

FINDING A TEST FOR PARKINSON'S DISEASE

Questions and Answers
on Biomarkers



THE
MICHAEL J. FOX
FOUNDATION

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Scientists are looking for objective medical tests for Parkinson's to help patients, doctors and researchers better diagnose and treat this disease. Biomarkers are the basis for those tests. Unfortunately, researchers have not yet identified any practical, definitive biomarkers of Parkinson's. Read on to learn more about these crucial tools and how The Michael J. Fox Foundation is leading the charge to find tests for Parkinson's disease (PD).

What is a biomarker?

A diagnostic biomarker is a measurable characteristic in the body associated with the presence of disease.

- » Blood sugar level is a diagnostic biomarker of diabetes. Levels of 6.5 percent or higher on two separate tests indicate disease.

A progression biomarker is a measurable characteristic in the body that changes over time in a way that can be linked to disease progression. This type of biomarker is critically needed for clinical trials — particularly trials of treatments to prevent, slow or stop disease — to objectively measure whether the drug is working.

- » White blood cell count is a progression biomarker of leukemia. Rising levels show the condition is getting worse, while a count moving toward normal shows improvement.

Why are there no biomarkers of Parkinson's disease?

There are a few advanced brain imaging techniques (e.g., DaTscan) that can help researchers measure the disease in its earliest stages, but no widely available and affordable biomarker tests have been conclusively validated. The variation in Parkinson's from person to person and the complex nature of brain diseases presents challenges in finding and validating PD biomarkers.

Why are biomarkers important?

Diagnostic biomarkers direct diagnosis and treatment. When doctors can draw blood or order a brain scan to confirm a diagnosis, patients and their families can get answers quickly and start treatment. These biomarkers also help select people for studies, giving trials the greatest likelihood of success and cutting time and cost.

Progression biomarkers help patients monitor disease and scientists develop new treatments. Researchers compare test results to see if a new treatment is slowing, stopping or reversing disease. Do biomarker levels move closer to normal? Do patients who did not receive the treatment have more or less biomarker change than patients who did get the therapy?

Biomarkers also may tell how far the disease has progressed and help predict the rate and nature of further progression.

How does the lack of biomarkers affect people with Parkinson's?

- » Diagnosis is subjective, based on observing and rating symptoms. This translates to a high rate of misdiagnosis and non-optimized care. A diagnostic biomarker would help people name their disease, watch for symptoms and start treatment.
- » There is currently no way to stop Parkinson's disease. By the time the first symptoms show, as many as 60 to 70 percent of a person's dopamine neurons may have degenerated. A diagnostic biomarker would allow us to identify people with PD — and intervene — earlier, maybe even before symptoms appear.
- » PD clinical trials are frequently and frustratingly inconclusive and take a long time.
 - » With no diagnostic biomarker, some PD trial enrollees may not have Parkinson's pathology, confusing results.
 - » With no progression biomarker to track the disease, there is no way to objectively measure treatment effects. Most trials use some form of symptom assessment, such as the Unified Parkinson's Disease Rating Scale (UPDRS), to determine



whether a treatment is working. But these methods are subjective, and symptoms can vary day to day, even hour to hour. These less-than-optimal measures may have contributed to a history of inconclusive trial results. They also mean trials often require more time and volunteers.

- » Some companies may not be interested in making Parkinson's drugs. Given the time, cost and uncertainties, PD trials are highly risky for drug makers. Fewer companies working on PD may mean fewer new therapies.

Where are scientists looking for PD biomarkers?

Researchers are looking all over the body for physical and cellular characteristics that show disease presence or progression. Here are the major avenues of pursuit today.

- » **Brain imaging** – Developing tools to visualize proteins linked to PD in the living brain.
- » **Fluid or tissue sampling** – Testing levels of proteins or other markers in blood, urine, spinal fluid or tissue.
- » **Non-invasive tests** – Using technology to diagnose PD with, for example, eye tracking or to monitor progression with wearable devices.

We likely need to use a combination of biomarkers (imaging, biologics and clinical) in the same individual over time to measure PD.

I thought a gene was a biomarker — and don't we know the genes that play a role in PD?

Certain genetic mutations can increase risk of PD, but they do not tell us enough to be a diagnostic or progression biomarker. It is possible to have one or more genetic irregularities linked to PD but never get the disease. Some drug trials do choose volunteers who have certain genetic mutations because their therapies target the cellular differences linked to those gene changes.

Do other brain diseases have biomarkers?

The lack of biomarkers is a particular problem for brain diseases such as Parkinson's, Alzheimer's and ALS. A study called the Alzheimer's Disease Neuroimaging Initiative (ADNI) has made important strides toward biomarkers of Alzheimer's and has reinvigorated research into stopping the disease.

What can I do to help identify a Parkinson's biomarker?

Parkinson's Progression Markers Initiative

In 2010, The Michael J. Fox Foundation launched a biomarkers study modeled after ADNI. The Parkinson's Progression Markers Initiative (PPMI) is looking for biomarkers and risk factors for PD. PPMI is following more than 1,500 volunteers for at least five years at 33 clinical sites around the world to better understand biologic changes over time.

PPMI is currently recruiting people with genetic mutations associated with PD. Certain mutations are more prevalent in certain populations. If you are of Ashkenazi Jewish descent and have either Parkinson's or a relative with PD, you may be eligible for the study. Given a genetic link to Gaucher disease, people with this condition or a relative with Gaucher also may be eligible. PPMI provides free genetic counseling and screening to all potential participants.

Visit www.michaeljfox.org/ppmi/genetics to learn more.

Fox Insight

The online study Fox Insight allows volunteers to take part in PD research from their own homes. This dynamic study lets people with Parkinson's and their loved ones contribute data on the experience of disease to help learn more about PD, which can help biomarker research and drug development.

Visit www.foxinsight.org to join.

Fox Trial Finder

Another online tool, Fox Trial Finder, matches volunteers to the biomarker studies and treatment trials that need them. Participants who sign up for Fox Trial Finder receive a list of trials in their area and email updates about new recruiting studies.

Visit www.foxtrialfinder.org to register today.

