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Study Looks for DNA Changes to Measure Parkinson's Disease

Two-year effort, funded by The Michael J. Fox Foundation, will look for molecular indicators in DNA that could aid diagnosis and treatment

Researchers at University of California San Diego School of Medicine and Arizona State University (ASU) have received funding from The Michael J. Fox Foundation for Parkinson's Research (MJFF) to launch a multi-year, $1.7-million effort to identify blood-based biomarkers of Parkinson's disease (PD), which could improve care and accelerate new treatments for the neurodegenerative disorder, which affects nearly 1 million Americans, with 60,000 new cases diagnosed annually.

"The exact cause of Parkinson's is unknown, but evidence points to a combination of genetic and environmental factors. Right now, there is no objective test or biomarker for PD, which increases the risk of misdiagnosis and delayed treatment," said Paula Desplats, PhD, assistant professor in the Department of Neurosciences at UC San Diego School of Medicine and co-principal investigator of the new study with Travis Dunckley, PhD, assistant research professor at ASU's Biodesign Institute.

The new study will analyze nearly 2,500 blood samples collected longitudinally over three years in the MJFF-sponsored Parkinson's Progression Markers Initiative (PPMI). These samples include donations from patients diagnosed with idiopathic (cause unknown) PD; PD patients and asymptomatic individuals who carry a genetic mutation in the PD-implicated LRKK2 gene; at-risk populations of people with REM sleep behavior disorder and/or smell loss; as well as healthy control subjects. Researchers will analyze DNA methylation, an epigenetic modification of the DNA that can change genetic activity without changing the underlying sequence. DNA methylation is critical to turning genes on and off and affects a vast range of cellular functions and fundamental development.

“This epigenetic analysis could help us better understand the pathology of Parkinson’s disease, pointing to biomarker candidates and, potentially, novel therapeutic targets,” said Samantha Hutten, PhD, MJFF senior associate director of research partnerships. “In addition, this DNA methylation data grows the value of the PPMI clinical, imaging and biological database, the most robust in Parkinson’s research.”

The goals of the new study are threefold: 1) Describe DNA methylation profiles of study participants, creating a new database for future studies; 2) Determine if methylation profiles are modified by PD genetic variants; and 3) Find out if any methylation changes can be linked to conversion of prodromal PD cases, from appearance of initial symptoms to full development of the disease.

“This study constitutes the largest appraisal to date of epigenetic changes during PD progression and may represent a major step forward in the design of a blood-based biomarker that aids in early diagnosis and evaluates the effectiveness of drug treatments,” said Desplats. “Early diagnosis is crucial to defining interventions since, by the time motor symptoms are evident, more than 70 percent of dopaminergic neurons have already been lost.”

Scientists have documented genetic mutations and environmental factors — such as exposure to toxins — that lead to Parkinson’s disease. Age is the greatest risk factor; the disease is rare in young adults. And men appear more at risk than women. But for most PD patients, the cause of their disease is not clear and likely a combination of multiple factors.

"The genetic and environmental causes of most cases of Parkinson’s disease are diverse and, to this day, remain largely unknown,” said Dunckley at ASU. “We believe that, through studying the genome, we can discover common factors underlying this disease that will enable an earlier and more accurate diagnosis to be made and that, using these DNA markers, we may enable more rapid clinical trials by providing an additional way for physicians to track progression of the disease."

PD is a degenerative nervous system disorder that affects movement and causes a host of non-movement issues, such as cognitive and autonomic dysfunction and mood disorders. Diagnosis is made by clinical observation of symptoms including tremor, slowness and stiffness. There is no definitive test to diagnose Parkinson’s onset or track its progression. Currently available treatments address symptoms of the disease; there are no proven measures to prevent, slow or stop Parkinson’s progression.

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