New blood signature analysis may help diagnose Parkinson's disease earlier

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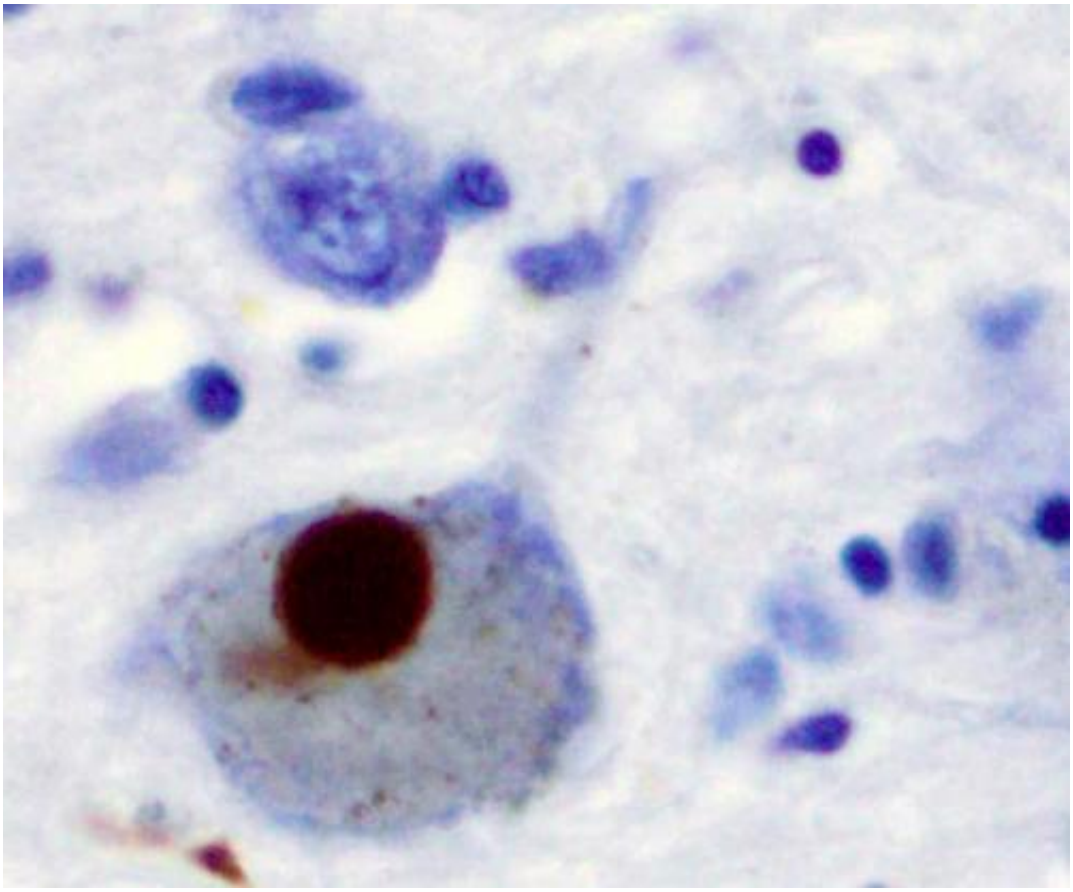

Immunohistochemistry for alpha-synuclein showing positive staining (brown) of an intraneural Lewy-body in the Substantia nigra in Parkinson's disease. Credit: Wikipedia

A new blood test may more accurately identify blood signatures, or

biomarkers, for Parkinson's disease (PD), according to a new study published in the journal *Movement Disorders*. The study, conducted by researchers at Mount Sinai and funded by the Michael J. Fox Foundation for Parkinson's Research, applies a new approach to looking for blood biomarkers for both patients with and without a known genetic risk factor for PD. This paper is the fourth in a series that report new computational techniques to improve the identification of reliable blood biomarkers.

While biomarkers—such as bad cholesterol level in the case of heart disease—hasten diagnoses by offering accurate measures of disease progression, there are currently no fully validated biomarkers for PD.

The Mount Sinai study analyzed the blood of four groups of mice with genetic material (e.g. ribonucleic acids or RNA) predicted by researchers to form part of a PD signature. Researchers also examined the blood of a group of Ashkenazi Jewish patients living with PD, as well as a separate group of healthy controls. About half of the human subjects—both symptomatic PD patients and healthy controls—have small changes in their DNA code called mutations, in a gene known to increase the likelihood of developing Parkinson's: leucine-rich repeat kinase 2, or LRRK2. Just one to two percent of Parkinson's patients carry this gene mutation, and many LRRK2 mutation carriers are from the Ashkenazi Jewish population. The other samples studied came from individuals without the mutation, half of whom had clinical PD.

After comparing the mouse and human blood samples, researchers identified RNA signatures that can be measured in blood samples that correlate with the disease-causing mutations in the LRRK2 gene in PD patients.

While LRRK2 mutations contribute to PD risk in a small percentage of patients, researchers believe related pathways also play a role in much

more common, non-inherited cases of PD. Studying it may speed progress toward treatments that would benefit everyone with the disease, not just those with genetic mutations.

"This is the first time we've studied animal models and clinical samples, and used them to look at RNA expression patterns of biomarkers in PD," said Stuart Sealfon, MD, Chairman and Glickenhaus Professor, Department of Neurology, Mount Sinai Health System and lead author of the study. "Our other goal is to use this approach to identify subtypes of the disease so that treatment can be targeted more accurately and in addition, incorporated with clinical trials that facilitate the ability to identify new therapeutic and disease modifying agents."

Parkinson's disease (PD) is a chronic and progressive movement disorder affecting nearly one million people in the U.S. PD involves the malfunction and death of vital nerve cells in the brain, called neurons. Some of these dying neurons produce dopamine, a chemical that sends messages to the part of the brain that controls movement and coordination. As PD progresses, the amount of dopamine produced in the brain decreases, leaving a person unable to control movement normally. The cause of PD is unknown and there is presently no cure.

"The goal of this research is to improve early disease detection, especially in people who are carrying a predisposing genetic mutation," said Dr. Sealfon. "If you can improve your ability to diagnose the disease more specifically and identify new subtypes, this can help overcome the hurdle in developing new treatments for Parkinson's and other brain diseases. The next step is to replicate this approach in a larger sample, where we track patients longitudinally and see how profiles are changing over time."

Provided by The Mount Sinai Hospital