Michael J. Fox: This is Michael J. Fox. Thanks for listening to this podcast. Learn more about The Michael J. Fox Foundation's work and how you can help speed a cure at michaeljfox.org.

Speaker 1: Navigating Parkinson's disease can be challenging, but we are here to help. Welcome to The Michael J. Fox Foundation Podcast. Tune in as we discuss what you should know today about Parkinson's research, living well with the disease, and the Foundation's mission to speed a cure. Free resources like this podcast are always available at michaeljfox.org.

Lydia Chain: Hello. And welcome to another episode of The Michael J. Fox Foundation Podcast's award-winning Parkinson's Science POV Series. I'm your guest host, Lydia Chain. My job here at the foundation is to bring you educational content like our third Thursday's webinars and this podcast where you can hear from scientists, doctors, and people with Parkinson's on different aspects of life with the disease, as well as research towards treatment breakthroughs. You'll hear a little from me today, but most of the voices you hear will be from our talented team of researchers.

I wanted to let you in behind the scenes and ask our scientists what they've been working on, what they're excited about, and how their work is going to help people living with Parkinson's, and how all of this will one day lead to a cure. We are so much closer to a cure than we've ever been before. The momentum behind Parkinson's research has only grown in 2024, and as you'll hear, our portfolio is wide-ranging, but there's still a lot to learn about the biology of Parkinson's. Scientists are working to understand why some people get Parkinson's and others don't, and how the complex set of environmental and genetic factors contribute to risk. They want to understand what the disease looks like at every stage, even before clinical diagnosis as possible.

Sohini Chowdhury: When it comes down to really developing therapies that will be impactful for people living with Parkinson's, you have to understand the biology of the disease in that person, and without biomarkers, we're not able to do that.

Lydia Chain: That's Sohini Chowdhury, Chief Program Officer at MJFF. A biomarker is a measurable indicator that gives information about someone's health. For example, cholesterol is a biomarker for heart disease. Doctors can measure the cholesterol in someone's blood and make a connection to their risk of heart disease. In 2023, in a monumental breakthrough, scientists created a Parkinson's biomarker test. It's for a protein called alpha-synuclein that in Parkinson's disease, misfolds and clumps in the brain. Scientists can now detect its activity in spinal fluid even before someone receives a clinical diagnosis of PD. But the hunt for biomarkers isn't over. More biomarkers mean more information about the disease and more options for treatments.

Sohini Chowdhury: I think that probably the project that I'm most excited about is a project where we put together a proposal to focus on the development of Parkinson's disease biomarkers in an incredibly accelerated fashion. And so the fact that we have this opportunity to go after biomarkers in an unprecedented way, I think is incredibly exciting and incredibly promising, and really lays the groundwork for the realization of new impactful therapies.

Lydia Chain: Senior scientific portfolio manager, Ariana Farrand says that more biomarkers will also mean faster trials because researchers can make sure that the right people are in the right trials.

Ariana Farrand: I think what most people are familiar with is being able to actually diagnose Parkinson's disease, but biomarkers can also be applied to make sure that the person is a great candidate for a clinical trial to also be able to measure how well a therapeutic is working in a clinical trial.

Mark Frasier: By finding better biomarkers, that is better ways to detect Parkinson's disease, we will be able to identify it earlier, treat earlier, and then measure that the treatments are actually working more effectively. So that's going to speed clinical trials and really get access and approved therapies to people living with Parkinson's earlier.

Lydia Chain: That's MJFF Chief Scientist, Mark Frasier. He also says that the work is well underway.

Mark Frasier: I worked on a program called The Quantitative Biomarkers Program that was focused on developing better quantitative measures of Parkinson's progression, and there are a number of grants that we made in 2024 focused on this challenge, and I'm actually really excited that all of them have made progress. They're all still working on this challenge, but we've seen some initial data that is looking really promising, that's getting to the goal of having quantitative measures of how Parkinson's changes over time.

Lydia Chain: To really discover and make use of biomarkers, scientists need tools to capture and measure them. A tool might be a blood test or a new way to image the brain. For the alpha-synuclein biomarker, it's a seeding assay. Here's director of research resources, Nicole Polinski.

Nicole Polinski: So research tools are the building blocks for how scientists perform experiments. So if you think of a big research initiative like wanting to build a skyscraper, in order to do that and to make a sound strong building, you need to have the right foundation, the right steel, the concrete and everything that goes into building it, otherwise it'll collapse. So the research tools are really those building blocks for the experiments that are going to help us build these large initiatives and uncover really critical answers for Parkinson's disease, and eventually develop therapies.

Lydia Chain: Brian Fiske, MJFF Chief Scientist, had more to say.

Brian Fiske: Much of the work that we're focused on right now is really about developing tools that can help us assess the biology of Parkinson's disease, and also how we can take those tools and actually use them in tests and in clinical trials for therapies for people with Parkinson's disease. And why that is so critical and important is because we can't really advance these therapies if we don't really know what biology they're hitting and what biology they're changing in people so that we can actually know if it's having meaningful benefits.

Lydia Chain: And the right tools can be used to tailor treatments so that individuals can get exactly the right treatment for the way the disease presents in their own body. Here's senior Vice President and Head of Clinical Research, Katie Kopil.

Katie Kopil: There's so much to be excited about. I think the opportunity to have new tools that help us understand what's happening in people's brains and bodies, not just what doctors are able to see, give people a sense of empowerment, and that we're moving Parkinson's research into a modern medical era where we're going to be able to deliver personalized treatments that map to what's happening in people's bodies.

Lydia Chain: But our scientists are quick to point out that to drive cures for all, everybody needs to get involved.

Alyssa O'Grady: If you don't include everybody in your research studies, you're going to miss something.

Lydia Chain: That's Vice President and Head of Clinical Research, Alyssa O'Grady, who works a lot on our diversity, equity and inclusion initiatives.

Alyssa O'Grady: I think the perfect way of illustrating this is talking about a research finding that GP2 and MJFF helped usher in 2023 with the Coalition of International Scientists. This was a new genetic change that was identified in individuals of African ancestry. It was the first time we had ever observed this genetic change simply because we hadn't looked in large numbers of individuals of African ancestry before to understand their genetics. So it was just a perfect proof point that inclusivity is so important for science so that you don't miss something.

Lydia Chain: Senior Scientific Portfolio Manager, Bradford Casey agrees.

Bradford Casey: In 2024, I worked on a lot of projects, but one that I'm most proud of is my work with the Global Parkinson's Genetics Project, GP2. This is a global initiative to collect samples around the world and connect that with the diverse research community to make sure that as we understand Parkinson's biology, as we drive things closer and closer to the clinic, that ultimately we are sure that that understanding is based around the most diverse representation of the patient population. So at the end of the day, we're developing things that are going to be a service to all Parkinson's patients around the world.

Lydia Chain: And here's Program Director of Clinical Research, J Solle.

J Solle: We work with researchers in hundreds of institutions who are contributing data into this resource project that are going to help us really better understand the genetics and the underlying biology of this disease. Better understanding of genetics will ultimately enable us to have therapies that work better and have better targets for Parkinson's disease.

Lydia Chain: Another way scientists are capturing a fuller picture of Parkinson's biology is through the Foundation's flagship Parkinson's Progression Markers Initiative or PPMI. In fact, the alpha-synuclein biomarker test was validated with PPMI data, and the study was a common area of excitement when I spoke with staff.

Maggie Kuhl: I would be remiss if I do not mention our Parkinson's Progression Markers Initiative, which is a real cornerstone of Parkinson's research and where we are learning so much about how Parkinson's begins and changes over time.

Lydia Chain: That's Maggie Kuhl, Vice President of Patient Engagement.

Maggie Kuhl: In 2024, we had more than 30,000 people take a smell test, which we're learning is a real canary, if you will, around Parkinson's risk and is a great way to allow us to understand more about the communities that are impacted by Parkinson's. Both people not yet with a diagnosis, but even people who have received a Parkinson's diagnosis.

Lydia Chain: Thousands of people have raised their hand for research through PPMI, which will accelerate our understanding of PD and lead to better treatments. Here's Katie Kopil again.

Katie Kopil: People have been contributing years and years of data, and new people are joining the study every day. That creates an endless resource for researchers to discover new ideas about what causes Parkinson's and how to treat it. And we don't have to start from scratch that people have been donating their time, their data, their bio samples, and that this resource is already banked to accelerate new research. So we're starting from really high up the mountain to reach the peak.

Lydia Chain: In 2024, PPMI started sharing back information with participants, from the alpha-synuclein test, DAT scan and physician assessments. Here's Maggie.

Maggie Kuhl: To me, this is a huge step in realizing the partnership of research participants, that they are not subjects of which we learn and discuss the findings amongst ourselves in the scientific community, but true partners who deserve to have those answers for themselves and now, which are enabling those individuals to take more ownership of their own healthcare decisions, lifestyle choices, research participation opportunities. I am very proud and heartened that PPMI made this commitment.

Lydia Chain: Our researchers have said this in different ways during the course of this episode, but the patients are the center of everything we do at MJFF. We share patient sense of urgency for improved treatments in a cure, and patients' unmet medical needs have shaped our decision-making around research priorities. Patients are our partners, whether it's participating in PPMI or advising us on which research initiatives hold the most promise to improve patient lives and much, much more, all of that information about the biology of Parkinson's disease, the tools, the biomarkers, all of it. It's all with the aim of developing better treatments like the two new drugs that were approved by the FDA in 2024. Biomarkers like alpha-synuclein often become targets of drug development, but so can genes or other pathways known to be involved in PD, and researchers are investigating and validating new targets to find new ways to address both symptoms and underlying disease biology. Here is Sohini again.

Sohini Chowdhury: I think it's all about really having therapies that address the underlying biology of the disease. So rather than having therapies that solely focus on symptom management, which is important because we want individuals who have Parkinson's to have the best quality of life as possible, but we want to go beyond that as well. And what we want to do is target the biology of the disease and to try to slow or stop it.

Katie Kopil: I work in the clinical research space, and this is where I think the Fox Foundation really shines in trying to bring together different stakeholders. So we don't just want researchers thinking about strong science, drug developers thinking about new medicines. We also want these solutions to be the types of solutions that the community is waiting for and the types of treatments that people want.

Lydia Chain: That was Katie Kopil. These new treatments enter the pipeline, the process of drug development and clinical testing that hopefully lead to new treatments to ease daily life with PD or stop it in its tracks. Here's Brian Fiske again.

Brian Fiske: So in my role as a chief scientist at the foundation, I spend a lot of my time looking at the clinical therapeutic pipeline for Parkinson's, working with our teams to think about what gaps we'd like to fill in that pipeline, where we see exciting progress in that pipeline, and where we can make advances with our funding and our other activities in helping to accelerate and enable that pipeline.

Gaia Skibinski: We're thinking about the next wave of therapeutics for Parkinson's disease patients. We want to have many different shots on goals.

Lydia Chain: That's Director of Discovery and Translational Research, Gaia Skibinski.

Gaia Skibinski: It's a really exciting time because we have many clinical trials that are ongoing for therapies that have been developed in the last 10 years. We just want to create more chances, more shots on goals. That's really what this Targets to Therapies Initiative is tempting to do. At the moment, we have several therapies being tested on patients that target LRRK2 and alpha-synuclein, and GBA. So these are quite familiar targets that people talk about for Parkinson's disease therapies. The Targets to Therapies Initiative that we're just setting up this year is trying to identify and prioritize the next emerging targets, like what are the new exciting targets that we should be working on, but will be the next wave of potential therapeutics that we'll get into patients.

Lydia Chain: And here's Shalini Padmanabhan, Senior Vice President and Head of Translational Research who works closely with Gaia and others.

Shalini Padmanabhan: This year, the team and I really focused on taking stock of what were those exciting Parkinson's disease targets that we should be focusing on. So we actually evaluated over 250 targets, almost close to 300 targets. We went through a very systematic evaluation, came up with a framework on how we should be evaluating these. What are those targets that we need to invest in so we can really push them from one stage to another. So we are very, very proud of that program because this is something that we built bottom up and we've already seen the results of that initiative.

Lydia Chain: Promising targets will begin to make their way through that treatment pipeline, and the pipeline has a lot going on. There's studies looking at disease modification. There's studies for motor symptoms, there's studies for a variety of non-motor symptoms, from pain to mood changes, to gait, and there's a lot to be excited about. Between you and me, it was quite a project to sort through all our interviews with our researchers because there's so much going on. But I did want to pull out a few interesting projects underway. Here's Bradford Casey, again, who is most excited about his work on big data.

Bradford Casey: Big data will definitely impact the future of people with Parkinson's disease. As we've learned more and more about the disease and as we've worked with patient communities to add collections of samples and data, all the power of big data allows us to use new analytical approaches and new algorithms of the type that we might use in the financial or communications world to really distill out the most important pieces of that data.

Lydia Chain: Here's Katharina Klapper, Principal Clinical Research Specialist who works on among other things, gait and walking.

Katharina Klapper: We have been seeing a lot of progress within the field, and we have been launching now two funding programs in this space where we are aiming to advance some of the knowledge around gait. We had a specific program on freezing of gait with a couple of projects that we are going to fund in the clinic that are either assessing non-pharmacological interventions to mitigate some of the freezing of gait patterns that patients are experiencing. And our new funding program is focused on personalized approaches to address gait, the whole continuum of gait. And the objective is very much to increase our understanding of what could be personalized interventions for the individual.

Lydia Chain: And Barbara Marebwa, Senior Scientific Portfolio Manager who works on using imaging to build an accurate, detailed, and analyzable picture of Parkinson's in the brain to learn what's going on in living people.

Barbara Marebwa: This is a picture that we can get on multiple scales, right? So we can look at it in terms of the structure, in terms of blood flow changes that occur, in terms of metabolites of interest. So we have a lot of scales, which we can be able to get this snapshot of the changes that are occurring in the brain and see how they affect the disease in terms of diagnosis and progression of the disease. And the idea at the end of this is to come up with biomarkers of nigro dysfunction that are useful for Parkinson's disease that can be used in clinical trials in the future.

Lydia Chain: And there is so much more to cover. For more information on how Parkinson's research changed in 2024 and what lies ahead, check out our November webinar to hear from industry experts and MJFF staff. You can find a link in the show notes. You can also read more in our year in review publication and consider raising your hand for research and being part of the work to find a cure. Take that smell test you heard about at mysmelltest.org/podcast. If you liked what you heard, share this episode with your community or leave us a review. It helps listeners like you find our show. That's going to be all for me for this time, folks. I am so excited to see what the new year holds for everyone in the Parkinson's community, and I'll be back with you in 2025. Thanks for joining us today.

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