large sample sets are able to identify these elusive genetic variations.

Collaborating scientists in the United States and Europe pooled nearly 14,000 DNA samples and data to confirm that mutations in the alpha-synuclein (SNCA) gene and microtubule associated protein tau (MAPT), both present in the general population, are risk factors for sporadic Parkinson's disease.

In an independent study from Japan, researchers also identified a different combination of genetic variants as risk factors in people of Japanese descent, a finding that highlights the power of GWAS in comparing risk factors among different populations.

The findings presented in the Nov. 15, 2009, online issue of Nature Genetics were supported in part by the National Institute on Aging (NIA), National Institute of Neurological Disorders and Stroke, National Cancer Institute, and the National Institute of Environmental Health Sciences, all components of the National Institutes of Health.

Parkinson's disease, which affects about 1.5 million Americans, is a progressive neurologic disorder caused by the degeneration of nerve cells in the portion of the brain that controls movement. The likelihood of developing the disorder increases with age and involves a combination of environmental risk factors and genetic susceptibility. GWAS studies require large numbers of DNA samples — a hurdle the international team of researchers overcame through collaboration.

"Because previous Parkinson's GWAS were too small and lacked power, we worked together to compile and analyze the large data sets needed to identify the elusive genetic variations that play a role in this complex disease," said Andrew B. Singleton, Ph.D., chief of the NIA Laboratory of Neurogenetics, who co-led the study with Thomas Gasser, M.D., of the Hertie Institute for Clinical Brain Research, University of Tubingen, and the German Center for Neurodegenerative Disease, of Tubingen, Germany. "With this better understanding of the underlying genetic variants involved in the progress of this disorder, we have more insight into the causes and underlying biology of this disease. We hope this new understanding will one day provide us with strategies to delay, or even prevent, the development of Parkinson's disease."

The two-phase GWAS first analyzed DNA samples of 1,713 people with the disease and 3,978 free of the disorder, all of whom were Europeans. The findings were then replicated in a similar group of 3,361 people with Parkinson's disease and 4,573 without the disorder. Following the initial findings implicating SNCA and MAPT variants as risk factors for typical Parkinson's disease, the team then compared results with

researchers performing a GWAS study in a group of Japanese people (2,816 with Parkinson's disease and 3,401 free of the disorder). This second GWAS also revealed the strong association for SNCA but not for MAPT. Additionally, both GWAS studies found evidence for two additional risk variants; the first, which was strongest in the Japanese population, was named Park16; the second is close to a gene, LRRK2, which Dr. Singleton's and Dr. Gasser's groups previously found contains mutations that cause an inherited form of Parkinson's disease.

"These findings support the notion that the sporadic and rare familial forms of the disease are related and that common genetic variability plays a role in developing the disorder," said NIA Director Richard J. Hodes, M.D. "Future GWAS involving greater numbers of DNA samples will likely reveal additional common genetic risk factors. As we continue to use these and other novel approaches to understand complex diseases, we move closer to a complete understanding of the genetic basis of Parkinson's disease."

Provided by National Institutes of Health

Citation: Researchers Identify Gene Mutations Underlying Risk for Most Common Form of Parkinson's Disease (2009, November 17) retrieved 20 April 2024 from https://medicalxpress.com/news/2009-11-gene-mutations-underlying-common-parkinson.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.