

Speaker 1:

Welcome to the Eye on the Cure Podcast, the podcast about winning the fight against retinal disease from the Foundation Fighting Blindness.

Ben Shaberman:

Welcome everyone to the Eye on the Cure podcast. I'm your host, Ben Shaberman with the Foundation Fighting Blindness. And for this episode, I'm really delighted to have as my guest Dr. Jacque Duncan, who is with the University of California, San Francisco. And we're going to tell you a lot more about Jacque. But Jacque, I feel like I'm having family on the podcast. You've been such an integral part of the foundation for so many years, and you and I have worked together for so many years. It's really great to have you.

Jacque Duncan:

It's a great pleasure to be here. Thank you for having me.

Ben Shaberman:

My pleasure as well. So a little background for our listeners, on Jacque, who is definitely one of the busiest clinical researchers on the planet. I can attest to that. Again, she's at UCSF. She is a professor and retinal specialist. She's also the director of the Retinal Degenerations Clinic and Retinal Electrophysiology Lab. She's interim chair of the UCSF ophthalmology department. And so important to the foundation, she is chair of our scientific advisory board, which I think is a full time job unto itself. Oh, by the way, Jacque also conducts some clinical research studies for inherited retinal diseases. So a lot going on in your professional life. So my first question, sort of a general reflective question, Jacque, is what inspired you to get into ophthalmology and the retinal disease space?

Jacque Duncan:

Yeah, thank you for asking that question. I did not know initially, first of all, that I even wanted to be a doctor. So it took me a little while to get to the point where I thought that that was what I wanted to do. I always loved biology, I always loved learning about science and how living things work. And then during college I decided that I also really love people. I love hearing their stories. I love finding ways to help them in any way I can. So the two together made it obvious for me eventually to know that I should apply to medical school. And during medical school also, I have no physicians in my family and I didn't really know which kind of medicine I wanted to pursue. But very early in my rotations I was assigned to a rotation in ophthalmology. It was actually the very first rotation I did with patients, and it was fascinating and beautiful.

The images were amazing, and it was a great way to get to know people and hear about their stories and think about ways to make their life better through intervention, whether that be medicine or surgery. So I spent the rest of my core clerkships trying to find something I liked as much, and I never did. And so that's how I became interested in ophthalmology. As it turns out, some of my family members, both grandparents on both sides had age related macular degeneration and lost vision later in life. So I kind of understood what it meant to lose your vision as an older person and the struggles that accompanied that. And so that was how I ended up in ophthalmology. During residency, I knew I loved the retina. Retina is the percipient element of the eyes, the part of the eye that takes light and turns it into a message the brain can understand.

I didn't love surgery though, because the surgeries for retina at that time were like six hours long and they didn't end up improving people's vision at the end of the day many times. And so I was interested in research and trying to learn more about how to make things better than they are. So I was introduced to one of the pillars of inherited retinal degenerations research, Matt LaVail, who was a basic scientist here at UCSF, and he convinced me that this was a unmet need in ophthalmology. This is where the future of ophthalmology resides, in that these are where all the really difficult, challenging unmet questions, unanswered questions remain, is in retina and in retinal degenerations. So I did a fellowship to learn more about these diseases at the Scheie Eye Institute with Sam Jacobson, Artur Cideciyan, Tomas Aleman, Stuart Fine. And came back to do research at UCSF with Matt LaVail, working with animal models, looking at different treatments that might help and the rest is kind of history.

Ben Shaberman:

That's a great story. And to have come through the ranks, the training at Scheie with Sam Jacobson and Artur Cideciyan and Dr. Aleman, I mean those are really impressive people in our space. And then Matt LaVail, for any of our listeners who kind of go back into the nineties and early 2000s, he was the go-to guy for animal models and neuroprotection. So you had a great upbringing in the retinal world. That's very cool. So you have a particular expertise in imaging, specifically adaptive optics. And I don't think a lot of people are probably familiar with that because that's not something, an imaging modality that one would get in their typical doctor's office. Can you tell us what interested you in that and maybe a little bit about what adaptive optics is?

Jacque Duncan:

I would love to. So as I mentioned, I was doing research with Matt LaVail on animal models of inherited retinal diseases and different treatments that might be helpful to them. And I kind of was bridging that research side of my career with my clinical side, where I was seeing patients suffering from the very same conditions that the animals were meant to model in the clinic. And a big challenge is trying to understand how the vision cells are being affected in these patients with retinal diseases. Different genetic mutations cause different effects on the vision cells. And no matter how hard I squint, I can't see the vision cells in living eyes.

So I was at ARVO one year and heard a talk by investigator who was soon to become a long standing collaborator, Austin Roorda where he had worked with David Williams at University of Rochester. And had patented a technique which was really based on technology from astronomy, where you could get a really clear image of the vision cells in living people's eyes by using a technique that was developed for astronomy, to overcome irregularities in the atmosphere that make it very hard for us to see distance stars.

So the way adaptive optics works is it measures irregularities in the light that is coming, entering and exiting from the eye that make it very hard for us to see individual vision cells. And it measures them very precisely, communicates that information with a special mirror that bends its shape to compensate for those irregularities such that we get a very high resolution image of the retinal structures. And this was really originally first developed to compensate for irregularities in the atmosphere that'll prevent us from seeing distant stars.

But Austin Roorda, who is my colleague at UC, Berkeley, working with David Williams, invented a way of using that same approach to look at eyes, look at the retina. And it's been, they developed that in the late 1990s, which is just about the time that I was completing my training. And to my good fortune, Austin Roorda had just begun his lab research career at UC, Berkeley, which is right across the bay from UCSF. And so I met him at ARVO and I said, "This is amazing technology. I have a whole career full of

patients that I want to investigate using it." And he said, "Come on over." So I visited his lab a few days later and we've been collaborating ever since.

Ben Shaberman:

That's cool. And thanks for that explanation. And for our listeners to understand how powerful adaptive optics is, you can look at and measure individual cone cells, cone photoreceptors and literally count them. And, aren't you able to see with the newer technology even rods now to some extent?

Jacque Duncan:

Absolutely. Yeah. So there are some... The resolution of the systems has improved since the early days of this technology such that you can see individual rods, certainly not at the fovea because there are no rods at the fovea. But as you get a little further away, you can see rods interspersed between the cones. And there's a special technique that was developed by an investigator named Alf Dubret at Stanford now, which is called split detection, where you take information that is not going through a pinhole and collect all the extra light and you can discern between cells that the light that's coming from the cones and discriminate that from the light that's coming from the rods. You can actually, with quick confidence, with certainty, determine which cells in the retina are rods and which are cones, and you can count them and you can see how they're changing over time in response to different genetic conditions.

Ben Shaberman:

Right. So you can use the technology to monitor disease progression and also tell the effect of the therapy if you're saving cells or even bringing some on the margins back. So, very cool stuff. So I want to switch gears a little bit because this is one of the most amazing things I think about you is that you chair our scientific advisory board, the foundation's SAB, and for those listeners who don't know the SAB, I think it's... Is it about 60 scientists from around the world that have for the most part expertise, great expertise in the retinal disease space? And among their many roles with us is they go through a long process of evaluating our grants. But that's such a really impressive, knowledgeable and experienced group of researchers and clinicians, again from around the world and someone to decide that they're going to help manage the SAB and all the processes toward grant evaluation and so on, that's just a very bold move. Can you talk about why you decided to do it and what it's been like?

Jacque Duncan:

Wow. No, it has really been the greatest privilege of my career to work with these leaders. Literally the world's greatest leaders in the field of inherited retinal generations are truly what makes the Foundation Finding Blindness the incredible powerhouse organization that it has been for many years and really the impactful organization that it is. We are so fortunate to be supported by, as you were just saying, the leading experts in all fields of inherited retinal degenerations research from around the world. And the greatest privilege of my life is to be able to reach out to them anytime and say, I don't understand this new question that I have, or this paper that just came out. And they are generous and thoughtful and kind and insightful and collaborative and so inspiring, like so inspiring. It's just really been such a joy to work with all of them. It's been an incredible privilege to be part of the scientific advisory board.

Ben Shaberman:

And so what motivated you to step up? You filled the shoes of your predecessor Eric Pierce, he was a very effective chair and obviously one of the best IRD scientists in the world. What motivated you to do that?

Jacque Duncan:

Right. Well, no one can fill the shoes of Eric Pierce, but I've been very fortunate to serve with him as my mentor for many years. Eric invited me to take on a larger role on the scientific advisory board one year at ARVO. And it felt to me like an opportunity to give back to the Foundation Finding Blindness, which have been so supportive of my career and made such a huge impact in the field. And so I very gratefully took advantage of the opportunity to be part of the scientific advisory board, and then to be part of the executive scientific advisory board, and subsequently to become the chair of the scientific advisory board.

And so it's been a very stepwise approach. I think Eric's many contributions was, he brought, I think a lot of organization and rigor to the scientific review process more. I mean, not that it wasn't there before, but I think he strengthened each of the review committees. I think he's initiated a review process that is so rigorous, and so fair, and so transparent and holistic and outstanding, that I think it can give everybody confidence that the work being funded by the Foundation Finding Blindness is just the top notch. And every year we get more high quality outstanding proposals than we can possibly fund. So it's a testament to the incredible expertise of the scientific advisory board that allows us to support really the very most promising research in the field.

Ben Shaberman:

Right. And I know one of my favorite days, it could be two days depending on how many grants we're reviewing, but is when you lead the study section where select SAB members come together and review the grants, and just the insights and the debate and the banter. It's just marvelous. And one thing I've consistently seen you bring to discussions like that with all these experts and heavy weights in our space is you bring humility and diplomacy. You ask good questions, but you do it in a way not to put somebody on the defensive. And I've always admired that about you, Jacque. Where did you learn humility and diplomacy? They're both so important in your role on the SAB and well, a lot of other aspects of life.

Jacque Duncan:

Well, what a nice thing to say. Again, the rigor of that process, which I agree with you, that is my favorite part of the job. The study sections are so fascinating. So thought provoking, inspiring, amazing, that was all set into place by Amy Laster and Eric Pierce. So that structure was created before I got here. I certainly can't take credit for that, but I'll tell you, it's very... The words you said to describe me were just incredibly kind. And I'll be honest with you, I am extremely humble in the presence of these people on the scientific advisory board. Every one of them knows more about many, many things, maybe most things than I know, right? So all of them have really established themselves as major contributors to our field. And it is nothing less than the greatest privilege to be able to ask them, what do you think about this?

And have these amazing, you participate in these amazing discussions of the topics and the challenges that are really the things that are preventing us from developing treatments and cures for these terrible diseases is wonderful. It's so exciting to hear what really smart people think are ways that we can make major progress. So I find that part of the job the best. It's my favorite part, because I get to reach out to people who I have admired for years, whose work illuminates our understanding of disease and mechanisms that will help us develop treatments, that will help make things better in the future.

Ben Shaberman:

But you still ask good questions and you do it in a way, again, that's very diplomatic. But continuing on this question, is there somebody in your life or was there a moment where you learned or appreciated the virtue of humility?

Jacque Duncan:

Wow. I think, I just come at all these questions with an appreciation for how much more everyone else knows than me about all of these things. And so I think that instills a sense of humility. I think training with experts like Matt Lavail, like Sam Jacobson, people who are just really thoughtful, knowledgeable resources, certainly instilled in me a sense of humility, and that I realize that there's a million lifetimes from now and I won't know everything I need to know about inherited retinal degeneration. So I think there's always interesting questions to ask and there's a lot of people with expertise and understanding that I can learn from. And so I bring that approach to every question.

Ben Shaberman:

Well that's great. And to foster the dialogue and the questions and the debate, you do such a great job.

Jacque Duncan:

Thank you.

Ben Shaberman:

So I want to switch gears again and start to finish things up here, but I know a lot of our listeners out there are affected by IRDs, or they have family members who are, and it's sort of a two part question. And one of the most difficult moments, obviously for anybody with an IRD is, and I'm sure so difficult for you, when you make the diagnosis, whether it's clinical or genetic or a combination of the two, what do you try to tell people besides you think they have RP or Stargardt's disease? What's the rest of that discussion?

Jacque Duncan:

Well, it differs for each person, to be honest with you. For each person, it's an individual experience and journey. And I think it's important to understand where people are coming from, and at what point in the journey that they are, when you're having this conversation. Some people have family members who are affected, and for them they have an understanding of what the disease might lead to or what... They also have a lot of mentors and supportive people in their lives that can help them understand what to expect, strategies that might be helpful for them going forward. Whereas sometimes people who have no idea, no other family members, I think the people for whom this is the most challenging are parents of affected children. And especially ones who don't have other family members who are affected, because they don't know what their child is going through.

They can't experience it firsthand and they want all the best for their child and nothing more than to make it better, to fix it so that their lives are going to be the best they can possibly be. So I think that's the group that finds this type of information the most challenging. I think some people bring a lot of, they've done a lot of homework, they bring... They've come to me with research papers and want to know my opinion. Other people are like, what does this mean? What do I expect tomorrow? What do I expect in five years? What do I expect in 20 years? And so, I think the conversation is uniquely tailored to each person. But that is absolutely a challenge. I always try to validate what people's experiences

have been. Sometimes it's a relief for people to say, "Oh my goodness, I've been struggling with this for a long, long time and I didn't really understand what it was and now I do."

And to let them know that there's a lot of work going on in the field and that this is really, in my opinion, the most important and impactful part of ophthalmology. This is the place where the most opportunity resides and therefore the most intelligent, hardworking, thoughtful people are inspired to be part of the solution. So, I spent a lot of time talking to them about how we can help them right now with low vision support and what I can do to help them adjust to the fact that they probably had this disease, they have had this disease their whole life. It's literally in their DNA and now they have a name to put with it. And the next steps are to try and adjust everything they can to make their life as easy as it can be by providing them with support, whether that be emotional, psychological, academic, career wise, or just helping them know that there's research going on to try and develop treatments and cures going forward. And that's where I often will connect them with the Foundation Finding Blindness.

Ben Shaberman:

And we appreciate that. And I think that kind of messaging, especially about the research, the trials, it can convey some hope.

Jacque Duncan:

There's always something we can do to help people. Absolutely. There's always research underway that's going to be helpful to them now or going forward. There's always something we can do to help them right now to adjust to the knowledge that they have this thing, and to try and help them make sure that they're going to be able to make the most of the vision that they have, and be safe in ways that they can continue to live their lives. So yes, I think there's always lots and lots of hope and opportunities to help people.

Ben Shaberman:

Right. Well thank you for being a doctor on the front lines that understands these IRDs so well and can help people move forward, because you're a rare commodity and you're kind of at the top of the space. I mean there aren't many clinicians out there who know as much as you do. But one thing I want to ask before we go, all this free time that you have, what do you do for fun?

Jacque Duncan:

Oh, I do lots of things for fun, lots of things. So, you know as well as I do, I like to exercise, I like to work out. I used to like to run, but my body doesn't really allow me to do that as much as it used to. So I've been doing a lot of Lagree Pilates lately and I ride a stationary bike every day. I exercise for at least 40 minutes to an hour. So that's fun. I have a dog that is my wonderful companion and best buddy, Peanut. So I take him for walks. I love Peanut. I'll have to introduce you to him sometime, if I haven't yet.

I have a wonderful husband named Keith and a daughter named Sydney. Sydney is currently a junior at Vassar, who's majoring in drama and pursuing her passion. I'm so proud of her. And so I have great connections with my family. I have wonderful friends that I work with, that do all kinds of fun things. I like to go see musical theater, I like to see other kinds of theater, I like to do... I love to see museums. I like all kinds of fun stuff. I love to travel. I've been part of several book clubs this year. Reading, I like discussing different kinds of literature with some of my colleagues. That's been fun too.

Ben Shaberman:

That's great. Well I'm glad to hear you have some of these other interests, because I know the work with the foundation and research keeps you very busy, the work with patients obviously. So Jacque, this has been a lot of fun. It's been awesome. It's good to learn a little bit about your history and perspectives on different things. And I just really appreciate you taking time out of your very busy day to be my podcast guest. So thank you.

Jacque Duncan:

It is my pleasure. And Ben, I want to thank you for all the times when I reach out to you for advice or thoughts or questions or information, you would never ever say no. You always turn it around in about two seconds and I'm grateful for all you do. Thank you for illuminating our community.

Ben Shaberman:

Well, you're very welcome. And it runs both ways, because I'm reaching out to you all the time, and I think that's kind of the way we work in this space, is that-

Jacque Duncan:

Yep.

Ben Shaberman:

We rely on each other for information. So-

Jacque Duncan:

Very true.

Ben Shaberman:

Thanks again. Listeners, thank you again for joining another episode of Eye On The Cure. Come back in a couple of weeks for the next episode. Jacque, thanks again for joining us.

Jacque Duncan:

Thank you, Ben.

Speaker 1:

This has been Eye on the Cure. To help us win the fight, please donate at [foundationfightingblindness.org](http://foundationfightingblindness.org).