AI technology uncovers genetic factors and treatment options for Parkinson's

Researchers from the Cleveland Clinic Genome Center have successfully applied advanced artificial intelligence (AI) genetics models to Parkinson's disease. Researchers identified genetic factors in progression and FDA-approved drugs that can potentially be repurposed for PD treatment.

The *npj Parkinson's Disease* report uses an approach called "systems biology," which uses AI to integrate and analyze multiple different forms of information from genetic, proteomic, pharmaceutical and patient datasets to identify patterns that may not be obvious from analyzing one form of data on its own.

Study lead and CCGC Director Feixiong Cheng, PhD, is a leading expert in the systems biology field and has developed multiple AI frameworks to identify potential new treatments for Alzheimer's disease.

"Parkinson's disease is the second most common neurodegenerative disorder, right after dementia, but we don't have a way to stop or slow its progression in the millions of people who live with this condition worldwide; the best we can currently accomplish is managing symptoms as they appear," says study first author Lijun Dou, PhD, a postdoctoral fellow in Dr. Cheng's Genomic Medicine lab. "There is an urgent need to develop new disease-modifying therapies for Parkinson's disease."

Making compounds that halt or reverse the progression of Parkinson's disease is especially challenging because the field is still identifying which of our genes cause which Parkinson's disease symptoms when mutated, Dr. Dou explains.

"Many of the known genetic mutations associated with Parkinson's disease are in non-coding regions of our DNA, and not in actual genes. We know that variants in noncoding regions can in turn impact the function of different genes, but we don't know which genes are impacted in Parkinson's disease," she says.

Using their integrative AI model, the team was able to cross-reference genetic variants associated with Parkinson's disease with multiple brain-specific DNA and gene expression databases. This allowed the team to infer which, if any, specific genes in our brains are affected by variants in noncoding regions of our DNA. The team then combined the findings with protein and interactome datasets to determine which of the genes they identified affect other proteins in our brains when mutated. They found several potential risk genes (such

as *SNCA* and *LRRK2*), many of which are known to cause inflammation in our brains when dysregulated.

The research team next asked whether any drugs on the market could be repurposed to target the identified genes. Even after successful drugs are discovered and made, it can take an average of 15 years of rigorous safety testing for the medication to be approved.

"Individuals currently living with Parkinson's disease can't afford to wait that long for new options as their conditions continue to progress. If we can use drugs that are already FDA-approved and repurpose them for Parkinson's disease we can significantly reduce the amount of time until we can give patients more options."

Feixiong Cheng, PhD, Director, Cleveland Clinic Genome Center

By integrating their genetic findings with available pharmaceutical databases, the team found multiple candidate drugs. They then referenced electronic health records to see if there were any differences in Parkinson's disease diagnoses for patients who take the identified drugs. For example, individuals who had been prescribed the cholesterol-lowering drug simvastatin were less likely to receive Parkinson's disease diagnoses in their lifetime.

Dr. Cheng says the next step is to test simvastatin's potential to treat the disease in the lab, along with several immunosuppressive and anti-anxiety medications that warranted further study.

"Using traditional methods, completing any of the steps we took to identify genes, proteins and drugs would be very resource- and time-intensive tasks," Dr. Dou says. "Our integrative network-based analyses allowed us to speed this process up significantly and identify multiple candidates which ups our chance of finding new solutions."

This research was supported by grants from the National Institute on Aging (NIA) and National Institute of Neurological Disorders and Stroke (NINDS), both under the National Institutes of Health (NIH).

Source:

Cleveland Clinic

Journal reference:

Dou, L., *et al.* (2025) A network-based systems genetics framework identifies pathobiology and drug repurposing in Parkinson's disease. *npj Parkinsons Disease*. doi.org/10.1038/s41531-025-00870-y.

News Source:

https://www.news-medical.net/news/20250128/AI-technology-uncovers-genetic-factors-and-treatment-options-for-Parkinsons.aspx