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.

Maggie McGuire Kuhl: Faith and science are not often discussed together, but science requires a leap of faith. I'm Maggie Kuhl, Vice President of Research Communications. We have been talking a lot recently about a biomarker breakthrough, the alpha synuclein seeding amplification assay that may help diagnose Parkinson's disease, including in its earliest stages. In our podcast today, we won't go too deep into the science. You can learn more about that in our blog posts and a webinar on our webpage. But we will focus on people who took that leap of faith and were there at the origin of this biomarker, including for one, our founder, Michael J. Fox, who visited our foundation to share his thoughts about this breakthrough.

Michael J. Fox: We've got a moment here where we can move ahead in a total gamechanging way. And we think about those things-- when we launched these programs, we asked people to do things--we asked people to get spinal taps when they clearly didn't have Parkinson's! But they would do it to be a part of the control. And I mean, what an astounding gift they gave us, those people that did that. And all the other people that showed up.

Maggie McGuire Kuhl: So showing up with me are three people who have showed up for Parkinson's science in different ways. I have Dr. Samantha Hutten and Dr. Katie Kopil who are both staff scientists at the Michael J. Fox Foundation. And I have Donna Rajkovic who is a PPMI (Parkinson's Progression Markers Initiative) participant since 2012, diagnosed with PD recently before that. And she's also the founder of Team Fox Detroit, a critical partner in our efforts to raise funds for research and to spread the word about research opportunities and the latest science. So thank you all for joining us.

Katie Kopil: Thanks, Maggie.

Donna Rajkovic: Thank you. Thanks for having me, Maggie.

Maggie McGuire Kuhl: So Michael referenced launching these programs and asking people to do things. So this biomarker breakthrough came out of our PPMI study, which is one of the programs that he discussed. PPMI was a big factor in this breakthrough. So Katie, maybe you can share with us, what is PPMI?

Katie Kopil: So the Parkinson's Progression Markers Initiative or PPMI for short is a landmark natural history study of Parkinson's disease. One of the most critical things in terms of getting to better treatments is understanding is the drug slowing down the disease? Is it improving symptoms? And the only way you can really benchmark that is to understand how Parkinson's happens and progresses naturally. So PPMI is a labor of love from patients and families, from clinical researchers and coordinators who are committed to understanding how Parkinson's naturally evolves. It's a global study, over 50 sites globally are participating, collecting data, neuroimaging scans and biofluid samples, and then making those resources available for the research community to be able to advance biomarker research, to advance understanding of Parkinson's disease. And I personally think it's one of the best investments that the Fox Foundation has been able to make.

Maggie McGuire Kuhl: And Donna, you joined PPMI in 2012. The study started just a couple years before that, but you joined recently after you were diagnosed. So tell me about that, again, leap of faith of, you've just been diagnosed, you hear about this study, what leads you to sign up?

Donna Rajkovic: So like most young onset Parkinson's patients, it took several years to diagnose. And it was only after this DAT scan that along with my symptoms did my neurologist say, "Yes, you have Parkinson'." Which when you're in your forties, you're kind of stopped in your tracks, so to speak. And so I did some research and I researched on the website of Michael J. Fox Foundation that they were doing a PPMI study. They were looking for volunteers with young onset Parkinson's, no medications. And the closest location for me was at the Cleveland Clinic. And there I enrolled in that study. I met their qualifications, I enrolled in that and I'm still part of the study today. So this is an important study for me because I have three children and no Parkinson's in the family. So I wanted to do my part to help not only myself and my family, but other people and researchers to study that.

Maggie McGuire Kuhl: You said do your part. I think that that was a pretty big action to take. Many people are doing their part in lots of different ways. So you have signed up for PPMI. You are contributing, as Katie said, very valuable data and biosamples, building this massive resource.

Samantha, you are recently starting at the Fox Foundation a couple years later at 2014, and doing your own part to advance our efforts here to create better tests for Parkinson's. So tell me about coming across this interesting paper and what you did next.

Samantha Hutten: Sure, Maggie. So I remember it so clearly, Katie, you and I were I think looking at the scientific article that we had seen in a journal from this investigator at the University of Texas, Claudio Soto. And what he was working on wasn't a Parkinson's disease biomarker test. It was a Prion disease biomarker test. And when we were reading it, we were thinking, hmm, this is really interesting. Do you think he could develop something similar for Alpha-synuclein for Parkinson's disease? And we cold called him. And I remember asking you, I was very, very new at the foundation, I remember asking you, "Are we just going to call him, out of the blue and ask him to see if he can take our money and develop this test for Alpha-synuclein and start working on Parkinson's disease? That isn't his area of expertise per se, but this test could be translated to Parkinson's disease just as easily." And you said, "We sure are."

So we called him out of the blue and we asked him about whether he could develop a similar test for Parkinson's disease. And he was very enthusiastic about trying. And what I love about this example is it really speaks to the foundation's core value of urgency, because we weren't going to wait for our next funding cycle six months down the road to invite him to submit a proposal. We were going to call him and invite him to submit a proposal in two weeks so that we could capitalize on this really exciting finding in the Prion world and see if we could transfer it to Parkinson's disease.

And I remember thinking to myself, this is my dream job. I can do anything I want. If in the pursuit of finding biomarkers and a cure for Parkinson's, if it makes scientific sense and we want to find the right people to work with, we don't have to wait for them to come to us. And as I said, this is so core to the way we operate with urgency, really keeping the patients in mind. And it was just so fun to be able to do that, I think within my first few months working at the foundation and then to kind of follow this over the last nine years.

Katie Kopil: Oh, it is a fun place to be. And you think we had been out of short postdocs and we're standing on the shoulders of giants. All the work that Michael and our CEO, Debi Brooks had done to make a smart team that balanced science with business. People took the Fox Foundation very seriously. And so when you have two new faces get on the phone and ask for a call and ask if you'd like to work in Parkinson's, and for someone to say yes, I think it's a real tribute to the organization and the vision that Michael and Debi have built. And we get to keep doing it every day.

Maggie McGuire Kuhl: I feel like I remember how excited you all were about this project. I take a lot of notes in my job and I consequently throw out a lot of notes, but I have saved this piece, this scrap of paper where you were first telling me about this project probably now how many, six, seven years ago, maybe more. And I just always thought there's just something, they were so positive and hopeful about this. So I'm just going to put that one in the do not recycle yet list. And I was revisiting it before this call thinking like, oh, this is a little piece of history, but it has turned into something with real tangible impact for research and patients.

So Donna, as I said, you were participating in PPMI. Samantha just said the sort of ethos of the foundation is this urgency and this patient relevance. And how does that make you feel to know that your contributions were being taken very seriously? They were valuing your resource and working to put it into action as quickly as possible.

Donna Rajkovic: Oh my goodness. I'm so grateful, so grateful for all of you. And because every year, you go to the research salons and you hear all the updates and you hear all this positive information that you know that you're making a difference. And science is just constantly evolving and growing and just, it's very thrilling to be part of something like that, part of that history. I feel like I'm helping my family, myself, my community.

PART 1 OF 4 ENDS [00:11:04]

Maggie McGuire Kuhl: So Samantha, that was a bit ago as we were reminiscing about. So what has it been like since then? Science is a rollercoaster. There's some steps forward, a couple steps back. What is the process?

Katie Kopil: Ups and downs. Mostly downs.

Maggie McGuire Kuhl: So how have you kept that faith though, and what's it been like stewarding this project since then?

Samantha Hutten: I mean this is sort of one of my favorite projects that I've been able to work on at the foundation. But like you said, I think some things moved very quickly and some things moved more slowly, that some things were more successful than others. So we were able to fund the investigator to develop this test and that took some time working out the Kinks, alpha-synuclein are very sticky different protein. So there were some initial hurdles that we had to sort of conquer to just enable the assay to work, the biomarker test to work. But then after that we wanted to test it in different types of patient samples. So PPMI is such a valuable resource that before we even go into PPMI samples, we test it on other resources that the foundation has access to. So it was really awesome to be able to see that this biomarker test could differentiate between Parkinson's patients and healthy volunteers in some of our other cohorts that are not associated with MJFF.

Katie mentioned one of the great things about working at the foundation is that our name really goes a long way. So once we started working on this test and the investigator had developed it, people started hearing about it. Things were being published in scientific journals, it was being presented at meetings, so there was a lot of buzz and certainly other organizations and other cohorts and other investigators that had biosamples wanted to try it out. So before we know whether a biomarker test is really rigorous, we need to test it in different patient samples and make sure that we get the same data and the same results time and time again. So we were able to do that in a lot of different studies and we were able to show that the biomarker test is really sensitive and specific to be able to detect Parkinson's disease.

And that was a really big step forward because the sensitivity and the specificity that we were seeing was in the high eighties and 90%. And just to kind of put that in perspective, we haven't had a molecular based biomarker test like that for Parkinson's disease. So this was the first time that we had something that was that specific and that sensitive in being able to separate people with Parkinson's disease from healthy volunteers. So that was such a breakthrough for us. But along the way we also wanted to look and see whether we could detect this pathogenic Alpha-synuclein in other Biofluids that weren't spinal fluid. Donna knows that a spinal tap isn't super fun. So being able to detect this pathologic Alpha-synuclein in more accessible Biofluids like a blood test or a saliva test, we tried a lot of different things.

And so far the spinal fluid test has been the most robust probably because we started first with that and that's kind of most advanced and for the long. But it's been so exciting over the last year, year and a half to be able to see the exponential growth in different groups around the world. Not just this one investigator that we funded, but we've been funding 10, 15, 20 other groups since then who have been able to work on this type of biomarker test, have tweaked it a little bit changed it modified it, made it faster or more accessible for skin.

For example, skin biopsies. So this one initial grant that the foundation gave in 2014 has exploded into 30 different grants, millions of dollars that we've invested and that other organizations have invested to be able to move this test along faster and with urgency to be able to detect this pathologic Alpha-synuclein and other biofluids in different ways. And it's been so exciting to see that growth and to track it. And there's so many opportunities to go from here. It's really just the tip of the iceberg.

Katie Kopil: Sam, you're very humble. I was going to say, I feel like I had the chance to sit next to you as we had that first phone call with Dr. Soto and then I moved on getting to explore different parts of the work that research team does at the Fox Foundation. And every two years I'd check up and you were running a new round robin or new bake off and it wasn't a linear journey, but I think that the tenacity that you brought to this and the investment, you said, let's attract more people. Let's not just put our eggs in one basket and hope this works out, but let's get other scientists working on this. Let's try it out.

Different samples or thank goodness the PPMI samples existed, but that, you know, really built the bank that now people can keep going back to over and over again to understand is this going to work? And I don't know how you didn't give up.

Samantha Hutten: I don't give up.

Katie Kopil: But it's, I'm glad you didn't and I think it's exciting to be able to see this breakthrough when it was not clear that that was what was going to, was the road that we were on and that's what it would lead to. And so I love that you bring that passion.

Samantha Hutten: Thanks Katie.

Maggie McGuire Kuhl: I think the whole Parkinson's community is glad that Samantha didn't give up, but what I heard Samantha when you were recounting was that there is this MJFF approach of leaving no stone unturned, urgency, leveraging partnerships, but also developing a real strategy and understanding how we might get not only to, A to B, but A to C, D, E, F G. And the other thing I think that Katie you just alluded to it too, that Fox does is builds the resources to be able to execute those strategies and we build them actually even in advance so that they're ready when the strategy is ready. And it's not such a sort of step-by-step approach of, well first we have to get all these samples and then we can start to test them. We've already made this investment, as you said. And so Donna, you have made that investment. You were the one who has contributed this bank of resources.

So Donna, tell us what's your experience been in PPMI and how have you felt about contributing? What does require a lumbar puncture, but to researchers is really liquid gold?

Donna Rajkovic: Well, I just want to tell say thank you for not giving up. I'm so grateful for all of you at the foundation. So yeah, I mean science is interesting and these lumber punctures aren't that great, but it's a small price to pay to help others and researchers because without it, science is the key to a cure. That's the way we're going to get there and we need everyone to participate. And the sense of urgency. Everyone in Michigan, in the Detroit area, they are very supportive of the foundation. They are very eager to help out wherever they can and participate in the studies. And we had a PPMI research salon last year and I think, well now I think I know that we have had so many people sign up to be part of research. So, I mean it's amazing. So I'm happy to do it because I could see a future without Parkinson's and that's hopeful for my family.

Maggie McGuire Kuhl: It says a lot that every time I ask you about yourself, Donna, you're talking about how your community is responding or how you're doing this for your children. So I think it's coming through that you really think of others a lot and that's amazing.

So I do want to go back to you though. How did you feel hearing about this biomarker breakthrough? What was it like and where did you first get the news about this success and what was that like?

Donna Rajkovic: I was thrilled. My whole family, we were thrilled. We got the news at the research salon in New York, during the MVP and of course I can't remember the doctor's name, but he was up there with all his whiteboard and everything. And of course I didn't understand any of it except that it's over 80% accurate and here we are. So I was like, yes, all of this and all the spinal fluids and all the DAT scans and I would be happy to do it all over again. So yes. Yeah, it was exciting for all of us. We were so excited.

Maggie McGuire Kuhl: That's amazing.

Katie Kopil: I love that you got the big unveil at the end. On the science side. We, Samantha was talking about, okay, we're going to run PPMI samples. That sounds casual, but when you realize there's 1,000/1,500 hundred people participating in PPMI and they have many study visits, we were getting the data back like it was a weekly release on Netflix and so you're waiting for the next episode, you're like, what's the data going to say? Because the best test is the one you.

What's the data going to say? Because the best test is the one you have the least data on, right? So if you don't have a lot of data, it always looks good. So each week as more data came in, you're like, "Is it going to look as good as last week? Fingers crossed, fingers crossed." And each week it did, which I think made it really fun to hurry up and wait, hurry up and wait. And it was so exciting to see it unveiled now at the end, but along the way it was pretty exciting too.

PART 2 OF 4 ENDS [00:22:04]

Maggie McGuire Kuhl: So Donna got the binge experience, right?

Katie Kopil: Totally.

Maggie McGuire Kuhl: Where all episodes are released at once. So I wanted to hear from someone else. We can play a clip here. Katie, you referenced before our CEO, Debi Brooks, who is a PPMI control participant herself. And she shared with us how Michael took the news of this biomarker breakthrough. So we can roll the clip hearing from her.

Debi Brooks: I really just wanted to make sure that Michael got a chance to hear it first. So he was on a family vacation in California and I flew out to visit with him and I set up some time, Todd Sherer the Chief Mission Officer at the Fox Foundation and the lead scientist for our team, he was joining us by Zoom. And so I kind of sat down with Michael and I said, Todd's going to going to be with us in a minute. I just need you to know he's going to tell you all the science. And Todd's a great science communicator. So it wasn't that it would be impenetrable, but I said, but you just need to know this is a breakthrough. And he just looked at me and then I hit go on the Zoom and Todd explained it all and Michael was nodding. He totally got it. Of course, we've been invested in biomarkers to the tune of hundreds of millions of dollars over the last 15 to 18 years.

And he knew exactly what the implications were and he was choked up. He was so proud and excited and felt like this is what we're here for. I mean, he immediately appreciated the full potential of this finding. But the cutest part was he picked up the computer screen, picked up his laptop and brought it forward and leaned over and kissed Todd.

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Maggie McGuire Kuhl: Certainly a lovely moment and I think a sentiment shared by a lot of us here. So Donna, you said I'd do it all over again and I think we are going to ask you to do it perhaps over and over again because our work is far from done. As Samantha recounted, she has big plans as she has a lot to do. So Samantha, what is next? What work remains and why do we still need really the whole community behind us to make this have an even greater impact?

Samantha Hutten: Sure, Maggie. Yeah, our work is never done. There's always more that we can do. So some of the things that we're really excited about right now are, as I mentioned, the opportunity to be able to employ this test in other non spinal fluid bio fluids or bio samples such as skin, olfactory mucosa, kind of the way we have been used to taking covid tests over the years. Certainly blood is very easily accessible. So there's that opportunity. I think another thing that we're really focusing on is taking the assay from its current form, which is binary to a more quantitative biomarker test. So right now when we look in the spinal fluid, we can say, yes, the assay is positive for this pathologic alpha-synuclein, or no, it's not for that particular moment in time when the spinal fluid was taken. But what we are moving towards and what we really hope for is something that can give us a number, like there's 400 micrograms of this pathologic alpha-synuclein. And you can imagine if you test, and now in 2023 and then you test again in 2024, that number could change. And that could tell us how the disease is progressing over time. If we have an at-risk person or somebody who has a family predisposition for Parkinson's disease or may have some risk factors like hyposmia, loss of smell or REM sleep behavior disorder, RBD, we would want to be able to track that person over time and we could potentially have the opportunity to use this test to see how the numbers are changing over the years or in clinical trials. If we had a quantitative assay, a quantitative biomarker test, we could see how a particular treatment is changing that number to know how that drug is affecting Parkinson's disease and specifically the alpha-synuclein readout. And that could inform clinical trials in a really big way.

I heard from Donna that she was really excited to hear these results and I can tell you that our pharma partners and people who are in the clinic right now are also really, really excited about the current results. And also thinking about the opportunities that this biomarker assay has in the future, particularly around being able to quantitate it and measure it in the same way that we can for cholesterol. So you can understand that having a cholesterol level above a certain amount predisposes you to various conditions, heart disease, things like that. And that's what we're going for with this pathologic alpha-synuclein. If we can figure out how to make it more quantitative, then we can develop a threshold and also understand how it changes over time. So those are two things that we're working hard on now and we have been working on these for a while, but with all the excitement and the enthusiasm around these latest results, like Katie said, we don't want to have all of our eggs in one basket.

So we're talking to leading experts around the world who are working on this and we're trying all of these different things. We're working with these different groups, having them collaborate with each other so that the research isn't siloed. Bringing these people together so that they can talk about their results and their challenges in real time and thinking ahead about the ways that the foundation can address these challenges or better enable this research as we think about the unmet needs and the gaps and what we can do to plug them and fill them and really capitalize on this really, really exciting finding so that we can move even more quickly to make the assay better and better and keep iterating.

Katie Kopil: Yeah, this is the beginning. It's a new frontier.

Maggie McGuire Kuhl: It is. So why is the Michael J. Fox Foundation, Katie, the best partner to push us toward that vision that Samantha just laid out?

Katie Kopil: Some of the things that I think make the Fox Foundation so special, we dare to be bold. And I think the return on investment and risk calculus we have, we're looking for things that make people affected by Parkinson's better. Donna, you were talking about it took you a long time to get a diagnosis. That can't be easy. And I don't know that this test is something that you're going to run out and do today, but for people that have to go on that journey in the future to have an easier journey to get a diagnosis, that's what gets us out of bed in the morning. Better treatments. Samantha talked about companies wanting to invest in clinical trials, in better treatments, understanding how do you know that you're changing the biology to slow down the disease? These are big challenging questions that have scared a lot of people off.

And I don't think Michael is scared. And the team at the Fox Foundation certainly isn't scared of taking risks. And we do this wisely. The donor dollars that Donna and her team Fox family helped raise for us, we want to deploy that quickly, want to put it onto things that other people aren't going to invest in. And so I think this is one of the reasons that the Fox Foundation is special. Some of the activities that are cascading from this biomarker finding include partnerships with other global patient organizations to make sure we have the same messaging that we can align our strategic funding to help really pave a pathway to better treatments. And it doesn't just stop here that we pat ourselves on the back. I mean, I would like to pat Samantha on the back, and I will. But that's not the end of the day that we now see, okay, well here's where we're going next and here's how we get up that mountain that we've been climbing.

Samantha Hutten: Katie, it's not just the Fox Foundation, obviously, it's Donna, it's the patients, it's the people donating CSF, it's the pharma partners. It's all of the different academic or researchers around the world. And being able to bring these people together, I think is the value add of the foundation. We're all speaking the same language and working together because we know we're all on the same page and we're all not competing, but collaborating in the most efficient way. And that's, I think, one of the strengths that we have. But it wouldn't have happened with just one of those resources or one of those groups.

It takes all of those different things together and I'm just so thankful to be a part of it. I'm thankful to Donna and all the participants in PPMI and our partners from the other organizations and PPMI leadership, the PPMI study, and all of the investigators who are working on this. Cause it took one person to take the leap and think about diving into the Parkinson's world with this type of assay. And now I think they're around 30 different groups working on it, working hard. And those are just the ones that we're affiliated with that we know of. It's just so exciting to see how it's exploded.

Maggie McGuire Kuhl: We can be bold and brave and take risks because we have the partnerships and the network and the community with us. So Donna, as we wind down our conversation and thank you to all of our folks here for joining us, but I want to give you the last words on how you have felt contributing in PPMI for the last 11 years and moving in this new frontier as Katie put it with the outcomes that your efforts have led to.

Donna Rajkovic: Well, I can't thank everyone enough for all the work they've done being, like I said, diagnosed young with Parkinson's disease is really, it's a challenge. And through all the resources and all the contributions that we do as a community and as supporters of research, I think it's important to have that trust factor with your organization and...

your doctors and things like that because you do see a difference. I see a difference in myself with the new medications that have been coming up through the pipeline. So I think the PPMI is, I'm so grateful to everybody. I'm grateful to Michael taking that risk, saying, "Hey, we're going to go in blind and let's see what happens." And here we are years later. There's progress. There's hope.

PART 3 OF 4 ENDS [00:33:04]

Katie Kopil: The field of dreams you built through PPMI.

Donna Rajkovic: Yes.

Katie Kopil: And now people are coming.

Maggie McGuire Kuhl: Thank you all, not just for your time today, but for everything that we've talked about in our time together. For you listening, participating in research like Donna has and continues to do is one way to feel empowered and make a difference, as she said, not only in her own disease, but in the future of how we approach and treat Parkinson's disease. So whether you have PD or not, you can help move research forward. Join the study that's changing everything. Visit michaeljfox.org/podcast-ppmi. Until next time, thank you for listening.

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