Maggie Kuhl: You're about to hear a conversation about the evolution of the Michael J. Fox Foundation's landmark PPMI study. In the course of our conversation, panelist Donna Rajkovic experienced Parkinson's symptoms. With permission from Donna, we've included those moments to give an authentic portrayal of the community we serve.

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.

Maggie Kuhl: Hello, I'm Maggie Kuhl, Vice President of Patient Engagement at the Michael J. Fox Foundation. Thank you for joining us today to listen to the latest update from our Parkinson's Precision Medicine Initiative or PPMI. You may know it by a different name. For the last 15 years, it was the Parkinson's Progression Markers Initiative. And today on this podcast, we're going to dive into what the aims of the study were back in 2010 when we launched and what they are today and what precipitated such a name change.

So we have some folks who have been with the study nearly since the beginning, if not well before even 2010. So to quickly introduce our esteemed panelists today here with me is Dr. Ken Marek. He is Co-Founder of the Institute for Neurodegenerative Disorders, and he has been the lead principal investigator for the PPMI study since its beginning. Ken, thanks for giving us your time.

Dr. Ken Marek: Thank you.

Maggie Kuhl: Sohini Chowdhury, the foundation's Chief Program Officer was also integral in helping launch PPMI and has stewarded it into what it is today and what it will be tomorrow. Sohini, thanks for giving us your input as well.

Sohini Chowdhury: Thank you.

Maggie Kuhl: And representing our most important partners in PPMI is Donna Rajkovic. Donna was diagnosed with Parkinson's in 2012 and joined the study soon after that same year. She's also the founder of Team Fox Detroit, a fundraising community and support network in her hometown. Donna, thank you for being with us and being part of the study.

Donna Rajkovic: Thank you for having me.

Maggie Kuhl: So to kick off our conversation to talk about what PPMI is, the impact that it's had, I think it's actually important to start with why we need more than just a therapy to move toward cures and new treatments. Donna, as someone living with Parkinson's and meeting many people with Parkinson's, some of the most common questions are what's going to happen to me and how am I progressing? And so what would, beyond just the promise of assessing new treatments in the future, how would better tests or measures of disease impact your care and how you interact with your doctor to manage your Parkinson's today?

Donna Rajkovic: It's my 1:30, is my medication time, so my brain is a little bit slow right now, so.

Maggie Kuhl: If you could go in every time that you have a doctor's appointment and have a blood test that gives you a, here's how your progression tracks, would that help you understand more how your Parkinson's is doing? Would it give you more insight into what might happen and how you would live your life?

Donna Rajkovic: Yeah, I think having better tests like blood tests and to see where my progression is in the disease process right now would be really helpful because the not knowing from day to day taking this medication and then it works for a minute and then it doesn't, I think it would be really beneficial to anyone with Parkinson's to have an idea of what we can do to either slow it down where it is at that time so it doesn't progress.

Maggie Kuhl: I think we launched PPMI because we needed tools to assess this next wave of treatments that was coming up. So with those goals in mind, Sohini would love to hear when we were identifying this need, when we were hearing from patients, these are our biggest unmet challenges, both cures and this long road to diagnosis, where was the foundation's mindset and how did PPMI crystallize or catalyze?

Sohini Chowdhury: The foundation's mindset from the beginning has always been what can we do to really develop things that have impact for patients? And so that really focused both on how we could improve the quality of life for individuals with the disease, living with the disease, their journey with the disease here and now, but also this holy grail of if we were to develop a therapy that could slow or stop disease progression, what will it take to do that? And so that was from the beginning and that really did reflect at the highest level what we heard from the community in terms of their unmet needs. But when we think about PPMI, and if you think a little bit about how that then reacted, I would say that in a perfect world, the story would be like, oh, and it connected with this incredible idea of PPMI.

But as Ken and I know, that's not quite how it went. And that's often the way these most impactful things happen is that things are happening in parallel and then before you know it, oh wow, they connected and they're in sync, but they didn't start that way. And so PPMI really didn't come out of conversations with the patient community. It actually came out from conversations with our scientific advisory board who were basically saying, "Hey, have you checked out and seen what's happening in the Alzheimer's field?" They have set up, and I think at that point, Ken, it was about maybe four or five years in existence, they've set up this study called ADNI, Alzheimer's Disease Neuroimaging Initiative, and it's this partnership with the government and companies, and it's all about developing these biomarkers, these tools to help really support drug development, to help us figure out what drugs are having an impact and is that the impact we want?

And maybe we should think about doing something similar in Parkinson's. And so that was way back in 2007. Ken was at that meeting, I and others were at the meeting and we talked about it and we started to move on this path of what would that mean? And we got it. I mean, at the scientific level, we totally were

like, oh, that's a no-brainer. Of course we want to do that because this is what our community needs. This what they told us. But it came through sort of a left hook or whatever. It wasn't quite a straight thing. But to our credit, we recognized that this wasn't something that we generated or that came directly from our community, but it very much fit the roadmap of how we wanted to ensure that what we were investing in, what we were supporting was all towards that effort of addressing the needs of patients.

Maggie Kuhl: So Ken, I'm actually going to read a quote to you of yours from 2010. When we first launched PPMI, you had said that, "With PD progression biomarkers, it will be possible to establish objective endpoints for clinical trials of disease modifying Parkinson's treatments. Endpoints are concrete ways to demonstrate that a candidate therapy is or is not slowing disease course. Without a biomarker, this sort of evidence-based decision-making is much more difficult." So that was a pretty academic way of saying that we need measures of disease to test if these therapies are working. Could you just ground us in the science a bit of why we need more than just a drug to get to treatments and why these measures matter?

Dr. Ken Marek: Yeah, I think that as you point out, in the most simple way, what we're saying is that it's important to be able to accurately and reliably measure the change over time in someone's disease state in order to know if a medicine has helped that process. And that's very simple, but the big problem in Parkinson's disease is that it's very challenging to simply measure the change in disease state by measuring symptoms because people, they're so changeable within a person, they are affected by medication. And of course they're very different among different individuals with Parkinson disease, a very heterogeneous disease.

So what we have sought is to have some more objective measure that we could use to really assess this change over time and likely not only one measure, but a group of measures that are going to be helpful in trying to understand whether a drug or an intervention might change the course of illness. And I think that's something that was, at the time PPMI began in 2010, it's something we've tried really hard to develop and it's a challenge to come up with these measures. But I think one of the benefits of PPMI is that it's enabled us to really come up with a group of biomarkers or objective measures of disease that will help us to really understand the change in disease over time.

Maggie Kuhl: We have made absolutely great strides toward that initial goal. So we talk about having crossed the 15-year mark in PPMI, but it sounds like we're actually closing in on the 20-year mark because it took a couple years. I would say still pretty quickly that we stood it up between late 2007 and early 2010, but to be able to build something at the scale of PPMI in a short time sounds like we've actually been at this for maybe close to two decades by now. And Sohini, I want to ask you too about when this idea was presented to you or the scientific folks said, "Hey, you should look over at Alzheimer's." They came to us, they came to the Fox Foundation, and they felt that we were in a good position. We were the right partners to move this forward. And so what about Fox really says we're the right leaders for this initiative?

Sohini Chowdhury: Yeah. Again, if you think about what their model was that they were thinking about ADNI, the partner who really catalyzed it and coordinated it and funded it was the US government. It was National Institutes of Aging, right? And so here in Parkinson's, it's the Fox Foundation. And Ken, I would be interested in getting your thoughts because you were part of the voices advocating for us to look at what's going on in Alzheimer's and not ignore it. But I think my perspective as being sort of a Fox staff member in that meeting is that part of the reason it came to us is that we did not have the same support from the government in the same fashion as it was with Alzheimer's. And that also there was a recognition here that there were things that had happened in Alzheimer's that pushed it in some ways a little bit ahead, and there was things that were still being built within Parkinson's.

And a lot of those building blocks, whether it be biomarkers, therapeutic development, that all was very much being catalyzed by Fox Foundation funding. And so we really were the right entity, that if you were going to think about who was going to take this on, who was going to advocate for it, who was really going to invest in it at a time when industry investment in Parkinson's was still quite low and spotty, we were really the only game in town. And this was, mind you, before we really also fully developed our ability, our patient engagement strategy. Now we have this incredible, like this podcast, this incredible suite of material and content that we share with our community. Back then we were a much smaller organization.

So we had reach obviously into the community, and it was a two-way dialogue, but it was not to the scope and scale that we have today, but still it was more than any other group probably had. And I think that also probably, in my mind, put us as the group that was most likely to take this on if it were going to happen. But Ken, you were on the other side of that conversation, so I don't know if you have different viewpoint.

Dr. Ken Marek: I was fortunate enough to be present at the start of the Fox Foundation's really efforts. And I think even from the very start, that it was clearly a foundation that was one, going to focus on understanding the science and biology of disease with the idea that that would lead us to better therapies, would lead us to where patients wanted us to be, which is to provide better treatments for disease. And the idea of biomarkers was a key part of that even at the very beginning, even before PPMI began, that it was something that had been identified within the foundation, within the scientific advisory board as a focus because we thought this would really be important in helping us to get to the settler promised land.

And it was really after a few years that it became clear in part because as you say, in part because we had an example from Alzheimer's disease, in part because it was just the growth within the efforts that had already been undertaken at the Fox Foundation, that we now could really develop this much more comprehensive strategy to try to get at this problem in the most efficient way. And I think on the one hand, it was pretty clear that we needed to do this. On the other hand, it was a huge effort and a huge risk to take this on because there really aren't even today and there certainly weren't then many studies that are focused on the development of biomarkers. And with a focus of the many and from the very

start we understood it was going to take a few years for really this to come to fruition.

So this is not the way clinical studies usually work. Usually their idea is that they're trying to develop quick answers and they certainly want to be sponsored by pharmaceutical companies that have a drug or drugs that they want to move forward. So this was a big change and a big risk and really was necessary to set the standard or provide a scaffold on which other trials could build and exist. And here again, it was really only the Fox Foundation that really had the vision, the energy to accomplish this. It was a remarkable effort that [inaudible 00:15:18] for what was a pretty young organization at that point to really take this on. And it's really been very successful and really grown in a way that has been very helpful in doing exactly what was the goal, which was to accelerate therapeutics. But I think it was a real visionary effort at that point.

Maggie Kuhl: And I think that that energy, that tenacity, that optimism really comes from our founder, Michael J. Fox. And I want to throw to a clip from him in 2010 talking to Dr. Sanjay Gupta where he shares more on our perspective here.

Audio: Michael J. Fox: Cures don't fall out of the sky. We have to go up and get them and we just assume. I think I always assumed that there was a Department of Cures, that there was a Minister of cures, Secretary of Cures, but there isn't. It's us.

Maggie Kuhl: So Donna, you are one of the secretaries of cures here in helping us launch and lead PPMI. And you joined so quickly after your diagnosis. What made you take that step?

Donna Rajkovic: Well, it's because first of all, I don't have Parkinson's in my family. At that time, I had three young children and I didn't know why I got Parkinson's. So I thought, well, I'm going to do some research. And I know that for me, science is the key to answers. It unlocks all the doors and windows to find the answers. And so when I joined... Sorry, my brain. See, this is where Parkinson's sucks. I can't get my thoughts out of my head.

Maggie Kuhl: I think a lot of our listeners would say, "Yeah, I'm having that day right now." And so don't apologize. If anything, thank you for sharing with our audience the reality of it.

Donna Rajkovic: Yes, it's really horrible where you feel trapped in your brain after 14 years of this diagnosis. And I joined the PPMI study because I really did want to help be part of a solution. It's my way of controlling my Parkinson's. I'm in control. It's not controlling me. And I wanted to make sure that I was helpful for unlocking some critical answers that needed to be answered for sure.

Maggie Kuhl: Well, we've been talking a lot about why PPMI is so important and its big goals, but for someone who's been in the study for 14 years, what is the reality of being in PPMI for you? What happens when you go to those appointments?

Donna Rajkovic: Well, right now, 14 years, I've been doing this. It's a annual visit and you go through the process of answering questions. You have a scan, you have some blood samples, things like that that they want to see because they're following you throughout the years. And so they want to see what's progressed, what stays the same. And so it really does help them understand the change that you're going through cognitively, physically, emotionally, things like that. And you yourself, as a patient, get to see how far you've progressed. I mean, I would answer these questions. I remember going, "Oh, why are they asking me this question? This makes sense." And now it's like, "Oh, okay, these are important. Drooling is important, swallowing is important. These kinds of things, this is where the doctors and researchers get to look at you and follow you throughout the course of the years and understand what's changed."

And for me, cognition has changed significantly, significantly, which I know that part of it is aging, part of it is that. But I don't know, I've never been this old and I haven't had Parkinson's for this long, so I don't know what it is. But I know the cognition is definitely really bothersome, really. It makes you disassociate from your friends as well. It's very isolating because you find yourself less of you and more of the disease, which is really frustrating.

Maggie Kuhl: You bring up, could it be aging? Could it be Parkinson's? At a certain age with women, hormones are always in play as well. And I think that's also one of the goals of PPMI, is that there won't be a measure for everyone. Can you use the term collection of measures, collections of biomarkers? How is PPMI helping us, from all of those tests that Donna said from so many different types of people, figure out how we can measure and tract disease in the complexity of the Parkinson's population?

Dr. Ken Marek: So this is really what Donna's describing, of course, is unfortunately not typical. Many people with Parkinson disease have these same kinds of challenges and difficulties, which are so frustrating. And I think cognition is a good example that often cognition is something which might occur later after you've had the disease for some period of time. So one of the real questions we have is what's driving these different changes that are occurring throughout the course of the illness? Again, I'm going to go back to the idea that if were smarter about being able to understand the biology of these changes, that can help us to both understand why these changes occur, in who they are going to occur, and when they're going to occur. And that's really what we would love to be able to do so we could, again, ultimately have a portfolio of drugs that could forestall this.

That's the holy grail. But I think it's really helpful to be able to, you pointed out so clearly, that people with Parkinson's disease have different challenges all the time. Even within an individual, one day is quite different from the next, but between individuals, also very different. And I think that we want to understand if we can use their objective biologic measures to predict who's going to have what problem. This is really the background for this name change that was mentioned earlier; when we're now, we think we're ready to use the terms precision medicine where we can use biology to be more precise in developing the information we need to predict what might be the symptoms that would occur, and when they might occur, and hopefully what drugs might be the best

drugs for different people so that they are really targeting those drugs to the people who are going to benefit from them the most.

And again, I can't say we could do that today. We can't. I wish we could, but that's where all of the information that Donna has provided and all the thousands of people in PPMI have provided are helping us to really get to that point.

Maggie Kuhl: I want to bring in another community voice here and touch on the need for different types of individuals to learn more about the different types of biology to, as you said, step into this precision medicine future, this right treatment, right time, right person. And so I'm going to throw to my friend Alan Dance who says this.

Audio: Alan Dance: I got a diagnosis for RBD last September and I joined PPMI the next week. One of the things that I found out before I was in this study is that a lot of the research studies in this area have a shortage of African Americans participating in it. And if you're doing research, you need to have people from all backgrounds. So I look to be an active participant.

Maggie Kuhl: So we are moving toward this future of precision medicine. Sohini, would love to hear from you about what precision medicine means overall, but also what does it mean for this study, for PPMI? What has changed in how we do this work, if anything?

Sohini Chowdhury: Yeah, so precision medicine is this term that's tossed around a lot. We see it in media, we see it in articles, we see it all over the place. And sometimes it's also called personalized medicine. But precision medicine essentially is just recognizing and taking an approach where an individual's biology, their genetics, their lifestyle, their environmental factors, all of these aspects are taken into account as you think about a therapeutic regime for a disease that you may be tackling or as you think about your own health kind of approach. And so it really is simplest nature, it's sort of moving away from a one-size-fits-all approach to recognizing that you want a bespoke approach that fits your characteristics, your variables, whether those be biological, sort of what's happening inside you, whether it's a combination of your lifestyle and your environmental, all of those things. And that's essentially what it is. And I think Ken and I have sort of chatted about precision medicine and Ken always is like, "We were precision medicine from the beginning." And in theory, yes, except in practice we weren't quite there.

That was always where we knew we wanted to go, but the science hadn't evolved as much. Our ability to be able to start to look at individuals and not just see the clinical diagnosis of Parkinson's disease, but actually start to go and look beyond that at the biological components, the molecular components, that was harder in the early days of PPMI. And I think what has changed, what has allowed us to start to be able to move in this direction is the ability to start to have tools that give us a sense of what is happening inside Donna and inside other thousands of participants in PPMI. So we're able to understand what's happening to the dopamine neurons. We have imaging that allows us to see that. We have

something that we've talked about at the foundation a lot. We have this alpha-synuclein seeding amplification assay, or called SAA for short.

It allows us to detect whether individuals have the form of synuclein that's relevant for Parkinson's disease, where we have genetics. Some people have genetics of interest, others don't. And so you're starting to build these variables of how you can look at an individual, not just again, sort of saying, "Well, here's this person with a diagnosis of PD," but sort of saying, "Well, here's this person with a diagnosis of PD, and do they have variables A, B, C, D, blah, blah, blah? Or what is their specific constellation of variables?" And that allows us to be a lot smarter about thinking about what is happening with this person. How do you tackle the things that matter to this person based on what is unique to that person? But it also allows us to start to say, "Okay, we always say that an individual's journey with Parkinson's is so different from one another, right? And that was just based on the symptom journey, the experience that you have day-to-day." Now we can actually say, "Well, no, there's also a biological difference between everyone."

And so we're seeing this there. And that actually means that maybe we have to be smarter. We have to think about different ways of tackling it from a therapeutic component. So it gives us more information and more precise information for an individual. And at the end of the day, when you have a disease that's as complex as Parkinson's, more information is only better. And the more people you have those information from, the better. And so going back to Alan, you want to have a representation of everybody who has Parkinson's because guess what? There is going to be differences and we want to capture that and you want to make sure that you fully understand the spectrum of what is the same because some things will be similar, but what is different? And so if you don't have a full representation of the community that is affected, you're never going to be able to really fully exploit the opportunities precision medicine can give us.

Maggie Kuhl: And Sohini mentioned a couple on the PPMI highlights reel, the dopamine imaging, the alpha-synuclein amplification assay test. What else is on your resume, so to speak, when we think about the accomplishments of PPMI? I'll prompt you if you don't mind to mention something that we ask folks to start with, which is the smell test.

Dr. Ken Marek: Well, I think that PPMI has contributed to how we now think about investigating Parkinson's disease in a number of ways. Probably the most important way is that, and this is really what, I've got to go back and credit the foundation for this vision, is that Parkinson's disease is a long-term process. It progresses slowly and it requires having a large number of individuals who we can monitor over time to understand these changes effectively and especially as we now have these tools Sohini was just talking about that might be able to differentiate one group from another. And in doing that, we learn a lot about how we might think about developing therapies for disease. And this has been utilized, the PPMI dataset has been utilized repeatedly over the last 15 years by pharmaceutical companies as they've tried to develop drugs. So that's a key issue.

More specific issues is yes, I think understanding this very simple way of identifying individuals who might have an important change within Parkinson disease, which is abnormal a faction, abnormal smell. We still don't know exactly why individuals with Parkinson disease have abnormal smell, but it's very, very common and it offers us this amazing opportunity because this is true even before any symptoms arise, any other symptoms. So we can use abnormal smell as a tool to identify individuals who might be at risk for disease.

Of course, not everyone who has abnormal smell is going to develop Parkinson disease, but it is a risk factor and it's very much associated with one of these other measures that synuclein just mentioned, which is the SAA or aggregated synuclein. So this is really a tremendous opportunity for us to reach into the community and be able to understand who might be at risk and how we can ultimately prevent the onset of disease moving forward. I think there are many other opportunities for us now. One of them going back to the area we were talking about a moment ago, which is cognitive changes, which are so difficult and have been such a black hole for us in Parkinson's.

We haven't been able to do anything. We now, building on some of the data from Alzheimer's disease, have developed some tools that we can potentially use to identify who might be at higher risk of developing these cognitive abnormalities. And ideally we might be able to borrow from some of the medications that exist in Alzheimer's disease to help those people. So I think these are all very exciting new ways in which we're able to, again, bring our understanding of the biology in very early aspects of Parkinson's disease to help us really do better as people progress.

Maggie Kuhl: So just to recap a bit, looking back, what PPMI has helped accomplish is better understanding the experience of Parkinson's and identifying some tests for risk assessment as well as some tests to really understand the biology such as alpha-synuclein and dopamine loss that's already changing how pharmaceutical companies are developing and testing therapies. Looking ahead where we're going toward this precision medicine, we're looking across diagnosis lines. Some people may have shared biology that could open up new treatments. And also we're looking towards prevention and we're looking at individuals really across the spectrum from even before diagnosis, as I said with prevention, but well to later stages and the issues that are not met today such as these cognitive impairments. So very resonant in science. Every answer, every new tool then opens up a whole new area of inquiry with many more questions. But we say often in PPMI, we don't know yet, but we're working towards the answers together.

Dr. Ken Marek: One other area which is really important and that we've now really taken to heart in PPMI and that's ensuring that the study participants are really recognized as partners in the research. And in one of the ways to do that, of course, the best way is to provide back information to those partners about themselves so that they understand what they're contributing and also just informing them about their disease. And so this is an effort which really is growing very rapidly where we are trying to develop the way and a responsible way to return research information even if we don't know all the answers. Of course, people who are

participating in PPMI are smart and able to understand that that might be true and they can take this into their worldview and discuss this with their families. So I think having this is an important way to, I think, continue research in general that I think PPMI is really pioneering. It's the idea of providing information back to participants as they participate in studies.

Maggie Kuhl: That's right. So if you take a smell test, if you have the alpha-synuclein test, you are able to have your results returned to you in PPMI and helping you understand what the precision medicine approach might be for you. Donna, how did that return of results impact your feelings around continuing in PPMI or just your feelings around being a true partner in the study?

Donna Rajkovic: Well, I started doing my PPMI study at the Cleveland Clinic, then I never actually got any results back. So I don't really know. I don't know how I've progressed. I just know myself of how I feel. I wish that they would have released some of that information to me, but they haven't. So I'm not really-

Maggie Kuhl: Donna, it's all in my PPMI.

Donna Rajkovic: Is it online?

Dr. Ken Marek: Yes.

Maggie Kuhl: It's all online.

Donna Rajkovic: It's online. Okay. No one ever told me to go there and take a look. I would like to see what my results would be. I would love to see my DaT scan changes. I would love to see my spinal fluid changes. I would love to see that. I haven't actually gone in there to investigate.

Dr. Ken Marek: This is now available and you can access these.

Donna Rajkovic: And when did that become available?

Dr. Ken Marek: It's been slowly progressing over the last-

Donna Rajkovic: Okay.

Dr. Ken Marek: Year or two. Yeah. So you're right, when you began, it was not available.

Maggie Kuhl: Oh, yes. Yeah. We haven't been sitting on it for 14 years. Don't worry. I promise you that.

Dr. Ken Marek: We've been-

Donna Rajkovic: Okay. Well, that's great because I would really like to know what my scan changes are, my-

Dr. Ken Marek: Exactly. That information is exactly available for you.

Donna Rajkovic: Yeah, thank you. Wow, this is great.

Maggie Kuhl: So I do want to make one important distinction. We have renamed the PPMI study to the Parkinson's Precision Medicine Initiative. Some people have asked, does the inclusion of medicine in the name mean that we are testing medicines or developing medicines? That is not the case. As we've been discussing, we are learning more about disease. We are informing individuals about their own biology such that they can take a precision medicine approach. PPMI itself is not testing any therapies, but it is enabling a future of precision medicine.

I want to go back, Donna. You shared that you have children and your motivation for joining PPMI was to do something, to feel like you were having an impact, not just on the broader community and your family, but also for yourself, to feel like you had some control. And that's something that I hear a lot from people in PPMI. And I want to bring in a couple other longtime participants to share their own reasons for joining and being in PPMI. First, we're going to hear from Jen Gaudio.

Audio: Jen Gaudio: I was actually diagnosed by the PPMI study because they had a DaT scan which proved that I did have Parkinson's. And from there, it was a no-brainer to stay in the program because I was devastated and could not think of any other way to fight this disease by providing data to help cure it. And that was the ultimate motive. It was a little bit altruistic and a lot of [inaudible 00:38:23] my own sanity, giving me a goal to fight for.

Maggie Kuhl: And here's Jerry Pollock.

Audio: Jerry Pollock: My father, brother, and sister were all Parkinson's victims. That in itself was motivation enough for me to join the PPMI study. Not only do I owe it to them and the rest of our family, but it's an opportunity to hopefully contribute in some way to the advancement of the research and ultimately positive outcomes.

Maggie Kuhl: Donna, you are such a pillar of your local and our Parkinson's community. I'm sure people ask you about joining PPMI. What do you tell them about why they should consider such?

Donna Rajkovic: Well, I think it's a really powerful way to be in control of yourself, your future, as well as changing the future of other families because there are families that are struggling and struggling quietly, but they don't have to. They can be in control of their future and be part of something greater than themselves.

Maggie Kuhl: Before we end, this is just one of my favorite topics. I think PPMI, as we've been discussing, is just truly the study that's changing everything. I'm so proud to be a part of it. I hope that those who are listening who are also part of the study, I'm sure there are many of you, are so proud of what you've built. Sohini, Ken, Donna, anything that you'd like to end on again as we look back, but also look ahead?

Dr. Ken Marek: I mean, I just would just build on what you just said, which is that when we began this project, it was really a question because we were asking so much of the participants, the scans, those spinal fluid, just the time and energy. And what has been striking is that individuals have stepped up gladly and are really, because this is important to them as well as to us of course. And we're just very grateful that we have such an amazing community that has been able, really enabled this project to exist. I think everyone who has participated should be extremely proud that they have played a role in this effort. So thank you all.

Sohini Chowdhury: Yeah, I would say something similar, which is that the ability to even think about precision medicine now in Parkinson's is because so many people raised their hand and have provided the information that has allowed us to start to look at this disease through the lens of biology and not just the symptoms. And it's a testament now of what we can do when we look at a disease with the individual who has that disease at the center of it as opposed to the periphery. And so I think that if there's anything to be learned about the last 15 years and how that's going to impact and build for the next 15 years, it's that power of partnership with individuals who have that disease that really is the way to move forward and truly understand and develop the treatments to affect that disease. So again, I echo Ken and you, Maggie, and just thanking all who have contributed and supported their partners or their family members who've contributed to PPMI.

Donna Rajkovic: Yeah. I don't know what to say. I feel so hopeful with all these years because it's hard to understand something that you don't know. And having research done on a disease that keeps on having layers, upon layers, upon layers and peeling those layers off, it takes time, but it's not that long. I mean, it's 15 years, but look at how far we've come in 15 years. And I feel very grateful for all the research that everyone's done and the understanding and understanding this disease and knowing that it takes time to get these answers.

Dr. Ken Marek: Thank you. Whether you're a beneficiary or not, you've contributed in a major way to helping-

Sohini Chowdhury: Yes.

Dr. Ken Marek: Others. And that's absolutely the case. Yeah.

Donna Rajkovic: It's my pleasure. I would do it over and over and over again and more if I could. But at that time, if you're in one study and taking medications, you couldn't be in another study. Now things are changing, which I think is amazing too. So let's work on the cognition, that I would like to... The fog is the worst, especially when you're off and I take my medicine every two hours, which is crazy.

Maggie Kuhl: Well, thank you for sharing your real experience with us and your PPMI experience. Thank you, Ken and Sohini for the conversation and for all that you've done for the study and the Parkinson's community. If you want to get involved with a study that's changing everything, visit michaeljfox.org/ppmi to get started. And if you liked what you heard, please rate and review our show. It helps listeners like you find and support our mission to end Parkinson's.

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.