Mark Masselli (00:04)
Parkinson's has been called one of the most mysterious diseases known, but recently there have been an important breakthrough. The Michael J. Fox Foundation announced it had developed a successful biological test for Parkinson's disease that detects it before symptoms appear.

Samantha Hutten (00:22)
So I think this is going to be a game changer for, clinical trials and for patient care in the future. But right now it is really a research tool that can be used to kind of inform research and also how we design clinical trials.

Margaret Flinter (00:35)
Our guests are Samantha Hutten, a PhD neuroscientist with a broad range of biomedical experience. She serves as the Vice President of translational research for the Michael J. Fox Foundation and Rebecca Miller, who holds a PhD and teaches at the Yale School of Medicine.

Rebecca Miller (00:51)
I think there's huge excitement around it, particularly about the, the impact on clinical trials. 'cause we're all looking for, you know, a drug that will really be, disease modifying.

Speaker 5 (01:04)
The only way we can get this data is by summing together, 20 or so patients and kind of adding all those patients together and looking at the overall effect. We can't quite do this, this kind of work on an individual person. So, I can see group differences. This is a Parkinson's versus healthy control difference. I can't do that on an individual person. I can only do that with group data.

Margaret (01:26)
This is Conversations on Healthcare.

Mark (01:37)
Dr. Hutten and Dr. Miller. Welcome both of you to conversations on healthcare.

Rebecca (01:43)
Thank you. Thank you for having me.

Samantha (01:45)
Happy to be here.

Mark (01:46)
Well, that's great. Let's, let's start with Dr. Hutten. The global rate of Parkinson's disease has doubled in the last 25 years in the us. The number of people diagnosed with Parkinson's is going up, because of aging population. You're here to tell us about the Parkinson's Progression Marker Initiative, also known as PPMI. And this has resulted in the advancements that's allowing healthcare providers to accurately identify people with Parkinson's disease. I wonder if you could fill our audience in on this new, important breakthrough.

Samantha (02:20)
Sure. I'm happy to. Maybe I'll just quickly describe, what PPMI is and how it's really served as the foundation for this breakthrough. 'cause we're really excited, to be able to capitalize on this, study, which is the Parkinson's Progression Markers Initiative that was launched in 2010. And the goal of PPMI has always been to identify biomarkers of Parkinson's disease. Biomarkers are things that we can measure in our body that tell us something about the risk or the onset or the progression of the disease. And the idea here is that if we can detect Parkinson's earlier, we can treat it sooner. Hopefully one day we can prevent the disease altogether. So in the 15 years since PPMI, started, it's really become the cornerstone of PD research. We have, over 3,400 participants to date. And PPMI, this is continuing to grow. It's very impressive. These are, participants who come to around 50 clinical sites around the world. These are newly diagnosed individuals, those who have a family connection to Parkinson's disease. People with risk factors for potentially developing Parkinson's, like loss of sense of smell or sleep disorders as well as healthy volunteers. And today, PPMI is still going strong. So there are some folks who have been in the study for 15 years now. They come in for regular visits to participate in clinical testing, brain scans. They donate their bios, samples like blood and spinal fluid. And this is the, the cornerstone of the new biomarker breakthrough that you mentioned, which is, now able to detect, pathology associated with Parkinson's disease in living people. So, as I mentioned, biomarkers tell us things about diseases. For other diseases like cholesterol or heart disease, we have things that can reliably, detect the pathology and then tell us with a

hundred percent certainty whether somebody has a disease or doesn't. So things like A1C for diabetes, cholesterol levels for heart disease, pregnancy tests. We haven't had that for Parkinson's disease until now, which is why this breakthrough is so exciting. So I can tell you a little bit about the biomarker, which is called the Alpha nucle seed amplification assay, or alpha nucle, SAA for short. It's a very long name. But you probably know alpha-synuclein is a protein that accumulates in the brains of everybody with Parkinson's disease. It's the pathological hallmark of the disease. And to date, it's been very difficult to measure this in living people, especially the aggregated or clumped up form that occurs in the brains of people with Parkinson's. So we funded work on this biomarker over the last 10 years. It's essentially a very novel way to measure, with clumped up alpha nucleon in a person's spinal fluid. So somebody comes in and they donate their spinal fluid, and then we can measure this pathological alpha nucle using a test that actually turns out to be over 90% accurate, for diagnosing people with Parkinson's disease. And the really, really cool thing about this test is that it doesn't only detect, alpha-synuclein, pathological alpha nucle in people with Parkinson's disease, but it's actually quite accurate in being able to identify people who later go on to develop Parkinson's disease even before they have manifest symptoms. So that's the, the test in a nutshell. And we're really excited to have been part of this advancement in biomarker research.

Margaret (05:45)
Well, Samantha, your comments raised so many questions. I think certainly in my mind, and probably in the mind of, our audience. So it can, the test can detect pathology and spinal fluid, not only of people diagnosed with Parkinson's, but in individuals who've not yet been diagnosed nor shown clinical symptoms of the disease, but maybe are at high risk because of family history. Maybe some other factors. So when should a patient ask a healthcare provider for the test? When should a healthcare provider think about raising the question and offering the test? How widely available? And of course, in our current healthcare environment, is this now accepted as something that would be covered by one's insurance generally, if they do not today have symptoms of the disorder? I know that's a couple of questions in one, but I think that's probably what people are thinking as they hear this.

Samantha (06:33)
Absolutely. And I think, you know, it's really important to, to highlight that. Currently this is a research test. So although it's been commercialized as a lab test that is available for clinicians to access, and we do anticipate that this is something that, you know, people will, will go on to use, more readily in the future. Right now, a positive test on its own, can't tell you which type of alpha-synuclein disease a person has. It might be Parkinson's, but it might be associated disorders like Lewy body dementia or multiple, systems atrophy. And on the other side of the coin is that, for at-risk individuals, if you get a negative test that doesn't necessarily tell you that you aren't gonna get Parkinson's in the future, it's only a snapshot of this particular point in time, and it does require a lumbar puncture, which isn't the most pleasant thing in the world. So for all these reasons, I think it's important to say out loud that the results of this test don't, broadly change how doctors diagnose and treat Parkinson's disease. So there isn't a, a real benefit at this time for patients going and getting the test right now.

Mark (07:39)
I think it's, I think, I think it's fair to say that it is a promise, really to transform clinical trials, right? And, and hopefully revolutionize the development of treatments. And I'm wondering if you maybe take us along that journey, what is PPMI working on and how close are we to this next step of, of transformation? It's a, it's a building block, an important cornerstone of the work that you're doing. But, what's the building look like in terms of next steps ups?

Samantha (08:09)
Yeah, I think you really nailed it. So for all the reasons that I said, I think if, if somebody's interested in, in potentially getting this test, they should talk to their doctor. 'cause it's a very personal decision. But the flip side is that this really is a game changer for clinical trials. And those do help patients too, right? We know that drug companies who are in the clinic right now testing very important drugs, are actually using this test to make sure that they're recruiting the right patients, in their trial. And this is important because we wanna set these trials up for success. So having a biomarker that indicates for sure that somebody has Parkinson's disease, instead of something that might look like Parkinson's disease, actually sets these trials up for success to make sure that the right people are there, which makes these trials more efficient and more effective. And one of the other really, great milestones that happened just this past summer was that the FDA issued a letter of support encouraging scientists and drug developers to use this biomarker test to improve the efficiency of clinical trials targeting Parkinson's disease. So this has been a really exciting landmark for clinical trials, using this biomarker to evaluate Parkinson's disease patients.

Margaret (09:16)
Well, that is very important and thank you for elaborating on that. Let me turn to Dr. Miller. Becca, you are very public about sharing your own Parkinson's story. Can we ask you to talk about it here with our audience?

Rebecca (09:29)
Sure, thanks. Yeah, I was diagnosed in 2013 when my daughter was nine months old. So that was, it was a very, very stressful time for me. And I'll just speak on the biomarkers piece that we didn't, back then, there was no biomarker test. There was purely a clinical diagnosis. And I had had symptoms actually for the previous 10 years, but hadn't, you know, hadn't known what they were. I was very young. I was only 38 when this all came about. So, but I've been so lucky to really access the really supportive Parkinson's community. I think that getting a diagnosis, especially when that young can be really, really stressful. But there is such a great and support of Parkinson's community, including places like the Michael J. Fox Foundation and other foundations that you can really reach out to and find kind of your people in the community. So despite, you know, the real stress and anxiety, I think that that, that has been something that's really been so positive. And now I'm actually on the Patient Advisory Council for the Michael J. Fox Foundation, which has been a huge, really, it's like a, a support group of other people with P'S as well as being part of one of the greatest foundations in our country, I think.

Mark (10:47)
Well, I know what is supportive is, you sharing your journey, with our listeners. So thank you so much for doing that. What are you hearing from patients about PPMI Becca in terms of, how, how they're taking it and maybe that patient advisory group, tell us a little more about what's happening there.

Rebecca (11:06)
I think there's huge excitement around it, particularly about the, the impact on clinical trials. 'cause we're all looking for, you know, a drug that will really be, disease modifying. So we do have wonderful treatments and we're so lucky as people with Parkinson's to have carbidopa levodopa, which is kind of the gold standard for treatment right now. But that only addresses symptoms. And we are really looking for something that will modify the course of this disease, to be helpful. So I think things like PPMI and the discovery of the biomarker is really huge in that we will hopefully be that much closer to really finding a cure.

Margaret (11:45)
Well, Becca, as we noted, you're a member of the Fox Foundation Patient Council. I will note that the organization that we lead also has patient councils hugely valuable in primary care as well as in, concerns like Parkinson's. Because it gives you an important platform to discuss, better care for patients. And I understand one of the areas that you all have, considered and talked about is, better care for patients when they're in the acute care setting, when they're hospitalized. What are your concerns and what do you see as solutions to them? I, I can imagine the challenges of home more than the hospital. So share with us what you've identified as concerns when people are in the hospital setting.

Rebecca (12:25)
Sure. I think there are a number, and I'll try and kind narrow it, but, some of the, some of the concerns as a person with Parkinson's in the hospital, really about getting medications on time and the right medications. So, you know, usually nurses are educated to give meds within an hour or two of when they're due. And that's fine if you're taking a daily blood pressure medication, for example, it's not a problem to get it, you know, at 10 o'clock versus 9:00 AM But when you're a person with Parkinson's, even a 15 minute kind of delay in medications can lead to one, losing the ability to really talk, walk, function in ways that are hard to kind of get back on track with them. So with the hospital being, you know, it's a challenge for all of us when, when we're in the hospital kind of, you know, that we're in this system, right? But for people with Parkinson's, I think it's especially hard when those systems are kind of not built at all to support the kinds of care that we need. There are also things like, you know, mo getting mobile after surgery is so important for people with Parkinson's to stay mobile, to, you know, when you're not supposed to have anything by mouth, not supposed to have water, that you still need to be able to take your medication or again, you're gonna be kind of off schedule. And then, I think one of the other dangers is contraindicated medications. So, for example, there's a very commonly used, medication, that is contraindicated with a lot of other kind of commonly used medications in the hospital. Pain medications, anti-nausea. So knowing what those are and having a list of those available, there's really, at this point a need for patients and their family members to advocate for themselves. So I went into the hospital in 2019 with an emergency appendectomy and was very, I'll say now, like, was very arrogant. 'cause I thought that I'd be fine. I was younger, I was educated. I, you know, I'd heard vaguely of these problems that people were having in the hospital, but I didn't think they would happen to me. And I really had all the experiences that others have had,

you know, in this country and actually internationally it's really a problem. But that I received contraindicated medications. I didn't receive my meds on time. I received, you know, sort of different classes of medication that were switched from the home regimen. So that really made me into a really strong advocate for trying to change our hospital systems using things like the medical record. So one thing that I've personally been doing is putting those contraindicated medications as allergies in my, you know, in my electronic medical record. Because that really is a system that is very much paid attention to by your providers. How many times when you're in the hospital or even an outpatient are you asked, do you have any allergies? You got a red bracelet, you got all kinds of things that are kind of attached to that. It's part of the joint commission requirements and focus at times the organization that, that, commission that provides certification to hospitals to say, you know, these are really important patient safety goals and will be included. So using that mechanism to try and, you know, make sure that you don't get those medications that will decrease dopamine. So there are certain antipsychotic medications like Aperol, that that's their mechanism of action is to re reduce dopamine, which is exactly what we people with Parkinson's need. So things like that have been really a focus of my work recently in trying to advocate.

Mark (16:08)
PPMI, the biomarker test is new, so I'm not surprised when we got this comment from a professor of neurology when he asked about the Parkinson test, he said, if a patient came to my clinic having done the test, I'd be a bit wary about knowing how to interpret it. And what I would tell the patient on the basis of the results is extremely interesting and helpful from a research point of view. But I'm not sure it really changes what we're doing, with patients in the clinic at the moment. I'm wondering what you think about that, statement. Is it a, is it a fair point?

Samantha (16:45)
I think that's accurate and you know, like I said, based on the current drug treatments that we have today, it's, it's not gonna make or break, a patient care perspective, or the medications that somebody's on. But I think where it is gonna have an impact is one, we're thinking ahead to potential prevention trial. So if we get to a point like the Alzheimer's field is, you know, starting to do, different clinical trials on people who are at risk that haven't yet been diagnosed, that's a situation where, you know, if we had a test that was available to people before they, you know, were diagnosed with symptoms that could identify them, they could potentially make decisions about whether they want to know what their risk is and whether they would want to potentially enroll in a trial that might prevent them from developing a disease like Parkinson's disease in the future. We're just not there yet, but this really sets the stage to enable those types of, of clinical trials that can really stop the disease in its tracks even before we start losing those dopamine cells in the brain that Becca was just talking about. So I think this is going to be a game changer for, clinical trials and for patient care in the future, but right now it is really a research tool that can be used to kind of inform research and also how we design clinical trials.

Margaret (17:57)
Well, Samantha, you've had over 3000 people enroll, in PPMI and you're enrolling more volunteers to sustain what you call critical progress. what are the volunteers needed for? Where do they go to learn more? Do they have to be diagnosed with Parkinson's already to participate? Tell us more about that. And I guess I'd, I'd add to that, and I'm thinking of the group patients like me that we talked to, several years ago, the benefit people derived from knowing that they were helping contribute, to the solutions. Is that part of the benefit of being in it? I know that's a lot of questions in one, but you can start anywhere you like on that.

Samantha (18:36)
Well, thank you so much for asking if anybody's interested in learning more about ppmi and how they could potentially participate, they can go to Michael j fox.org/ppmi. But PPMI is sort of an all comers study right now. So anybody that wants to get involved, whether they have Parkinson's disease, whether they have, excuse me, a family member with Parkinson's disease, whether they have risk factors like loss of sense of smell or REM sleep behavior disorder, whether they know they have genetic mutations or if they're just healthy volunteers that wanna get involved. PPMI is seeking all of these folks, and if you go on the website, it'll ask you a few questions and help find the best entry point for you. But, we couldn't do what we do as far as the biomarker research without the study volunteers. So I think it's just really critical to recognize that, you know, certainly from a patient perspective, this is something that you can do to get involved, and to, to be part of a community. But PPMI wouldn't be anything without the volunteers with Parkinson's and without that come in year after year. Some of them have been in the study for, you know, 15 plus years donating their, spinal fluid and their blood taking clinical tests, really participating in research in such an extraordinary way. And, you know, one of the things I I just wanna highlight about PPMI is that it's an open access resource. So once the data is generated, it's made publicly available to researchers around the world. So in addition to the, the patient community and the volunteers, we also have some of the most brilliant scientific minds that can look at any of the PPMI data. Obviously, it's all de-identified, so you wouldn't be able to see or tag that data to a particular subject. But having

that research data available, for anybody to download really opens up, the doors for different types of people who have data analytics expertise or a particular biology expertise, or a clinical expertise to all think about this Parkinson's problem and sort of apply their expertise to, to answer those questions. And that's how we move science forward by making it available and easy to access so that everybody can, can really look at the data.

Mark (20:38)
Samantha, you used the, the term a few minutes ago, a game changer. So I wanna ask you about GLP one drugs, which helped treat, type two diabetes. Every study goes into a long list of things that it's, had an impact on, and Parkinson's, is, is listed in that. What do we know about the potential, effectiveness of the GLP one, for treating Parkinson's disease?

Samantha (21:09)
Yeah, this is a good question and it's getting a lot of attention now because of these Vago vs. And ozempic, you know, a lot of people are taking these medications. So I think there's, a lot of interest here. So, GLP one is actually a naturally occurring hormone in the body that affects insulin production and appetite. But it's also thought to play a role in things like reducing inflammation, which is a pathway that's implicated in Parkinson's disease. So, whether drugs that mimic GLP one actually provide benefit through this or other mechanisms, has really been an active area of research, not just for Parkinson's disease, but also for other neurodegenerative disorders like Alzheimer's. And there was recently a publication in Lancet. This was looking at, exenatide, which is one type of GLP one receptor agonist, and this was the largest study to date of GLP one receptor agonists in people with Parkinson's. And this was a study that concluded last summer, really aiming to test whether if you give this regular dose of IDE this would slow or stop the progression of Parkinson's disease. So I think unfortunately, the results from the trial indicated there was no evidence that this IDE administration slowed the progression of the disease. But I think there's, you know, a lot of different formulations that people are testing and looking in different populations. So this is still an ongoing and active area of research because there's a lot we don't know about GLP one agonists. We don't know how it, it, it affects different people differently as far as people's weight and other medications they're on. So this is still something I think that's, interesting and worth pursuing. Just because a medication's FDA approved for one condition doesn't necessarily mean it's safe and tolerable for another condition. So we really need to go through this rigorous and standardized testing to really evaluate some of those questions.

Mark (22:55)
Is that something the foundation is gonna, make as a, a target or is that something you're, watching other people, work on and and collaborating with them?

Samantha (23:05)
That's a good question. So, you know, we've, we funded research in this area, many years prior to this study, and some of the work that led up to this most recent publication was funded by Fox. It's still something that we're, pursuing through some of our therapeutic activities. So we have our eye on it and we're funding, different work in this area, but I think it takes, different studies and different types of populations and different people. So yeah, I think it's a combination of different types of approaches and efforts.

Margaret (23:32)
Well, Samantha, turning back to PPMI, I understand this is a $500 million initiative, and one way it's different is that it's the foundation as a nonprofit that's conducting the research. It's not being done by the government, it's not being done by, pharma. Maybe take us through that history and why, 15 years ago, I guess it was, when you started down this road, finding an objective biomarker for Parkinson's was so critically important to the foundation.

Samantha (23:58)
Yeah, I think that the foundation was really a thought leader here 15 years ago, thinking about how we would set up the infrastructure to be able to find biomarkers. And I think the impetus there really was, it's a chicken or the egg argument. You can't have, successful clinical trials if you don't have a way to measure whether drugs are working. But you can't have, you know, different ways to diagnose and measure Parkinson's disease if you don't have the bio samples and the resources and the infrastructure in place to be able to collect those BIOS samples and then rigorously test whether there are ways to, to measure the things that are important to Parkinson's disease pathology. So we did launch a Parkinson's progression markers initiative in 2010. At that point we were collecting bios samples from, you know, 400, people with Parkinson's and I, I think around 200 healthy controls. And we've really been able to expand the scope of the study as research has changed over the years to then include genetic mutation carriers to include people who have risk factors for Parkinson's disease and now

including people who, you know, can take a scratch and sniff smell test because smell a loss is a risk factor for Parkinson's. And we have now an online component so people can engage where they are. We have, tests that we can send by mail and some of the, questionnaires that we can administer online. So PPMI has been, I think something that has rolled with the punches and changed with the times. And it's only continuing to expand. And it's been really exciting to see the progress and how, there have been actual clinical trials that have been designed based on, the research that's coming out of PPMI and the way that PPMI itself, was set up. So it's really been, I think, to use the same phrase again, a game changer for Parkinson's disease research.

Mark (25:44)
Well, I think it's fair to say that Michael J. Fox is a rockstar and a force of nature. Tell us a little more about the bigger foundation. It's really doing remarkable work, not only here in the United States, but around the globe. This is such an important initiative, such an important, effort, that he, launched and so many people are working on. But maybe give us a little bit of the size and shape of the, the work the foundation is engaged in.

Samantha (26:14)
Sure. Yeah. I mean, the Fox Foundation has funded more than $2 billion in high impact global research programs, which is astounding. Just really proud to, to be part of that over the years. And, this has been not only through biomarker research, but also through looking at different therapeutic, modalities and being able to understand Parkinson's disease biology. So we think that the best measure of success, is really looking at the, therapeutic pipeline because that's what's telling us, whether we're moving the dial. So there have been a growing list of priority proteins and pathways that we've been establishing links to, Parkinson's disease onset and progression. There are currently more than 150 unique therapeutic approaches in clinical testing across phase one, two, and three trials. These are varied approaches, so immunotherapies, small molecules, gene therapies, really, one of the goals of the foundation is to make sure that there's a diversified portfolio. And we fund things across the pipeline from basic science, looking at the pathology of disease all the way into preclinical development and clinical testing with the goal of really, de-risking the field, and specific programs so that other folks with deeper pockets can come in, you know, and invest in these areas. So, you know, this is something that we can really tangibly measure the success of. And in the last decade, there have been 20 Parkinson's disease therapies that have been approved by the FDA. So really progress in Parkinson's disease has exploded, and that's thanks to, you know, obviously not just the foundation's efforts, but all of the different companies that are engaged in this space and the patients and their families who are willing to participate in research and get involved towards, you know, participating in clinical trials and finding biomarkers.

Margaret (28:03)
Well, Samantha, I know we're, close to our end here, but I just thought this was such an important thing for people to know that PPMI has reported that dementia and Parkinson's disease was seen less frequently or later in the disease course than previously reported, and it had been thought that dementia occurred in about 80% of Parkinson's patients. This seems like another, important, issue certainly for, scientists, patients, advocates. How, how has that changed, the messaging about Parkinson's in the community of both scientists and patients?

Samantha (28:37)
Yeah, that's a great question. I think, you know, previous estimates around the 80% mark, were based on other smaller scale studies, and since PPMI has been around for so long and we've had the same patients coming in year after year, we've been able to track not only their biomarker, progression through tests like the Alpha Nucle, SAA, but also their clinical progression. So they're being given the same cognitive battery of tests and then assessed year after year. And I think it's, it's good news for patients that a cognitive decline is, not happening at such an exponential rate. And it's also, maybe not as, is sort of affected in younger individuals as previously reported. But we can continue to monitor that thanks to studies like PPMI that are bringing patients in year after year.

Mark (29:22)
Well, that's great. Then, thank you Dr. Hutten and Dr. Miller for joining us. And thanks to our audience for being here. Just a reminder to be sure to subscribe to our videos on YouTube and find us on Facebook and X. You can also share your thoughts and comments about the program, take care and be well.

Margaret (29:42)

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