Researchers discover genetic link between immune system, Parkinson's disease

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A team of researchers has discovered new evidence that Parkinson's disease may have an infectious or autoimmune origin. "Common genetic variation in the HLA region is associated with late-onset sporadic Parkinson's disease" appears online in *Nature Genetics*.

The study was conducted by the NeuroGenetics Research Consortium, an international team of researchers led by Haydeh Payami, research scientist at the New York State Department of Health Wadsworth Center. The clinical directors for the study were Dr. Cyrus Zabetian, associate professor of neurology at the University of Washington and VA Puget Sound Health Care System, Stewart Factor at Emory University and John Nutt at Oregon Health and Sciences University.

The research team studied more than 2,000 Parkinson's disease patients and 2,000 healthy volunteers from clinics in Oregon, Washington, New York and Georgia, assessing clinical, genetic and environmental factors that might contribute to the development and progression of Parkinson's disease and its complications. Some of the research subjects were tracked for nearly two decades.

"Over the years, there have been subtle hints that immune function might be linked to Parkinson's disease" said Zabetian. "But now we have much more convincing evidence of this and a better idea of which parts of the immune system might be involved."

In the study, researchers detected a new association with the HLA

(human leukocyte antigen) region, which contains a large number of genes related to immune system function in humans. With the new findings, and link to HLA, researchers will now be encouraged to take a fresh look at the possible role of infections, inflammation and autoimmunity in Parkinson's disease.

HLA genes are essential for recognizing foreign invaders from the body's own tissues. Similarly, HLA molecules are supposed to recognize a body's own tissue as itself and prevent immune reactions against them. But the system doesn't always work perfectly. HLA genes are highly variable from individual to individual. Certain variants of the genes are associated with increased risk or protection against infectious disease, while other variants can induce autoimmune disorders in which the immune system attacks the body's own tissues. Multiple sclerosis, a neurological disease caused by autoimmunity, is also associated with HLA-DR. The genetic variant that is associated with Parkinson's disease is in the same region as the one associated with multiple sclerosis.

People who take non-steroidal anti-inflammatory drugs (NSAIDs, such as ibuprofen) have a reduced risk of developing Parkinson's disease, which also supports an immune-related mechanism. The protective effect of NSAIDs is not the same for everyone, likely because of genetic differences, and NSAIDs can have side effects. Pursuing the connection between Parkinson's disease and inflammation, especially in the context of variable genetic makeup, may lead to better, more selective drugs for treating Parkinson's disease.

Consortium leaders recognize the study would not have been possible without the precious help from volunteer patients. "This type of research could not be done if it weren't for the willing and dedicated individuals who volunteer as research subjects," said Payami, who acknowledged that some study subjects participated for nearly two decades.

What's next for the team? "Our results also pointed to several other genes that might play a role in developing Parkinson's disease, and these findings need to be confirmed, so we have a lot of work ahead of us" said Zabetian. He and others in the consortium will now mine the data even more for gene-environment interactions, with a goal of finding environmental triggers and protectors to develop genetically-personalized therapeutics for treatment and prevention of Parkinson's disease.

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