



**FOR IMMEDIATE RELEASE**

**Parkinson's Is Partly An Autoimmune Disease, Study Finds**

*First direct evidence that abnormal protein in Parkinson's disease triggers immune response*

*June 21, 2017*

**LA JOLLA, CA**—Researchers have found the first direct evidence that autoimmunity—in which the immune system attacks the body's own tissues—plays a role in Parkinson's disease, the neurodegenerative movement disorder. The findings raise the possibility that the death of neurons in Parkinson's could be prevented by therapies that dampen the immune response.

The study, led by scientists at Columbia University Medical Center (CUMC) and the La Jolla Institute for Allergy and Immunology, was published today in the Advance Online edition of *Nature*.

"The idea that a malfunctioning immune system contributes to Parkinson's dates back almost 100 years," said study co-leader [David Sulzer, PhD](#), professor of neurobiology (in psychiatry, neurology and pharmacology) at CUMC. "But until now, no one has been able to connect the dots. Our findings show that two fragments of alpha-synuclein, a protein that accumulates in the brain cells of people with Parkinson's, can activate the T cells involved in autoimmune attacks.

"It remains to be seen whether the immune response to alpha-synuclein is an initial cause of Parkinson's, or if it contributes to neuronal death and worsening symptoms after the onset of the disease," said study co-leader [Alessandro Sette, Dr. Biol. Sci.](#), professor in the Center for Infectious Disease at La Jolla Institute for Allergy and Immunology in La Jolla, Calif. "These findings, however, could provide a much-needed diagnostic test for Parkinson's disease, and could help us to identify individuals at risk or in the early stages of the disease."

Scientists once thought that neurons were protected from autoimmune attacks. However, in a 2014 [study](#), Dr. Sulzer's lab demonstrated that dopamine neurons (those affected by Parkinson's disease) are vulnerable because they have proteins on the cell surface that help the immune system recognize foreign substances. As a result, they concluded, T cells had the potential to mistake neurons damaged by Parkinson's disease for foreign invaders.

The new study found that T cells can be tricked into thinking dopamine neurons are foreign by the buildup of damaged alpha-synuclein proteins, a key feature of Parkinson's disease. "In most cases of Parkinson's, dopamine neurons become filled with structures called Lewy bodies, which are primarily composed of a misfolded form of alpha-synuclein," said Dr. Sulzer.

In the study, the researchers exposed blood samples from 67 Parkinson's disease patients and 36 age-matched healthy controls to fragments of alpha-synuclein and other proteins found in neurons. They analyzed the samples to determine which, if any, of the protein fragments triggered an immune response. Little immune cell activity was seen in blood samples from the controls. In contrast, T cells in patients' blood samples, which had been apparently primed to recognize alpha-synuclein from past exposure, showed a strong response to the protein fragments. In particular, the immune response was associated with a common form of a gene found in the immune system, which may explain why many people with Parkinson's disease carry this gene variant.

Dr. Sulzer hypothesizes that autoimmunity in Parkinson's disease arises when neurons are no longer able to get rid of abnormal alpha-synuclein. "Young, healthy cells break down and recycle old or damaged proteins," he said. "But that recycling process declines with age and with certain diseases, including Parkinson's. If abnormal alpha-synuclein begins to accumulate, and the immune system hasn't seen it before, the protein could be mistaken as a pathogen that needs to be attacked."

The Sulzer and Sette labs are now analyzing these responses in additional patients, and are working to identify the molecular steps that lead to the autoimmune response in animal and cellular models.

"Our findings raise the possibility that an immunotherapy approach could be used to increase the immune system's tolerance for alpha-synuclein, which could help to ameliorate or prevent worsening symptoms in Parkinson's disease patients," said Dr. Sette.

The study is titled, "T cells of Parkinson's disease patients recognize alpha-synuclein peptides." The other contributors are: Roy N. Alcalay (CUMC), Francesca Garretti (CUMC), Lucien Cote (CUMC), Ellen Kanter (CUMC), Julian P. Agin-Liebes (CUMC), Christopher Liang (CUMC), Curtis McMurtrey (University of Oklahoma, Oklahoma City, OK), William H. Hildebrand (University of Oklahoma), Xiaobo Mao (Johns Hopkins University School of Medicine, Baltimore, MD), Valina L. Dawson (Johns Hopkins University School of Medicine and Adrienne Helis Malvin Medical Research Foundation, New Orleans, LA), Ted M. Dawson (Johns Hopkins University School of Medicine), Carla Oseroff (La Jolla Institute for Allergy and Immunology, La Jolla, CA), John Pham (La Jolla Institute for Allergy and Immunology), John Sidney (La Jolla Institute for Allergy and Immunology), Myles B. Dillon (La Jolla Institute for Allergy and Immunology), Chelsea Carpenter (La Jolla Institute for Allergy and Immunology), Daniela Weiskopf (La Jolla Institute for Allergy and Immunology), Elizabeth Phillips (Murdoch University, Perth, Australia, and Vanderbilt University School of Medicine, Nashville, TN), Simon Mallal (Murdoch University and Vanderbilt University School of Medicine), Bjoern Peters (La Jolla Institute for Allergy and Immunology),

April Frazier (La Jolla Institute for Allergy and Immunology), and Cecilia S. Lindestam Arlehamn (La Jolla Institute for Allergy and Immunology).

The study was supported by grants from the JPB Foundation, the William F. Richter Foundation, the Parkinson's Foundation, the National Institute of Neurological Disorders and Stroke ([P50 NS38377](#)), the National Institute of Aging (90071017), and The Michael J. Fox Foundation for Parkinson's Research.

Columbia University filed a patent application for use of alpha-synuclein peptides as biomarkers (US Patent Application No. 15/300,713). David Sulzer (CUMC) and Alessandro Sette (La Jolla Institute) are listed as inventors. The authors declare no other conflicts of interest.

### **About Columbia University Medical Center**

[Columbia University Medical Center](#) provides international leadership in basic, preclinical, and clinical research; medical and health sciences education; and patient care. The medical center trains future leaders and includes the dedicated work of many physicians, scientists, public health professionals, dentists, and nurses at the College of Physicians and Surgeons, the Mailman School of Public Health, the College of Dental Medicine, the School of Nursing, the biomedical departments of the Graduate School of Arts and Sciences, and allied research centers and institutions. Columbia University Medical Center is home to the largest medical research enterprise in New York City and State and one of the largest faculty medical practices in the Northeast. The campus that Columbia University Medical Center shares with its hospital partner, New York-Presbyterian, is now called the Columbia University Irving Medical Center. For more information, visit [cumc.columbia.edu](http://cumc.columbia.edu) or [columbiadoctors.org](http://columbiadoctors.org).

### **About La Jolla Institute for Allergy and Immunology**

The [La Jolla Institute for Allergy and Immunology](#) is dedicated to understanding the intricacies and power of the immune system so that we may apply that knowledge to promote human health and prevent a wide range of diseases. Since its founding in 1988 as an independent, nonprofit research organization, the Institute has made numerous advances leading toward its goal: *life without disease*.

###

### **Media contacts:**

#### **La Jolla Institute for Allergy and Immunology**

Jessica Roi, 858-752-6645

[jroi@lji.org](mailto:jroi@lji.org)

#### **Columbia University, Medical Center**

Lucky Tran, 212-305-3689

[lucky.tran@columbia.edu](mailto:lucky.tran@columbia.edu)