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Podcast Host: In this episode of the HD Insights pod, we were fortunate to catch up with dr Victor Sung. Now, Dr. Sung is an HSG researcher at our University of Alabama Birmingham site and he's been involved with HSG and HDSA and he's just a really generous, caring person working with patients in the HD field. We were fortunate to catch up with him and spend some time with him at the 34th Annual HDSA Convention in June of 2019 held in Boston. So here's that interview.

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Podcast Host: All right, so we're pleased to be joined today with Dr. Victor Sung. He heads the HD Clinic at UAB. He is a member of the Huntington Study Group and he's one of our neurologists who's a PI on all our HD studies. Dr. Sung, we're, we're very happy to have you join us today for this podcast.

Dr. Sung: Kevin, thanks having me. We're here at the HDSA Annual Convention in Boston. It's an exciting time. This particular meeting is a patient facing meeting, so a lot of the stuff is directed towards patients and family members. But I have to say the thing that all the patients and families want to know the most about is what's going on in the world of HD research. This is kind of an unprecedented time. I took over our HC Clinic in 2010. But even in that short amount of time, since I've been really working in the field of HD, the way I've seen the research grow, I mean it's really been exponential.

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Dr. Sung: Back in 2010, 2011, when I was first getting started, our clinical trials were not as many. They were mostly symptomatic therapies. They were things that... My first HSG study that I participated in was the CREST-E Study, which was looking at creatine for the treatment of HD. For me, we hoped that maybe it would work. But really in the back of our minds, did we really think that a nutritional supplement that you could get over the counter was going to be the end all, be all cure for Huntington's Disease. I don't think any of us really thought that. Could it do something? We hoped that. Unfortunately, that didn't work out, but a lot of us scientifically are attracted to Huntington's Disease because of the genetic aspect of it, because of the scientific aspect that it gives us a target to focus on.

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Dr. Sung: I talked to a lot of my... Well, a lot of people, my colleagues even in the field of neurology, ask me, "Why would you choose Huntington's disease?" Huntington's Disease is so daunting clinically. These patients have multifaceted clinical issues and tackling that. But one of my answers scientifically, as a a scientist, as a researcher, is that compared to other diseases that myself as a neurologist might be treating, we don't have a clear idea of one single cause of Alzheimer's Disease or a one

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single cause of Parkinson's Disease or a one single cause of ALS. Whereas in Huntington's Disease, we have a pretty clear cause. It's that mutated HD gene that causes the disease, so it's as simple and as complicated as targeting that.

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Dr. Sung:

And while we're still excited about symptomatic therapies, I think that's still hugely important in this field. I mean, it's both therapies that we already have and therapies that we're going to look at in the future. I think I'm excited about more symptomatic therapies. We need more of those also. The exciting thing right now is all the potentially disease modifying therapies. I think disease modifying therapies really exist in a lot of other fields in neurology. You have revolutionized the

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treatment of diseases like MS, but they've been lacking behind in a lot of the... particularly the movement disorders, but the prospect that we might have that in Huntington's Disease... I think we'd all love to think about these drugs as or these

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therapies on the horizon as potentially curative therapies. And yes, we would all love to cure Huntington's Disease, but I think a step towards that is if we can modify the course of the disease by targeting the root causes of these by targeting the gene.

Dr. Sung:

I think those are the studies that we all are the most excited about, generate the most buzz, generate the most questions for all of us as clinicians and scientists is where are all of those things? I think the way in my mind that I think about break those therapies down or you have your RNA based therapies and your DNA based

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therapies. For the RNA based therapies, which are the ones that are in clinical trials now, you have the phase three ASO study, which is a non allele specific ASO study that's being run by Roche Genentech as it's known in the United States. There's been a lot of talk about their trial here at this meeting. The Wave Life Sciences ASO study, which is using a different mechanism also with an ASO, but slightly different mechanism to be allele specific. I think both of those are very interesting.

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Dr. Sung:

Will either have them be curative on their own? No, I don't think so. But could they significantly slow the progression of the disease? That would still be huge. My perspective on that is I ask my patients, or my patients kind of say this kind of thing,

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"Well, what is the point of that?" The point would be if you are... hypothetically, if you could take these therapies and you're presymptomatic, then maybe and you are maybe with your repeat number that you were going to start showing

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symptoms at 50, now maybe with these modifying therapies like an ASO drug, then maybe with that then your disease starts at 60 instead of 50. And 10 more years, 10 more productive years in the working environment, 10 more years of wage earning and 10 more years to see your children graduate from high school and from college and to be able to walk them down the aisle. The significance of that is huge.

Dr. Sung:

All of these potentially disease modifying therapies, you can still use symptomatic therapies on top of it. Right. I think all of this kind of works together. At the HSG meeting last year, Sarah Tabrizi, who's a Clinician Scientist at UCL in London, she did a lot of the initial work with this Roche at Genentech ASO. She's the lead author on a lot of these publications. At the HSG meeting last fall someone asked her,

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[00:08:30] "What do you think? Like with all the stuff, this amazing stuff that we have going on scientifically in the field of HD, give us your candid take on all of these things." I still quote her on this as I thought her answer was spectacular, which is, in her mind, we have potential of a total body cure for HD. I think that's what it's going to take.

Dr. Sung:
[00:09:00] We'll need all these therapies. We need all these treatments to come down the pipeline and work and we'll take any and all of it. She talked about there's an ongoing HSG trial of an IV infusion therapy that could be disease modifying. So you have an IV infusion that goes into the rest of your body that might slow the progression of the disease, combined with an intrathecal or a spinal tap delivery ASO that really gets a lot of penetration into the cortex of the surface of the brain and slows the disease there. And then you have a therapy, like the uniQure therapy that is directly injected into the basal ganglia of the brain and you have a deep brain cure that way. Between slowing the disease in the basal ganglia, the cortex of the brain and in the rest of the body with an IB infusion, maybe that's what we're looking at as a cocktail, as a kind of total body cure for Huntington's Disease. The prospect of those things on the horizon, that's really neat.

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Podcast Host: Yeah, I think that's one of the things that I've heard people talk about is it's not necessarily that any one of these clinical trials are going to end up with the cure because there's always variances from person to person, so it's more of do we look for something like in cancer treatments where it is a cocktail like you said.

Dr. Sung:
[00:10:30] Right? Yeah. I think that's if you look at any of our major diseases where we've made major breakthroughs... A big one that I compare it to is HIV. Right? We've come so far in the treatment of HIV that it's essentially... You can essentially eradicate HIV in patients. They need to continue to take their therapies. But like you said, it's a cocktail. It's a multi-drug regimen that keeps the disease under control. I think that's what it's going to be. Each of these horizon therapies in the field of HD, exciting? Yes. As clinicians, as scientists, we're all very excited about all of them, but I think it will take a combination of all of them to really get on top of this disease. Any one of them, we'll take all of them. We'll take this one and that one and the next one. There's still plenty of work to be done, but that there is this work to be done is super exciting.

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Podcast Host: I want to go back to something you let off with at the beginning, the fact that you took over the clinic in 2010 and just the progress in the new types of trials or treatments coming out has been amazing, but that in fact in HD it's kind of lagged behind some of the other diseases. Do you think it's because HD is considered rare? It's been more of a growing field or... Is it just that we're reaching a point now where we're starting to make a lot of progress? Now we're getting more people involved in it.

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Dr. Sung: I think there is this kind of cumulative momentum kind of effect. I think some of the slowness in getting into it is like you alluded to, it's a rare disease. Big pharmaceutical companies with big money weren't as attracted to it initially

[00:12:30] because they want the glamorous, high-profile diseases that will impact more patients so they can make that money back, which I get that. But I think some of it too legitimately is that our scientific technology just wasn't there. The gene was sequenced in the early 90s. I think people legitimately thought back then like, "Oh, we know what the gene is now. We're within a few years of being able to cure this disease." 20, 30 years later, we're still not there yet. I think it's just a technology is not there. And over the last five years, finally our science is catching up to being able to do the things that we've wanted to do once we discovered the gene.

Dr. Sung: [00:13:30] It's a culmination of those things. The science is getting there. And as the science gets there, I think these companies, they've had enough failures that they see like, "Wait, if the science is there, even if this a rare disease that won't impact the same number of patients as some other higher profile disease, if we can make this work in this disease and make this technology work in this disease..." One, there's good PR for a big pharmaceutical company like says, "Hey, we were involved in the first gene silencing or curative study in Huntington's Disease," but then also maybe they can apply the technology and their learnings to other diseases and then take the next steps into higher profile diseases.

Dr. Sung: [00:14:00] Certainly for those of us who have a passion for HD patients and families and wanting to bring new therapies to them, we'll take it however HD garnered this attention from pharma to to have these big studies going on now. However we got there, I think we'll take it.

Podcast Host: [00:14:30] You mentioned passion. I heard you speak last year at the HSG Annual Meeting on the Ask the Experts Panel at our family day. I was really moved by not only your responses to family's questions, but everybody that was on the panel. Tell us a little bit, for those that don't know you or your background, how did you end up in neurology and getting into HD specifically? What kind of led you down that path?

Dr. Sung: [00:15:00] Yeah, I mean I think I have a... Everybody has their own unique story, but I think the way I ended up in HD is very similar to how a lot of my colleagues in this field ended up in HD, which is you kind of backed into it. I don't have any particular personal story. I kind of backed it, but once we got into it, the patients and families inspired us. I think there's a unique aspect to the disease, right? So Huntington's Disease is a purely genetic disorder with usually an adult onset. Because of that, people often live their lives until the point, mid adulthood, when they start showing symptoms. But up until then they have a normal life and then it hits them like a ton of bricks in the middle of their life, in the middle of their prime wage earning years, when they start to show symptoms and takes them out of those wage earning years, so the crippling effect of that on their whole family, but then also the constitution of symptoms that they get with the motor symptoms, the cognitive symptoms, the behavioral symptoms. [00:15:30]

Dr. Sung: It really affects all aspects of their life and it really can be really devastating on the patient and their whole family around them. You add in the genetic aspect of that so that someone who's taking care of their loved one with Huntington's Disease,

[00:16:00] then may not be able to be their caregiver anymore once they start to become symptomatic themselves. It really has this profound impact on the whole family. But in spite of that, or maybe because of that, I don't know, just the resilience of these HD patients and families and seeing the whole family rise up to meet the challenge of the disease is just so inspiring. We all get this feeling like, "Okay, we have to do something to help these people. If they can put up this much of a fight and be inspirational to us, we need to step up and meet this scientifically." I think that's kind of how we all get hooked into it.

Narrator: We'll return to the interview on the HD Insights Podcast in a moment. We hope that you're enjoying this episode. As a nonprofit organization, the Huntington Study Group relies on the generous support from the community and listeners like you to continue bringing you in depth content on HD, like this podcast series. If you like what you're hearing and are interested in supporting HD Insights through a grant or donation, please contact us through our email address, info@hsglimited.org or by calling toll free at 1-800-487-7671. We greatly appreciate your support. And now, back to our episode.

Podcast Host: Looking back, is there a particular instance that really inspired you more? What was your most memorable experience dealing with the patient population?

Dr. Sung: Yeah, I mean, I think we all have these amazing hooks of stories. The one for me, the story that I always tell, it was very early on when I had taken over the clinic. There was a patient who... My clinic is in Birmingham, Alabama and this patient lived in New Orleans. New Orleans is about a five hour drive from Birmingham. I saw that this patient had come to see me from New Orleans I thought, "That's an awfully long way to come, five hours to come to Birmingham. How did you guys find me here in Birmingham?" They said, "Well we looked on the website, looking for major centers." At the time, there wasn't a major center of excellence in New Orleans. They said, "Well, the next nearest center were either Houston or Birmingham and they both were five hour drives from New Orleans." And they said, "Well, we figured that Houston traffic would be worse than Birmingham traffic, so we chose Birmingham." I said, "Well, I think you chose wisely. I grew up in Houston. I love Houston, but the traffic is certainly worse in Houston than it is in Birmingham."

[00:19:00] Dr. Sung: There were two things that struck me about that patient. She was a young patient and she had profound chorea and profound depression. I started two therapies for her. One to treat her depression, one to treat her chorea. One pill for each and pretty straightforward. I saw her back in follow up. When she came back for follow up, her follow up appointment fell around Christmas time. It was in December. She and her family came with this big basket of goodies, Christmas themed food, goodies. UAV is a state institution. We're not allowed to accept gifts. I kind of took the basket, kind of towed the typical party line, "I accept this gift on behalf of the whole clinic. I will share it with everyone here in the clinic. I'm not going to take any of it home," blah, blah. This typical party line kind of thing.

Dr. Sung: The family said, "Whoa, Whoa, Whoa, Whoa. You do not understand the gravity of this gift that we're giving you." I said, "Well sorry, please enlighten me." They said, "Well, one, we're from new Orleans and we take our food seriously in New Orleans, so you need to take our food more seriously." I thought, "Yes ma'am. I've been to New Orleans. I know you take your food seriously, I will take the food seriously."
[00:20:30] They said, "But more than that, before she became symptomatic with HD, she was a chef and because of the chorea that she's have been having and the depression that she's been having, she hasn't been in the kitchen for the last five, seven years. But because of these treatments that you gave her, she's doing so much better that she participated in making every single thing in this basket."

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Podcast Host: Oh wow.

Dr. Sung: "So on behalf of our whole family, thank you for giving us our sister back. Thank you for giving us our daughter back. Thank you for giving her her sense of self back." I was crying and they were crying. We all had a big cry about it, but it was that. And ultimately, many years down the road, I mean, this patient has
[00:21:30] succumbed to her Huntington's Disease and she's no longer with us, but even for that amount of time, that with the limited options that we had available, we're still able to make clearly such a big impact on that patient and that patient's whole family, that was the hook. It's like, "Okay, that." Even if we can't do that with everybody, if we can do that every once in awhile, that's enough and we need to fight for these patients.

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Podcast Host: That's an amazing story. It goes right along with what you said. I mean, even though she's no longer with us, even that treatment gave her that much more time to be more productive or get involved with something that she couldn't have gotten into up to that point. So I mean, that's amazing. Kind of keeping in the theme with working with families and the motivation that... This past year you, you
[00:22:30] became part of the board of directors at HDSA. What's your experience been like working in that capacity?

Dr. Sung: Yeah. I think like a lot of things, it's definitely a labor of love. All of the volunteers on the board of trustees for HDSA volunteer their time and give it freely. About half the board has HD in their family and the other half have a story like mine where they interacted with HD patients and families and just fell in love and felt like they
[00:23:00] needed to do something to help. I think that's HDSA's mantra, right, is help for today, hope for tomorrow. I think that's very true. I think that's kind of how we all live and breathe it. It's been hugely rewarding to be a part of the board, to shepherd their mission. It's great. HDSA's mission is really providing help and hope for patients and families. It's a really patient facing organization and they really do
[00:23:30] have a nice collaborative working relationship with the other HD organizations like the Huntington Study Group, which is much more research focused, which I think is really important.

Dr. Sung: HDSA doesn't take as big of a role in shepherding the clinical trials because they are the patient facing organization, but I think there's a place for everybody at the table to really work to help eradicate this disease.

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Podcast Host: Absolutely.

Dr. Sung: I think I've heard HSG people say the same thing. I've heard HDSA people say the same thing is, "We'd love to put ourselves out of business. Right? We'd love to, through the work that we do, there's so much out there that, we've eradicated the disease or eradicated the need for Huntington Study Group to exist or HDSA to exist." And that's kind of what we're all passionately working towards.

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Podcast Host: Absolutely. One of the things people may also not know about you in terms of your role at Huntington Study Group, you also have helped out with our CME for HD program. You've provided some training, lecture based training, in the course of the disease. I think the one thing that's... the takeaway from that course is it's a holistic look at how you handle care and treatment of the disease. It's not just prescribing a drug. But like you said, there's symptoms that we can treat. There's

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the psychology, the psychiatric treatment. There's cognitive issues. What, in your experience, or what do you foresee changing that overall dynamic over the course of time? We have these new treatments coming out, but the key is not to lose sight of the fact that you need social workers. You need to think about financial planning. You need to think about eventually care in the home, whether it's family members or professionals. What are some of the things that maybe you're doing at UAV that

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kind of look holistically at the-

Dr. Sung: I think that's really important. It's one of our goals with CME for HD. The program that HSG's put on, is really showing that... Okay, right now, a lot of our big a disease modifying therapies, they're all in clinical trials, meaning that none of them are clinically available to treat our patients and it may be a number of years before we have any of those. But it doesn't mean that right now there's not things that we can do. And just because we don't have a curative prescription that we can write on a prescription pad and order for our patients doesn't mean there's not things that we can do that have a significant impact on the whole patients and families lives. It's more than just the medicines. We talked about in my story about some medicines that I gave that did have a big impact on that patient and family, but there was definitely more than that like you alluded to.

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Dr. Sung: Just getting the awareness out there I think is hugely important for there are things that can be done, kind of dispelling this myth that just because we can't cure it, doesn't mean that there's nothing we can do about it. I think that's part of the goal of CME for HD. But forward looking, definitely I think that's something that is huge that we are all talking about. As center directors, we're having a big meeting

[00:27:00] tomorrow specifically to talk about this. What if one or more of these disease modifying therapies gets approved in the next couple of years? If we don't have our infrastructure ready, our care model ready on how we're going to provide this care, provide patients access to these new therapies, then we won't be ready and we will fail the patient and the community.

Podcast Host: Right, because it's one thing to be able to deliver it in a controlled trial setting, but then when you're talking the entire population.

[00:27:30] Dr. Sung: Yeah. A number of these trials, while the therapies are exciting, they are invasive, right? So the two ASO trials that are ongoing now, they're intrathecally delivered. If the therapies workout scientifically and come to market, then we're talking about a therapy that has to be delivered via lumbar puncture. The vast majority of the neurologists in the United States haven't done a lumbar puncture themselves in a long time. If you've been in private practice for 30 years, it may have been 30 years since you've done a lumbar puncture. Are they all going to feel comfortable all of a sudden bringing an HD patient in who's symptomatic and has chorea and doing their first lumbar puncture in 30 years on an HD patient with chorea to deliver them this therapy? I would venture to say that they're not going to want to do that, but patients will be clamoring for it, so how are we going to operationalize that?

[00:28:00] Dr. Sung: I think it's going to be up to us as the investigators, as the Center of Excellence Directors, to come up with a care plan that operationalizes that. At the same time, all of us as investigators, HSG sites Center of Excellence Directors, the majority of us are at tertiary referral centers where we're already being inundated by patients and we have an access issue already. What are we going to do when all of a sudden all of these patients have to come to us to receive these invasive therapies? How are we going to accommodate that? The ASO therapies are going to require multiple treatments a year. How are we going to accommodate that? How are we going to meet the demands?

[00:28:30] Dr. Sung: It's a complex thing, but I think... To me, I look at it as a double edged sword. It's going to be a hard question to answer and we're going to have to figure out something that's going to work for everybody, which is going to be really difficult, but at the same time, if we are having to have that discussion, it's a good thing. Right? I mean, at least we have therapies that have a lot of promise that we're talking about how are we going to deliver these promising therapies to our patients. As opposed to the opposite, which is, "Well, we don't have this difficult problem to solve because we don't have good therapies to deliver to our patients." It's this double edged sword.

[00:29:30] Podcast Host: Yeah, it's a good problem to have, but the more prepared we are, the better it will be for the entire population for sure. Before we finish up, there's really just one last question I wanted to ask you and that's, in your growth in this field or getting into

this field, who has been your greatest mentor? Who's the role model that you look to or still do maybe that's really kind of inspired you to grow?

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Dr. Sung:

Yeah, I mean our community is really tight knit and I think that's been one thing that's been attractive. All of us who do this are passionate about it and we see that same passion in all the other investigators. The other thing is it's very collegial. I mean, that's been my experience in movement disorders in the broader sense, but definitely within the HD community. Everyone is looking for the next person

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coming up and looking proactively to reach a hand out and help them to come up to their next stage. The person, the single person in our field of HD, who has been that person for me is Sam Frank.

Dr. Sung:

I tell this story all the time about I never would have known how clinical trials and being involved in clinical trials would've helped my career. I knew pretty early that I wasn't going to have a lab, a basic science lab and chase NIH grants that way, but how was I going to be an academician and do research, which I still was interested in, and the thing that was most apparent to me was in clinical trials. One of the early trials that I was involved in was the HSG trial, First-HD, which led to the commercial approval of deutetrabenazine. And Sam, as you know, was one of the PIs on the First-HD study, the global PI for the study. I remember at the first investigator meeting for First-HD, wide eyed, I didn't know anybody, sitting down and Sam was looking around the room and saw a new face that he didn't know and proactively came over and sat down next to me and we just hit it off.

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Dr. Sung:

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I mean, I could tell he had the same energy, the same passion for HD patients and we hit it off really well. This is my first year on faculty. A few months later, I got an email inviting me to chair a session at the American Academy of Neurology. I thought, "How in the world did I get invited for that? Because I'm brand new. I don't know anybody. I literally haven't done anything in my career." It turns out Sam was the Chair of the Scientific Committee for Luma Disorders for the American Academy of Neurology. He chose that. I mean, that is him directly mentoring and directly helping me. Things like being a chair for a committee for our big national meeting, those look really good on your resume, on your CV and that's how you move up. It's those direct things, like proactively helping me up to the next step. I'm forever thankful for those things.

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Dr. Sung:

Now I'm not the new guy anymore and I'm proactively trying to reach to the next generation, but that's how we do it. I mean, that's how we get more investigators to be involved in clinical trials. We have to have this proactive mentoring thing and we definitely have that in this community. It's all facilitated in my mind by HSG, but there's really this attitude that kind of pervades our whole community and it's been fantastic to be a part of.

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Podcast Host:

That's outstanding. Well, Dr. Sung, we appreciate your time stepping away from

the HDSA Conference to speak with us today. Thank you so much for your passion and dedication to the community and we look forward to continuing to hear from you in the future.

Dr. Sung: All right, thanks for having me, Kevin.

Podcast Host: All right, thank you.

Podcast Host: That concludes our interview with Dr. Victor Sung. It was great catching up with
[00:34:30] him at the HDSA Convention in Boston and he has some really great stories to share about his experience with patients, as well as research. I really hope you enjoyed this episode and this interview that we were able to bring you.

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