Marie: Hello and welcome to *The Parkinson's Research Podcast: New Discoveries in Neuroscience*. I'm your host, Dr. Marie McNeely, and I've partnered with The Michael J. Fox Foundation for Parkinson's Research to bring you to the forefront of the field of neuroscience to discuss the latest advances in discoveries with leading experts.

The Michael J. Fox Foundation created this podcast for researchers, clinicians, and industry professionals with the hope that these conversations and the resources we share will advance your efforts and partnerships to improve brain health. We are welcoming guests with a range of experiences and viewpoints. The views expressed belong to the guests themselves.

Today, we are excited to be welcoming our guest, Dr. Monica Rivera-Mindt. Listeners, Monica is Professor of Psychology, Latinx studies, and African and African American studies at Fordham University. And she has a joint appointment as Professor of Neurology at the Icahn School of Medicine at Mount Sinai. She is also a board-certified neuropsychologist. And today, we'll be talking more about Monica's research on brain health inequities and strategies to improve brain health outcomes and healthy brain aging across the lifespan, particularly for minoritized, underrepresented populations. So, Monica, we are delighted to have you here with us today. Welcome to the show, and how are you?

Monica: I am well, and I'm so excited to be here, Marie. Thank you so much. I feel really honored and happy to be here with you and your listeners today.

Marie: Well, Monica, we're excited to learn more about you and your work. And perhaps we can start with some background first. So, can you share what was your career path, and how did you get to the position where you are today?

Monica: So, as you said, I'm a board-certified neuropsychologist, which means I'm interested in the relationship between the brain and behavior. I have a PhD, and I'm going to take a step back before I move forward to say that my grandfather actually had dementia while I was growing up. So, I think that that piqued my interest in brain-behavior relationships. I was also a part-time caregiver for different family members.

And so I think that was part of my interest specifically in neurocognitive disorders and conditions, and I was always interested in science, passionately, since I was little. And so, as I was going through my career trajectory, as I went forward, I became more and more interested in the connection between neuroscience and neuropsychology as it related to groups who I did not see represented in the studies that I was reviewing, learning from, the studies I was participating in as a graduate student at the University of Nebraska at Lincoln.

And that experience carried on through my residency at the University of Washington, where I observed very acutely that we did not have a good evidence base for assessing, diagnosing, and treating individuals who would come to see us from minoritized backgrounds — ethnoculturally minoritized backgrounds and others. And so, that really set me on a course by the time I got to my post-doctoral fellowship at UC San Diego to really focus on this interplay to understand what was available, what we knew about brain-behavior relationships and outcomes for individuals living with neurologic conditions and what we could do. And that just sent me on this path of what ultimately became brain health equity.

Marie: Now, Monica, you mentioned in talking about your background that you have family members who have had these neurological conditions. So, there is this personal connection there. And I know your family also has a personal connection with Parkinson's disease plus syndromes. So, Monica, can you share — to the extent that you are comfortable — your family's story, and tell us how this has really motivated, or inspired, or even perhaps changed the work that you do?

Monica: Absolutely. So, my family is from Puerto Rico and Colombia. And on the Puerto Rican side of my family, my uncle, who was a veteran and who worked so hard in this country, you know, he was a business owner and a really active, incredible, dynamic man. His name was Carlene Rivera. He, unfortunately, in later life was diagnosed with progressive supranuclear palsy or PSP, which is a Parkinson's plus syndrome. And it's a rare chronic neurodegenerative disorder, and it has some similarities with Parkinson's.

So, it can affect your motor functioning — so, how you walk — and also can impact your thinking — your cognitive abilities. And it was really hard for our entire family. My uncle, luckily, had an amazing wife, and his two youngest children were really involved in his care, and served as caregivers. And it was an incredible lift, but it was done with a lot of love, and all of our family were very saddened by it. And unfortunately, he passed a couple of years ago. But I think the way that it changed my lens through which I see my own work, you know, it's so interesting. I've been working on brain health equity for over 20 years.

And now that you're in your career, you're doing this work for so many years, and then when somebody who's really close to you suffers from a neurodegenerative condition like this, it certainly changes your lens. And I think it builds more empathy between me as a scientist and, you know, how I think about the folks who could be touched by the work that I do. And it makes me feel more passionate about ensuring that the research that we conduct isn't just for some of us, but it's for all of us so that we can do a better job of assessing, diagnosing, and treating individuals living with these conditions and also their families.

Marie: Definitely. I think, Monica, seeing firsthand the impacts of these diseases, whether it's Parkinson's disease or one of these Parkinson's plus syndromes, how it's impacting people in their everyday life is something that not all physicians really get to see. And can you share maybe some of the things that changed for you or some of the ways that you've shifted how you look at your work?

Monica: Right. Well, for instance, one thing that I was really, really concerned about and remain concerned about is that when you look at the literature, for instance, in these different types of neurodegenerative conditions and dementia, there's not a whole lot of research for people from minoritized, underrepresented populations. And this is important because even for something like PSP — or even more broadly for Parkinson's — I don't feel, based on my review of literature, that we have a really good sense about the prevalence and incidence even in these different populations. And we need to do better as a field because again, we want everybody to have better outcomes. And we can't do that unless people are represented and included in the research. And the research is tailored to understand brain-behavior relationships in these different populations.

Marie: I definitely agree. And perhaps we could dive into your work in a little bit more detail. We mentioned that you're an expert on brain health inequities in minoritized, underrepresented populations. So, perhaps to start off with, Monica, how do you define brain health inequities?

Monica: So, I'm going to give you my personal definition. And I have, you know, an academic definition that I share, but I really want folks to be able to connect with this. Essentially, to me, brain health equity has to do with the fair distribution of brain health determinants and outcomes across different segments of the population, regardless of social standing. So essentially, what I'm interested in when I'm talking about brain health equity is that everybody, no matter what part of the population you're from, where you're born, you know, what country your parents are from, what language you speak, your gender identity, your sexual orientation, regardless of your background, that everybody across the lifespan have an equal chance for good brain health as they age. That, to me, is brain health equity and what I am so passionately working on in my own work.

Marie: Wonderful. I like that definition. And, you know, you mentioned that in some cases data is missing, or we don't have it yet. But what do we know so far about brain health inequities and maybe differences in cognitive aging in different populations?

Monica: So, most of the work has been done in Alzheimer's and related dementias. And in that body of literature, so now we're already circumscribed to a segment of

neurodegenerative conditions, right? And in that literature, most of the work that has been done has been done in individuals 65 and older. So, I really want to highlight here that we don't have a whole lot of research across any of these neurodegenerative conditions for people under 65. And I think that's a real weakness in the work from a lifespan perspective. So that said, with regards to Alzheimer's and related dementias, what we know has mostly come from research with Black African American and Latinx populations here in the United States. I'm just focusing on work here in the United States.

And what that literature suggests is that Black and Latinx adults are up to twice as likely to develop Alzheimer's and related dementias compared to non-Latinx white adults. Not only that, so not only do we have this issue around prevalence, but also when we look at the clinical manifestations within those populations, multiple studies suggest that Black and Latinx adults demonstrate a younger age of onset and greater severity of initial cognitive symptoms.

And if current demographic and epidemiological trends hold, it looks like that by the year 2030, Latinx and Black African American adults will make up almost 40 percent of the over eight million families here in the United States affected by Alzheimer's and related dementias. So, what we're talking about here is, to me, a public health emergency. We're in a situation here in the United States where our country is rapidly becoming more diverse — ethnoculturally diverse. And at the same time, we know that the country is aging. Our population is getting older. And so we have these two trend lines, and there's a vector that we're dealing with where we are not prepared, from a public health perspective, from a clinical perspective, and a scientific perspective for that matter, to really address these issues at the present time. Just as a field we're not ready.

Marie: That makes sense. And I think you highlighted a really important point here that we don't really have much data on people under the age of 65. Are there other big gaps that you're seeing that remain in the literature that really stand out in your mind?

Monica: Yes, multiple. First, the research that I just shared with you, again, it's in the context of Alzheimer's disease and related dementias. And I think there's a tremendous gap in the literature with regards to Parkinson's and Parkinson's plus syndromes in terms of the prevalence and incidence of those conditions with those populations, as well as clinical outcomes and other things. And again, I think this is so important because until we have data that is externally valid, right? That's generalizable to these different populations, our ability to assess, diagnose and treat in an evidence-based way is going to be diminished.

Marie: Definitely. And I think you really highlighted what was going to be my next question, just the importance of ensuring that there's diverse representation in

research in these neurological diseases. I guess, how do you encourage people to start making these changes? What steps need to happen to start ensuring this diverse representation?

Monica: It's a millions of dollars question that NIH, I think, and others are working on tackling now. And from my perspective, first of all, the research to date in neurological diseases is primarily in non-Latinx white, highly-educated, high socioeconomic status (SES) populations. So, from the available literature, that's what we know. So, there are these tremendous gaps around, not just age, and neurological conditions, and ethno-cultural identity, but also education, SES, and these other things.

That said, for not just days, weeks, months, years, but for decades, folks in the scientific community and other communities have been talking about how we can increase the diverse representation in research in neurological diseases. How can we do this? And people have been wringing their hands about this for a long time and talking about it for a long time, but not a whole lot has changed in the last 20 years in terms of representation overall. Yet, there is research that shows that there are evidence-based approaches to increase the representation of these minoritized groups in dementia research and neurological disease research. And that's culturally informed community-engaged research methods. And again, I'm going to say it so that your listeners can make sure they didn't miss it. It's culturally informed community-engaged research methods.

There was a wonderful review article a couple of years back by Andrea Gilmore-Bykovskyi. And she demonstrated in this systematic review very cogently that if scientists really focus in their studies on these genuine community-engaged approaches to working on outreaching, including, engaging individuals from these diverse communities, that they do get involved in this research. They will get involved. And this has been a focus of my work now for many years locally here where I live and work. I live and work in the village of Harlem, USA in New York City.

And I was formally trained in these methods when I was early in my career. I was very lucky to the Icahn School of Medicine here at Mount Sinai, where I have my laboratory, that they were very supportive of me getting this training. And in this training — so, I received didactic training and experiential training, mentored training. And it's its own expertise. So, yeah, I have expertise as a neuropsychologist and a neuroscientist, but also this other expertise in how you can take an evidence-based approach to inclusion and engagement of these diverse populations. And when you take the time, money, and effort that it requires to really do this work, you can make significant changes in the representation of your study samples. We've achieved this quite successfully here in our group.

There are also other groups to highlight the folks at Columbia, so Jennifer Manly, Adam Brickman, also Lisa Barnes at Rush in Chicago, and others have achieved these outcomes, utilizing this more community-engaged approach. But again, it takes more money, more time, and a particular expertise. And I think that when prior work has tried to address this issue, they haven't had those three factors in alignment, and it really requires all three.

Marie: Certainly, and Monica, I am really glad to hear that you and others are making important and much-needed progress in this area using these evidence-based approaches. When you are talking about the importance of increasing diversity in these research study participants — and perhaps to even just take a step back for listeners out there who might be trying to figure out how to do this with their own research. What are some of the different dimensions of diversity, Monica, that you think it's important to consider?

Monica: So, I'm so glad you're asking this question and that we're on the same page because I think people get caught up in this error of thinking about diversity just along the dimension of ethno-cultural status, right? But there are many different aspects of diversity that we need to be thinking about that can have significant impacts on outcomes and all the things that we've just been talking about. So, ethno-cultural status is certainly one, but as I mentioned earlier, socioeconomic status, education is another big one, social adversity is another, and certainly some other dimensions that I think we need to be thinking about as we move forward in this work. Things like geography. Does somebody live in an urban area, a maybe exurban area, or suburban, or rural? For instance, we know that rural populations also experience significant health inequities that could have serious implications for dementia and neurological diseases as well.

So, I think that it's really important, first and foremost, that we, like you said, take a step back and really think about these different dimensions of diversity. And I also think that we need to be mindful when we're studying these different populations, that we avoid always comparing a given population to the referent group of non-Latinx white, highly-educated, high socioeconomic status folks, and that it will likely be more fruitful to look within a given population to really understand the many variables within that population that could be contributing to their unique neurological disease burden and outcomes.

Let's just take the Latinx population, for instance. If we just looked at that population and were trying to understand these issues within that population, it's not just race/ethnicity. We are looking at things I mentioned just now. So, socioeconomic status, education, stress, social adversity, quality of education (not just years of education), and many other sociocultural and structural

determinants of health that we think could be impacting both disease burden and outcomes.

Marie: Certainly, and I think when we look in the literature and just kind of in the field as a whole, there are some problems, unfortunately, with things like bias and discrimination. So, Monica, what steps can researchers be taking to reduce the risk of discrimination and bias in the research that they're doing?

Monica: We're also looking at the effects of discrimination, both racial discrimination and LGBTQIA+ discrimination in our work as well. But what you're talking about is on the other side for scientists and team members. And this is a really big issue that I think we all need to think about. The reason is, right now, there's such a push, and rightly so, to address the issue of under-inclusion of these different populations in neurological research, and for good reason.

However, if we don't have well-designed studies with individuals who are competent to work with these individuals, then we can be contributing to the problem by putting out biased research, allowing our findings to be open to racist, incorrect interpretation. And it is incumbent on all of us, no matter what your background, and I'm including myself. So, I am a woman. I am an ethnoculturally diverse woman. I'm Afro, Latinx, and Indigenous by background. But those demographic characteristics about myself do not make me an expert or competent to do the work that I do. I am competent to do the work that I do with the populations I work with, primarily Black and Latinx, but others as well.

What makes me competent to do this work is that I've gone and become an expert. I've done the work I've studied. I've received mentored training. I've collaborated with experts, and I've developed my own competence in this area. And I think that all scientists would do well with a good helping of cultural humility to understand that we all — even including myself — that we need to do the work in order to become an expert so that we can work in a valid, ethical way with these populations. And in doing so, we do reduce the risk of discrimination. We do reduce the risk of bias.

But it has to start at the top. If the principal investigators of these different studies aren't doing this work, then it's not going to become really taken up in a meaningful way by the research teams that are on the front lines working with these participants. And the worst thing that we can do is to do harm in the science that we're conducting by not being competent to effectively include and engage these participants into our research studies. Or being in these communities for a limited amount of time, just to get the research questions that we want answered, and then to come right out. I call that a “conquistador approach” to research. And it's absolutely what we want to avoid.

And myself and most scientists are trained in this more transactional approach to research, right? Where somebody gets a grant for five years of funding, they go to that community at that moment, do the research, and then they leave. Those communities were not involved in the preparation of that study. They did not inform the recruitment methods, the methods for the surveys or the different instruments that were going to be utilized. They don't have an input on how the data are interpreted or how and where they're disseminated.

And this kind of transactional conquistador approach does harm in our communities because it makes people trust less and makes those folks less likely to engage in research. And I will tell you from my own experience that when community members see that a principal investigator is willing to show their face and come to community meetings or meet people in person and that they make those efforts and they stick around that that makes all the difference. You know, we as scientists need to earn the trust of the communities that we want to understand and serve. It's not that those communities are distrustful and I have really been rankled about that framing of the situation in the last couple of years. It's not that Black and Brown folk don't want to be in research. It's that scientists haven't oftentimes proven themselves trustworthy, and we need to do the work.

Marie: Definitely. I think, Monica, it's so much bigger than just having a diverse team or hitting these diversity numbers. I think you brought up some tremendously important points. I think the experience, the training, just critical thinking in some cases, and self-reflection can go a long way. And I think for listeners out there, it might be daunting to try to jump right into this culturally informed community-engaged research method. So, are there specific strategies or maybe starter action items that you can recommend for researchers in neurodegenerative diseases that they can implement to really start on that path of increasing diversity in their studies?

Monica: First of all, researchers don't need to become experts in all populations, right? So, this doesn't have to be a black or white kind of situation. Researchers, though, should become more informed and competent in working with the specific populations that they believe will be coming into their studies, right? And understanding that very foundational issue means reaching out to get experts onto their studies who know how to do this work. So for instance, can you imagine running a neuroimaging study without having a radiologist or somebody with neuroimaging expertise on your team?

Marie: Right. That would be impossible.

Monica: Right? Impossible. It makes no sense. It's not logical. Yet when it comes to the issues that we're talking about today, I think many scientists don't appreciate how important it is to have the appropriate expertise on their teams so that they can help inform and guide the research so that you can come out with a good

outcome, a good study. And the study and the work, it doesn't have to be perfect. One study can't meet all the needs for all the people, right?

But if you're working with experts and looking to available literature as it pertains to your specific area, you can start developing a really good plan on how to do better research that will end up being more externally valid, right, and more generalizable, which we like, and also more internally valid, because you've worked with an expert to really understand the instrumentation, the normative data, everything that is pertinent so that you can get the best data possible. You know, we all work so hard to get these data, and for me, every data point is a jewel, and we need to really make sure that we provide the highest integrity of those data when they go out into the world when we disseminate them.

Marie: Definitely. So, it sounds like a really important kind of first step for people out there would be to just include these experts on their study teams and in the study design process to make sure that you're sort of starting from the right place.

Monica: That's exactly right. And note that I say the word expert, not just somebody who might look like me or talk like me, but somebody who actually has the expertise. Because again, somebody who happens to be from a certain background — that does give them a certain amount of knowledge, absolutely, and lived experience is so important. But what I'm talking about are experts. And oftentimes, I think another possible pitfall is that sometimes investigators will identify somebody who's from a particular background, but they might not have developed the requisite actual expertise needed to actually do this work. So really being discerning about that and thoughtful is really important. And I also wanna say, look to the literature. There is an evidence base in this area, and you can look to that literature to get guidance as well, right? We would do that if we were working with a new method or something else, and it's the same here.

Marie: Definitely, and Monica, I'm really glad to see that there are starting to be more initiatives, both nationally and internationally, that are working towards increasing or improving diversity in research participation, and also trying to eliminate or reduce some of these inequities in brain health. And I know, Monica, you have been involved with the Alzheimer's Disease Neuroimaging, or ADNI, Diversity Task Force. So, can you tell us what is ADNI, and how did you first get involved with this initiative in their diversity task force?

Monica: Yes. This is one of the biggest and longest-standing efforts that I know of in the United States to address Alzheimer's and related dementias. And so ADNI stands for Alzheimer's Disease Neuroimaging Initiative. And this study, in fact, this year, we celebrated 20 years of ADNI, which is incredible. So, this is an ongoing longitudinal study, essentially to identify and validate biomarkers for clinical trials in Alzheimer's and related conditions.

And this study has been an innovator in the field overall, initially working on neuroimaging biomarkers, and more recently, blood-based biomarkers for Alzheimer's and other dementias. It's a national study. There are about 60 sites all in the United States and in Canada, and there have been spinoffs of ADNI around the world, including, I think, Korea might be one and there are others. So, this is a large-scale study of incredible magnitude, and its impact on the field has been tremendous. I think that there's something like over 5,000 articles have been published utilizing ADNI data, because ADNI, if I'm not mistaken, was the first study — and this is way back from the beginning in 2004 or around that time — that started by being open (open data approach). So, the principal investigator is Mike Weiner, and he's a real maverick in this space to really revolutionize the field for this research and advance both our understanding of the etiology of Alzheimer's and also to inform clinical trials.

And then I guess your other question was, how did I get involved? So back in 2020, Dr. Mike Weiner, who's at UC San Francisco, reached out to me to see if I would be interested in getting involved in ADNI because as important and transformational as ADNI has been, ADNI, like most other studies of Alzheimer's and other dementias, has done a profoundly poor job — and he would admit this as well — of including the types of populations that we've been talking about here today. So, when I joined ADNI, historically, the cohort has been primarily non-Latinx white, highly-educated, high SES. That's the landscape, but I don't want to just pick on ADNI because that's the field more broadly as well. That said, here we have a PI of one of the largest, longest ongoing studies of Alzheimer's, and he reached out to an expert. So, he found me. He asked around, he found out about me, and we started collaborating together, and he invited me to co-lead the ADNI 3 diversity task force.

So, ADNI 3 is one of the iterations — about every five years it gets updated. So, myself and Dr. Ozioma Okonkwo out of the University of Wisconsin at Madison, we became the co-leads for this ADNI 3 diversity task force effort. And in our time — so essentially, what we were asked to do was to conduct a pilot intervention, where we were given funds and were able to work with a subset of ADNI 3 sites. And I believe we identified and worked with about 13 of the sites in ADNI 3. And we gave them a certain amount of money. We gave them our expertise and lots of time, consultation, collaboration, troubleshooting. And in our time working with those sites, which was about 18 months, we made tremendous changes, including the rate of enrollment of individuals from underrepresented populations — and we focused on Black and Latinx populations. For those 13 sites, before these efforts, they were enrolling about one person per month from those backgrounds (Black or Latinx background). After our efforts, they were enrolling about four people a month. That's an exponential change.

And during our time doing this intervention, 95% of the individuals who were enrolled in ADNI 3 were from underrepresented populations. And at those sites, the rate of overall enrollment was about 20% people from underrepresented populations. And after, it was almost 50%. And these are really big effect sizes and really exciting results. Again, they're pilot results, but what this shows is that when you put the time, money, and expertise, apply that to the problem in a consistent manner with the support of leadership, we can make big changes. We can move mountains.

And I also want to note that we did this during the heat of the pandemic. We were deeply in the moment of the pandemic when this happened, and we were still able to achieve these results. And as a result of that work, when it was time for ADNI to apply to be renewed to National Institute of Aging through National Institutes of Health for ADNI 4 — when it came time to submit the renewal application, we were invited to become our own core within ADNI. And eventually, that's what we did. We submitted a proposal within this larger application to become the engagement core.

And now in ADNI 4, which we're in year two of ADNI 4, we have three main goals in our core, and I continue to co-lead this effort with Dr. Okonkwo at University of Wisconsin. And our three primary goals are to do exactly what we've just been talking about, right? So, our first goal is to increase the representation of underrepresented populations in ADNI, and speaking of dimensions of diversity, for this first goal, we have gone beyond just the initial populations we worked with in our pilot. So, here in ADNI 4, we're defining underrepresented populations to include people of all ethnoculturally minoritized backgrounds, so not just Black and Latinx, but also Asian, American Indian, Alaska Native, Native Hawaiian, and other Pacific Islanders, for instance. That's one aspect of how we're defining this underrepresented population or URPs.

The other two include people with 12 years or less of education, and the third are people from rural backgrounds. So again, we are working, we're thinking about intersectionality and thinking about these different populations and making an effort to scale up our efforts to these other populations that have been under-included. And our goal in ADNI 4 is to make it so that at least 50% of the individuals who are newly enrolled into ADNI 4 at our different sites for in-clinic visits — that 50% of those new ADNI participants are from underrepresented populations. So, it's a very ambitious goal, but we've started out strong and we're really excited about our efforts.

So, that's the first aim. The second aim of the Engagement Core within ADNI 4 is to advance brain health equity research within ADNI and beyond. So, we have been looking at ADNI data, we've been writing papers, we've been documenting our methods on inclusion science. We have a paper in press right now in *JAMA*

Open Network that myself, and Dr. Miriam Ashford, and Dr. Okonkwo co-first authored. We also have a paper in *Alzheimer's & Dementia* that's in press that documents our ADNI 4 methods as we've gotten started. So, that's our second goal, and we have a monthly writing group working with other ADNI investigators to advance that goal.

And our third goal is to create a culturally competent, more diverse dementia research workforce for the 21st century. And we're doing that through something that we call the Health Equity Scholars Program. So, our study ADNI and another study HABS-HD, which is a study out of the University of North Texas. Sid O'Bryant is the PI with a couple of other great folks. We have joined forces to develop a scholar training program that is lifting up scholar scientists from diverse backgrounds and scientists of any background who are interested in brain health equity research to train them on many of the things that we've been talking about today. So that as we move forward in the field, we won't have such a dearth of scientists and clinicians who are ready to do this work.

Marie: Well, Monica, I think this is remarkable, and congratulations to you and your colleagues on all of these exciting successes. And I know ADNI, specifically, is for Alzheimer's disease, but can you share what have been some of the lessons learned in ADNI that could potentially be applied to PD research?

Monica: I think that what we've demonstrated in ADNI is that it is possible to do this work in populations that have been considered hard to reach. And I think that what we've done in ADNI could be replicated in Parkinson's if investigators were given these tools. Again, funding, time, and expertise. Those are the three key ingredients to making meaningful change in the scientific landscape to advance science, and research, and treatment for neurological diseases, especially Parkinson's. So, I think my biggest lesson learned is that it is possible to do. And I think that what we've done could certainly be scalable to Parkinson's disease.

Marie: Well, that's wonderful to hear. And I think you are making incredible progress. And I know we've touched on some different areas and things that are helping people make progress in this area of having more diverse research populations and just improving the area of brain health inequities. So, when you look at the field as a whole, Monica, are there particular things that rise to the top of your mind as tools, or resources, or collaborations that you're seeing — or that you're involved with — that you think are really moving the field forward?

Monica: Certainly ADNI, which I've just spoken about. And what's exciting about ADNI is how we're taking these highly intensive, very local, in-person, boots on the ground types of efforts and scaling them up to the national level. Right? And so, there are resources through the papers that we're currently publishing. We want it

all out there so people can utilize this and try to replicate it in their populations of interest.

I have other collaborations that I'm also really excited about where we're also working in these directions. And we started out our time together talking about the lack of research in individuals under the age of 65. And I'm co-principal investigator on another study called BEYONDD, which stands for biomarker evaluation and young onset dimension diverse populations. And this is a collaboration between myself and Drs. Adam Boxer and Gil Rabinovici at UC San Francisco and also Dr. Desiree Byrd at Queens College at City University of New York. And we're working on looking at all-cause dementia in individuals under 65.

And that would include some of the things that we're talking about here, right? So, it could be frontotemporal dementia, early onset Alzheimer's. It could be PSP. It could be other types of dementias. And in that study, we're looking to really focus on younger populations from these ethnoculturally diverse backgrounds. And I'm very excited about that collaboration as well. And I think that will have — since we're looking at rarer types of dementias — I think what we learn from there could be particularly of interest for both Parkinson's research and Parkinson's plus syndromes.

Marie: Very interesting. Well, Monica, we talked about a lot of areas that remain to be explored, that are related to some of the topics we talked about today. But what are some of the future directions or perhaps areas of opportunity in Parkinson's disease research that you think are most promising or that you're most excited about?

Monica: Well, I'm going to tell you one thing I'm really excited about. Some of my work that you've heard a little bit about today is focused on blood-based biomarkers, which is a really exciting area of research for neurological diseases. So, these blood-based biomarkers have been developed and validated, for instance, with Alzheimer's disease. And they have very strong sensitivity and specificity. And essentially what they do is they provide us with a really great way to identify individuals at risk for Alzheimer's in the community.

So, they don't need to go to a big, fancy academic medical center to get a very expensive amyloid PET imaging evaluation, or tau PET, or both imaging evaluations. Because those cost thousands and thousands of dollars, and they're not readily available to people from these different types of diverse backgrounds that we've talked about ethnoculturally, socio-economically, and geographically. And so, these blood-based biomarkers are a really exciting opportunity for us to get diagnostic tools that would be more readily available to clinicians and researchers in these communities that have been so profoundly under-included

to date. But these blood-based biomarkers that we're talking about are really more to date, more for Alzheimer's and other related dementias.

But what I'm so excited about when we talk about Parkinson's are the new blood-based biomarkers or CSF-based biomarkers that seem to be gaining some traction, looking at alpha-synuclein seed amplification assays. And ADNI actually has been collecting some of these data and just some of the ADNI investigators.

In fact, there's a great paper that was recently published this year by Dr. Duygu Tosun, also at UCSF. And it's a cross-sectional study looking at the prevalence of alpha-synuclein, which we know is a biomarker for Parkinson's (for Lewy bodies and Parkinson's), and how it's related to different biomarkers and cognitive function. And it looks like, at least in the ADNI cohort, it seems to be this marker again, this alpha-synuclein seed amplification marker, seems to be a very sensitive and specific marker for this pathology. And it could open up a whole new avenue for research to make Parkinson's research, and Lewy bodies, and other research more accessible to people. So, it's really exciting. And I think it's a new area worth investigation, and especially to validate this biomarker in diverse populations as well, I think is an important next step to advance this research.

Marie: Certainly. Well, I definitely agree with you. I think you brought up some really important points there and just the big picture that these biomarkers, whether they're blood-based or even CSF-based, would just increase access for so many more people from diverse populations. And I think, Monica, you were doing amazing work in the field, but can you share with us how you see your work bringing us closer to finding a cure for Parkinson's or contributing to improved therapies for people who have Parkinson's today?

Monica: One of the challenges of doing this work and being in this area sometimes can be that sometimes we might not feel hope or, you know, feel discouraged. Science takes a long time to move forward, but I really think that as we wrap up, I want to leave your listeners with a sense of hope as we look forward. We're really in a golden age of science and research in Parkinson's, and Alzheimer's, and other dementias. The emergence of these blood-based and CSF biomarkers, really, it's an exciting time. And as we develop and refine these biomarkers, that provides targets for treatment. And good biomarkers can help us develop and test new and better treatments for Parkinson's.

So, I think that's really hopeful. And as this work has been accomplished in the area of Alzheimer's, with regard to brain health equity, this gives me hope that we can do this in Parkinson's so that Parkinson's disease research can be more generalizable, more externally valid, more representative of everybody who is at risk to get Parkinson's, not just some people. And in doing so, this work can touch more lives, touch more families, have more of an impact, and we can

develop better, more evidence-based interventions to improve the lives of all people living with Parkinson's and their families.

Marie: Absolutely. Well, Monica, a wonderful note to end on. Thank you so much for joining us. It's been such a pleasure to chat with you today.

Monica: Wonderful to chat with you. Thanks to you and also to the Foundation. Again, you're all doing such incredible work, and I feel truly honored to be here with you and your listeners today. Thank you so much.

Marie: Well, Monica, we truly appreciate you taking the time to share your expertise and your insights with us today. And listeners, it's been great to have you here with us as well. If you want to know how The Michael J. Fox Foundation can help your research, please visit michaeljfox.org/researchresources. And you can find new episodes of this show each month on the MJFF website or on your favorite podcast platform. When you have a moment, please subscribe to our show to make sure you don't miss our outstanding lineup of upcoming episodes. We look forward to connecting with you again in our next episode of *The Parkinson's Research Podcast*.