ROUGH EDITED COPY

USHER SYNDROME CONFERENCE

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>> MARK DUNNING: We're going to get started in about five minutes. We're going to get started in about five minutes, but I want to let everyone know we're trying to make this as accessible as possible. So, if you don't need to see the interpreters and you're in a seat where you can easily see the interpreters, we're trying to make sure we have seats for everyone who needs to see the interpreters. And part of the reason we have these round tables here is so that you can move your chairs around however, you need. So feel free to -- you know, situate yourself in whatever way works best for you. We sort of expect chaos at these things. So -- we'll get started in about five minutes.

Testing.
>> MARK DUNNING: Hi, if we can ask everybody to get settled, we'll get started. You guys are a great crowd. Very well organized.
So as people get settled in here, I want to thank you all for coming. My name is Mark Dunning. I'm the chairman of the Usher Syndrome Coalition and this is our 8th annual Usher syndrome family conference. We try to make these conferences as accessible as possible, so we understand the needs of the interpreters and we understand that the interpreters are in charge. So they'll be taking breaks about every 15 minutes or so.
I'm looking to the people who are in charge. Yeah, they're going to switch every 15 minutes or so we'll be taking breaks in between while they switch. And they will be telling people like me to slow down if we're talking too fast. And if you have any issues seeing the interpreters, please, we'll be happy to arrange the room in any way that's necessary to make that happen.
I know that we tried to get assistive listening devices here and I understand that we've had some issues with them. It's one -- I can't apologize enough for that. We are very aware of how important that is and we thought we were getting one device and when we showed up today, it was a different device. So we apologize for that and again we'll do whatever we can to try and address those communication issues.
I want to talk about a couple of really important things and they're not necessarily in this order. But the first is if you have not found the bathrooms, they're straight down the hallway, almost to the very end on the left-hand side.
The food if you have not found the food yet, is just past the tables in the front lobby to the left and then you take a quick right and all the food is in there.
So those are two important things.
The third important thing is Robyn Stidd asked me to make sure that I said happy birthday, happy 20th birthday to Robyn. She's here with her sister. This is her second time attending. [Applause.]
And her parents were unable to make it but they made sure they got a message through to you. So happy birthday.
It's great to be back here in Seattle and to see such a wonderful crowd here today. This is -- you may not know this, but the Usher Syndrome Coalition had its genesis right here in Seattle. About nine years ago my daughter Bella was diagnosed with Usher syndrome. And at the time we had a very difficult time finding other people who had -- other families dealing with Usher syndrome.
In fact, we only found one. And they were out here in Seattle. It was the McKittricks, Lane and Todd. Lane and Todd McKittrick here in Seattle. So we packed up the family and flew out to meet the "other" Usher syndrome family in the country. Sitting at that table with them, the two families there, I kind of realized the real power in having an Usher syndrome community.
They saved me that day in many ways. They empowered me. Because they were just like me. They were terrified just like me. They were confused. And they wanted to do something. They just didn't know what. To try and address this. That gave me hope that I was not alone. That there were other people just like me out there. And that's what drives this community today. Look at this community. There's -- we have not just people with Usher here but we have interpreters and

SSPs and we have doctors and we have researchers and we have families. We have 31 kids here today. Siblings, parents, friends who have all come together to support us in this community. And we're bursting at the seams. We actually sold out this event this year. That's why we had to open up the doors to the rooms because we have other people here today. We have over 200 people in attendance. And as much as it broke my heart to have to turn people away from this event, it also makes me want to dance a jig across this table -- I could dance on the table but -- (chuckling) across the stage. Because from that community of two families sitting at a table, nine years ago, we now represent families in all 50 states and in 52 different countries around the world. And so this Usher syndrome community is growing and growing and growing.

But we have a lot more work to do.

Usher syndrome affects somewhere between 400,000 and a million people worldwide. The research community is in touch with less than 1% of those people. And that is a big problem for us. Because the -- at the Usher syndrome symposium that we held at Harvard medical school a few years ago, I asked researchers what was the most difficult challenge they faced in treating Usher syndrome. To a person they said the biggest barrier is that we were not in touch with enough Usher syndrome families. And it makes sense when you think about that.

Because Usher syndrome families are the source of funding for research.

Not just writing the checks, but companies like pharmaceutical companies that are the big investors in new medical research are looking for a market that they can deliver a product to. And so you need to be able to present a reachable market to those companies if they're going to invest.

So we've tried hard to make us reachable. And we've done that by developing a -- the Ush trust, which is a registry for people with Usher syndrome. And the idea is we want to get everyone who has Usher syndrome to enter their information, their contact information into that registry so that they can be reachable.

So that when we have treatments, we can reach them.

And because then we can demonstrate to these pharmaceutical companies that we can -- we do have a market for their products.

And families are not simply important to funding on that level. They're also the reason we have any sort of federal funding.

We go and spend a lot of time in Washington, D.C., these days. And I have pictures of us with Senator Elizabeth Warren, who is one of the leading democratic senators and I have pictures with Senator Roy Blunt from Missouri who is one of the leading Republican senators and they're both supporters of Usher syndrome research.

And with their help and the help of a number of other members of Congress, we have been able to get language into bipartisan support for language into appropriations bills to urge NIH to make Usher syndrome research a higher priority and to invest more in Usher syndrome research. And that happens because of you guys, because it's not just me going to visit Washington, D.C. This group, this Usher Syndrome Coalition has been called by people who have been in Washington, D.C., for a long time the best grassroots organization in Washington, D.C.

And that is an incredible compliment and it's because people who are deaf and blind and have difficulty traveling and community, they go to Washington, D.C., or send

emails or get in touch with their Congress people any way they can, and their message is incredibly compelling. So the reason that that language is in those bills is because of you. And because you're out there and pressing this stuff.
The Usher syndrome community isn't important just for funding. We're also the pool of candidates for clinical trials. Now, you don't have to participate in clinical trials. But there may be one that's out there that is appropriate for you.
That you want to get involved in. But to be able to identify candidates for clinical trials, you need a huge pool of people. Because not everybody wants to be involved in clinical trials. And those that do want to be involved in clinical trials may or may not actually be candidates for those clinical trials. So you quickly dwindle a large pool down to a few people who are appropriate for clinical trials. We need a huge pool. We're a rare disease, there is an orphan disease. 400,000 to a million people sounds like a lot of people but it's not when you start doing the math for clinical trials. So we need to be in touch with everyone for that. A lot of the treatments that are coming -- and there are a lot of treatments coming, you'll hear a lot about them today -- are genetically specific. So it's important that people with Usher syndrome be genetically tested because the treatments are not necessarily only specific to a type of Usher syndrome. In some cases they're specific to a specific mutation in a specific type of Usher syndrome.
So you need to be -- to have that genetic testing done. So we have partnered with the University of Iowa to start a program called unraveling Ush, which aims to ensure that every person with Usher syndrome gets genetic testing. And we even have a program where if you can't afford genetic testing and you're an appropriate candidate for it, we can get free genetic testing for people like that.
Not everyone knows about all of the stuff that we're doing and not everyone has heard of Usher syndrome. So raising awareness is a very important thing that we do. Krista will come up here in a little bit and talk about the Own the Equinox campaign. But today right now we have a group called Kidz B Kidz who are here and they're doing an art party with -- we have 30 kids in there doing an art party this morning. And the art is going to be used as part of that Own the Equinox campaign to try to help raise awareness. But they're also doing a -- they're also asking for people to be photographed. So everyone who is here with Usher syndrome today is invited to be photographed by Evan McGlynn, who is a well-known photographer who has done photography for the "New York Times" and for "National Geographic" and he's here taking portraits of people with Usher syndrome to help us to promote Usher syndrome. So, if you'd like to be involved in that, you can go get your picture taken near the food. And Evan do you want to come out here and wave so everyone can see who you are? This is Evan back here in the back. So, if you can track down Evan, he'd love to take your picture. If you look on your table, you'll see some post cards. If you flip them over, you'll get a sense of what we're trying to do with these. You'll see pictures of Connor and Dalton McKittrick on there and you can see the photos they're doing and the type of information that's going to be on these. So we hope you'll be involved in that as well.
If you have not already signed it and you're a parent, we have release forms for kids to be photographed. So please make sure you sign those if you'd like your child to be photographed. We'd love to get pictures of the kids. The neat thing about the

kids we have is we have kids from just about every age from 4 years old up to about 18 years old. So that would be a great photo essay of all the kids from 4 all the way up and we have adults of every age including Robin over here, who is 20. So we go on from 20 on upwards. So it would be great for a photo essay for that stuff to help us promote Usher syndrome. So we do a lot -- we make a great effort to try and make sure families don't feel like I did way back when I first learned about my child having Usher syndrome. We run a number of different programs to try to connect families. So in addition to this Usher syndrome family conference that we run, we also have the Ush blue book which is formerly known as the Usher syndrome family network where you can enter your information to be connected with other families who have Usher syndrome. And my daughter has met her best friend in the world, Clare, through these programs --through the Usher syndrome family conference and through the Ush blue book. Bella lives in Boston with me, and her best friend lives down in Tampa. So those are the types of connections we're able to make for families. We also have the Ush yellow book, which lists all the leading Usher syndrome experts and their contact information in there. So you can get in touch with all the leading Usher syndrome experts. And it's really important for us that we connect not only families to one another but also connect families to the researchers. So that they can establish a personal relationship with them. Many of them are here today and you'll meet them over the course of the day. And we also started a program called Ush talks which will be similar to TED talks, on our Web site. They'll be captioned videos with interpretation on all of the videos and all of the leading experts on Usher syndrome will be posting their work on there. So you'd be able to keep up to date on that stuff.

So we want you to feel connected. We want you to feel empowered. The point of the Usher Syndrome Coalition and this event is to not only give you hope but also to give power to this Usher syndrome community and you guys have a great power that you may not even realize.

And to talk a little bit more about that, I'm going to introduce our executive director, Krista Vasi.

And we're going to do an interpreter switch right now before Krista comes up.

>> KRISTA VASI: I want to first thank you all for being with us here today at our largest family conference yet. It's a real milestone for us. So it's an exciting day. And thank you, Mark. I'm Krista Vasi and I'm the executive director of the Usher Syndrome Coalition.

As Mark mentioned, I'm here to encourage you all to participate in our second annual awareness campaign.

You make a huge impact on people. I should know because I'm one of those people. I've served in this role for just over three years, but Usher syndrome and the Coalition became part of my life about 8 years ago when I first met a little girl named Bella who is standing right there. Weeks after starting my new job at the Decibels Foundation, the non-profit that Mark and Julia Dunning founded to help children with hearing loss, I met their kids. Bella and Jack. We met at a Walk for Hearing. I remember 9-year-old Bella as sweet and smiley and I remember six-year-old Jack trying to make me hold his empty soda can. Soon after that first

meeting, Bella's dad told me she named her favorite doll after me. No sweet gestures from Jack like that but I knew they'd become special people in my life. Wise beyond her years, Bella has taught me the value of focusing on the good stuff and letting the rest go. I've also been inspired by the dogged determination and fearlessness of people like Moira Shea. I've been awed by the tenacity of people like Mani Iyer, who used his skills as a programmer and his narrowing vision to build our registry character by character. Who just last week received his masters in poetry. I've been honored to be on the other end of the phone with parents seeking answers that will make the new diagnosis of their child a little less terrifying. I've listened while people with Usher syndrome, people who have been through their share of battles have offered their support to us.

The coalition community talks a lot about our Ush family. We use that word because the definition of family can transcend the traditional meaning of parents and children, blood relatives and genetics.

A family experiences life together. A family is connected through hopes and dreams, through hardship and laughter. What every family has in common though is that they're telling the world these people are important to me.

Eight years ago, Bella became my first Usher syndrome family member. And today I feel my family has grown exponentially. I wasn't born into it, but this family has changed me all the same. I've been part of all eight of these conferences we've held across the country, witnessing first hand as over 500 people have come together to learn, to share, and to grow.

I've observed the change that comes over someone when for the very first time they meet someone else with Usher syndrome. Someone who gets it. I felt the energy and excitement that comes from the world's leading experts meeting face-to-face with families they're working tirelessly to treat.

I've advocated with this community. I've sat down on Capitol Hill with Congressional representatives fighting with you all to make Usher syndrome research a higher priority.

I've seen how powerful you can be. How loud your voice has become. We hardly have to explain what Usher syndrome is on the Hill. They've heard from you, they're getting to know you and they know we're not going away. You are a force to be reckoned with.

Above all, my greatest joy in this job comes from connecting people. I get to bring people together. I get to do that every day.

And I know that it's a privilege to do work that I love and work that matters.

It's a privilege I don't take lightly.

This is what I meant to contribute. Not only to our Ush family but to the rest of the world who hasn't had the pleasure of meeting you yet. Last year I joined this community in our first global awareness campaign. We owned the equinox. Around the third Saturday of each September the fall equinox takes place here in the northern hemisphere.

This marks the start of days containing more darkness than light.

It can be a scary time for people with Usher syndrome. A time when their independence is incrementally shortened each day. A time when their surroundings disappear into the darkness of night. So what does it mean to own the equinox?

Last year for 26 days people from Australia to Alaska ran marathons, mile-a-thons, and media campaigns. On our first Usher Awareness Day, Cleveland's terminal tower even lit up blue and gold in honor of you. Hundreds of our Ush family members showed the world how they owned the equinox. This historic day was even entered into the Congressional record. We're going to own the equinox again this year starting on August 23rd and leading up to our second annual Usher awareness day on September 17th. The equinox is a powerful metaphor for the state of Usher syndrome Usher syndrome and the state of research. This community has the power today to stop their world from sliding into darkness.
This community also has the power to change people. You've changed me. You've enriched my life.
I know you can make that same impact on everyone else who hasn't heard of Usher syndrome yet.
So on August 23rd, I'll be joining my Ush family to help push off the darkness for their sons and daughters, for their partners, for themselves, and for their friends. And I hope you'll join me too. Thank you. [Applause.]

>> MARK DUNNING: Thank you, Krista. So I have a couple thank yous I would like to say but before I do that, Nancy, I see you but I don't see Jan. I know you don't like public speaking.
Would you like to talk about this or do you want me to try to track down Jan?
>> Where is she? She's back there.
>> We'll find her.
>> MARK DUNNING: Kay. I'll say thank yous first. So I'm going to have Jan come up here and talk about Kidz B Kidz and the photo campaign just a little bit so you can know how you can participate in that. I also want to say thank you of course to Lane and Todd McKittrick, you probably saw signs for the hopes event they helped to arrange everything. They were feet on the ground in Seattle. They had connections to get us all the interpreters and the room and this wonderful location that we have. So -- and they have been terrific supporters of the Usher syndrome from the start. So thank you, guys.
I also want to thank the Decibels Foundation. Cochlear, usher 1F collaborative, Ush 2020 foundation and two more people: Moira Shea and I'd also like to thank my parents, here from Boston, for their support. This is the first time my mother has ever gotten on a plane so you guys were important enough for her to fly out to Seattle to see you.
I also want to thank our Board of Directors who are around here. Whole bunch of different people who are on it. But particularly I want to thank our Vice Chair Moira Shea. If you haven't met here yet she's worth meeting and Finnigan her guide dog is here and I also want to say thank you in advance to our interpreters and to our CART for all of their work here today.
And the audio-visual staff, thanks, Ricky for all your help today. And so I see that Jan is here. You want to come up and say a little bit about the art party and what the kids are up to? And then we'll get started on our program.

>> Jan: Hi, everyone. I'm Jan and this is Nancy and together we're Kidz B Kidz. We're a non-profit based in Boston. Our entire mission of our non-profit and our life is to bring awareness to Usher syndrome, raise funding for the Ush trust registry and even eventually be part of finding a cure. What we do, Kidz B Kidz teaches empathy through art. And so what we do is we hold art parties where children and adults can draw and express their feelings. We're in the room the other room with 31 children now. I think half of them have Usher and half of them are siblings and I just got finished talking to them. And about -- and they said what do we draw? And I said draw what it feels like. What does it feel like to have Usher syndrome? What makes it hard? What are some of the things you can do really easily? What do you love about life? How does it feel as a sibling to see someone you love have challenges in their life?

And, man, they're just going for it. We're just starting a partnership with the Usher coalition and it's our goal to begin a campaign which will be Owning the Equinox to have portraits -- and as Mark said earlier, every single one of you with Usher syndrome now becomes the face of the campaign, faces and voices and stories. So what we're hoping is in the days leading up to the equinox we're going to hold art parties and if any of you with Usher syndrome are interested in helping us find someone in your community in which to hold an art party, we'll hold these art parties leading up to the equinox and we're going to start putting the portraits along with your stories, along with the artwork together and get this campaign out everywhere to raise awareness. I'll turn it over to Nancy now who is shy. But two of Nancy's four children have Usher syndrome.

>> Nancy: So we started Kidz B Kidz when my children were born with a hearing loss. I had never even heard of Usher syndrome. And probably about three years ago my older daughter who is now 22 started having trouble seeing at night. And she said, "Mom, I just -- my eyes -- I just can't adjust at night any more."

And so through testing and so forth, we found out that she in fact had something called Usher syndrome, which we had never heard of.

And we were told that it was probably Ush 2 and we did genetic testing and it has been confirmed. And then we were also told that we needed to test the rest of the family. Her younger brother who's 20 now, he also was born with a hearing loss. And so then we tested him and of course he also has Usher syndrome. We have two other children, one now is 18 and one is 15 who do not have Usher syndrome. We feel it's really important, even before we knew what Usher syndrome was, to teach children that it's so important to be empathetic, to learn how to put yourself in somebody else's shoes. And that's where Kidz B Kidz began from our hearts to teach -- and Jan and I are both artists and she is just like a sister to me. And we knew this was our background and this is our way that we could reach the world was through teaching empathy first. And then they could understand what Usher syndrome is. So that is our point. We're using art to each empathy and then we're going to bring this out into the world with these photographs and with the art and we're going to make a difference and we're going to try and get -- if there's 400,000 people in the world that have it, we're going to bring light to this to have everybody register and have the genetic test done and we're trying to raise funds to change the

registry that can handle this type of data and we're going to make a difference. And it's really, really important. So we're going to start small and we're starting today and Evan who is this amazing photographer is here to help us begin. And we've had some other PR people who are willing to help us. So let's just hope this whole thing just gets out there. So thank you. So we're going to do an interpreter switch. Okay. I'd like to invite our first speaker to come up and join us. His name is -- he's Dr. James Philips from the University of Washington and Seattle Children's Hospital. Am I saying this correctly? Or wherever you'd like to be from. Jim is one of my favorite presenters to have come to this thing, whenever we are here in the Northwest, we try to make sure we have Jim involved. He's going to talk about a combined cochlear and vestibular prosthesis to treat the balance issues in Usher syndrome. And it's always very interesting stuff. So Jim Philips.

>> JAMES PHILIPS: I'm going to start a timer so I don't run over.
I also have my laptop up here, it's not connected to anything, but I noticed that since the screen's over there, I would spend about half my time with my back to half the audience. So I have my laptop to help me get through this. I'd like to thank the organizers and also all of you for giving me an opportunity to talk to you today about our work, which is to develop sort of a modified cochlear implant, a combined cochlear and vestibular prosthesis for the treatment of Usher syndrome.
Okay.
Our group is comprised of a lot of people and I'm just the one who gets to talk to you today.
And I just wanted to at the outset a lot of people have a slide at the end that shows everybody that's working on this stuff. I just wanted to acknowledge everybody in our group that's contributed to the development of this technology.
I'd also like to acknowledge the support of a lot of agencies and organizations and companies and people who have funded our work to help us develop these technologies. Especially the national -- the NIDCD, the hearing institute at the NIH.
And finally, I have a disclaimer. And that is that some members of our research team, not all of us, some members of our research team, the University of Washington and a company call Cochlear limited have intellectual property associated with the technology I'm talking about today.
So I'd like to start by talking a little bit about what is the vestibular system.
You may not all know of this. The vestibular system includes the structures of the inner ear that contribute to balance and orientation.
This includes the nerves that relay that information to the brain from the inner ear. It includes neurons in the brain that make sense of that information by combining lots of different sources of information from different parts of the inner ear, from both ears, from the visual system importantly, it contributes a great deal to your sense of orientation. And finally, from muscles and joints.
What parts of the inner ear are parts of the vestibular system? It turns out I think you're all acutely aware of this -- whoops. I'm going to need help here. How do I make this thing shine a light? The top one? All right. Great. You're all aware of this part of the inner ear. It's the cochlea. And it's the part that hears. But it turns out that most of the inner ear doesn't hear. Most of the inner ear helps you to

maintain your balance and your orientation. It turns out that there are a bunch of different parts to that system. These parts up here actually help you to know when you're turning. So every time you turn or if you go through a series of turns and you're trying to figure out where you are now, that part of the inner ear is telling you that. They're call the semicircular canals and there are other parts of the inner ear located down here which tell you if you're tipping or if you're moving forward or backward or right or left or up and down.
And all of these work together to inform you of where you are in space. And where you are relative to objects around you. They help you to maintain your orientation. And then -- and these contain hair cells just like the cochlear of the inner ear and these hair cells can get sick and one of the things that can make them sick is Ush. And then there are also nerves that carry all of this information to the brain and the cell bodies for those nerves are located back here. Called the vestibular ganglia. Those cell bodies are immune to a lot of things that cause this system to fail. So that means that the nerves are still healthy, they just need to be informed by something that you're moving in space.
And that gives you an opportunity just like with a cochlear implant, to create a prosthesis that can inform the brain by bypassing the part of the inner ear that gets sick.
So it all starts with hair cells. Hair cells are the cells in your inner ear -- hair cells are the cells in the inner ear this is going to be tough that are responsible for turning motion information into signals that the brain can use and these hair cells can get sick and do get sick and their nearest neighbors to and also kind of cousins of the hair cells in the cochlear.
So a lot of things that make cochlear hair cells sick also make hair cells sick in the vestibular system.
The semicircular canals are actually the part of the inner ear that tells you if you're turning are actually fluid filled rings. When you turn your head, that fluid sloshes around and there are parts of those fluid filled rings that contain little fins or sails. And those are located right here.
And those things have the hair cells embedded in them. This is sort of an expanded picture of those. And you can see -- let's see if I got this right. Yeah. I can't even see it. Over here there's sort of a sail that's sticking up into that fluid space. And that sail billows and when it billows, the hair cells actually are activated or deactivated and that then signals nerves to tell you that you're moving in space. You're turning. The other end organ is called the otolith organs. They actually have hair cells, which are embedded in Jello. And that Jello has crystals on top of it and when you tip or when you move forward and back, the Jello bends. And when that mushes back and forth, the hairs of the hair cells bend and they tell you that you're tipping and you're moving forward or up and down or side to side.
So it's a cool system. But of course that system is totally dependent on the activity of the hair cells. When they get sick, the system gets sick as well. What happens when the vestibular system gets sick?
When both ears fail to send balance information to the brain, a lot of things happen. But one of the things that you might think would be the primary problem doesn't happen. If you lose one ear, you get vertigo, you get whirling vertigo, you have a

sensation of spinning, okay?
But, if you lose both ears, both ears stop working you don't get that. That's the one thing you don't get. What you do feel is significant disorientation. You have a swimmy headed feeling. You don't know where you stop and where the world begins. People talk about being in a fog when they have a vestibulopathy. You may experience fatigue or nausea. The reason for this is that your brain detects that there's a problem. Your inner ear is saying you're not moving but your vision, or your body, your movement of your body is telling you yeah, absolutely you are. Your brain says uh-oh, maybe you've been poisoned. Better throw up. Maybe you're sick, better lie down. It makes you nauseated and tired. Anxiety is a very big consequence vestibular loss. You say that makes sense, you feel anxious about not knowing how that's going to affect you. But it's more than that. It's the largest sensory inpulled too something called the limbic system and that's responsible for attaching emotional significance to events. So the vestibular system directly affects activities in structures like amygdala, which can directly influence anxiety. There's a structure in the brain called the hippocampus, which is responsible for working memory. What you think of is what you and I think of as consciousness. And it allows you to process the events of your life put them in a context that's meaningful to you and store them away. The largest sensory input to the hippocampus is from the vestibular system. So when the vestibular system doesn't work, the hippocampus doesn't work as well and people describe significant memory impairment and inability to focus their attention when they have vestibular disorders. So these are all significant contributors to the situation that people experience when they lose vestibular function. There's also Oscillopsia. The balance part of your brain doesn't just balance your body, it balances your eyes. When I turn my head back and forth I can see you because the vestibular system is working. If I hold my thumb out and shake my head back and forth, I can see it. It's crystal clear. If the vestibular doesn't work you can't do that. There's a steady cam system built into your brain that allows you to see the world when you move.
That system, if it fails, makes the world move just like a sort of an unsteady handheld camera, like when you try to film someone's meeting or you hand your camera to your kids and they take pictures of you. That system when it fails it makes it impossible for you to stabilize the world. So people experience motion of the world when they walk around in the world. It doesn't exist for people who don't have loss of vestibular function. And then finally, of course, there's postural and gait instability. You use your balance system to balance your body. All of these things are important. When I first came to the meeting a few years ago I was invited to speak. I had this impression and the impression was wrong. It was totally incorrect, really. And that is that because there's compensation for the loss of inner ear function, that kids especially young children who have no vestibular function from birth kids don't have significant balance problems. They have balance problems initially, but they can adapt their way out of it. They can compensate for that. So over time yes, we compensate for vestibular loss. That's especially true of children. How do we do that? Compensation is dependent on learning. We learn not to misinterpret cues from a non-vestibular learning system. We learn to use cues that are appropriate in a specific context to make sense of the world. We learn to

develop a strategy that adapts over a range of situations. And we do this by substituting information from other sensory systems. We say Okay. My inner ear is off line. That's really bad, but I can use vision, that's mainly what we do. We can used somatization, appropriate input from muscles and so on. So you substitute visual information and you get better, and kids do really well with that. You talk about the situation, which I admit I hadn't considered -- what about the situation where vision is progressively affected, where your vision fluctuates depending on the environmental situation you're in? Under those circumstances, compensation can't take place. Because compensation requires sensory disability, it's defeated by change or fluctuation. So this is really a significant problem and it's a significant problem for people who may have adapted early to their loss of vestibular or their absence of vestibular information. But now are confronted with a new challenge as other sensory systems that allow them to compensate are changing. We're going to change interpreters, now.

What about vestibular loss and Usher syndrome? It's characterized by varying degrees of congenital hearing loss, retinitis pigmentosa and also vestibular dysfunction. I'm not going to provide a comprehensive review of vestibular function in Usher's disease because I'm not the expert on that and there are lots of other people here who can tell you about that more than I can. I will tell you this. I know there are three clinical subtypes of Usher's and some of these are associated with loss of vestibular function. Usher's type 1 which accounts for a large number of cases of Usher's that as a classic vestibular phenotype, severe vestibular dysfunction, bilateral areflexia, that means no vestibular function within the first year of life. Now, there are either subtypes of usher's type 1. Some have classic phenotype and some have non-syndromic hearing loss but many, many people are affected with vestibular loss as well as with hearing loss with usher's.

Ushers's type 2, these patients have normal vestibular function. This is not a challenge for them. Their vestibular function is working just fine.

Usher's type 3. These patients have progressive vestibular loss. This also, by the way, defeats any strategy that the brain has to compensate for this loss. They have varying degrees of vestibular dysfunction. In summary, Usher syndrome can produce bilateral complete loss of vestibular function along with bilateral sensorineural hearing loss and hearing loss. It can produce bilateral sensorineural hearing loss and later progressive vision loss. It can produce partial vestibular loss, it can produce progressive vestibular loss. So, it is affected by these syndromes and it would be good to be able to address that along with addressing the two primary complaints that you're usually most focused on.

So the question today for the rest of this talk is can we replace the inner ear vestibular system with a gadget? Can we supplement this incredibly cool physiologic system with hair cells and these neat structures with a device that is sort of like a cochlear implant that electrically stimulates the end organ? And we believe the answer is yes and we believe that we've proven that. We actually even have a clinical trial that's ongoing that's demonstrating that these technologies work. Who would you treat with a vestibular prosthesis, when a device that treats vestibular loss? About one third of people in this room are going to have an acute transient loss of vestibular function. A lot of them with experience rolling vertigo. I have but it

gets better even if your ear doesn't recover. Those patients aren't patients who will be getting a device like this. But patients with bilateral acquired vestibular loss due to exposure to ototoxic drugs like certain antibiotics and cancer chemotherapy agents, yeah, they could use this. Patients with uncompensated unilateral loss of function, they can potentially benefit from this. Or patients with extreme intermittent vertigo sort of fluctuating vertigo, all of these patients could potentially benefit from this technology.
Now, you notice I didn't mention Usher's patients in this list. They weren't on our original list.
Why not? Why not treat Usher's patients with this device? It's obvious. They may experience a bilateral loss of balance function but it's combined with hearing loss. That often is not the case with people who have vestibular loss. This means that Usher's syndrome patients already have inner ear implants often. They're cochlear implants. It provides standard of care therapy for their loss of hearing. You can't put a vestibular implant in that ear because there's already a cochlear implant there.

So to effectively treat Usher syndrome vestibular loss you need a combined cochlear implant. One that can stimulate the hearing system and also stimulate the balance system.
So we set about to modify our device and make something that can do that. This is our original device. Shown up here. It has stimulating arrays that can activate the vestibular system and replace loss of vestibular function. This is our current device located down here.
These are some diagrams showing the evolution of our technology. And the thing about this current device is that down here at the bottom there's a cochlear implant array as well as vestibular implant arrays. So this device does both. It restores hearing because it's a regular cochlear implant and it also can restore vestibular function. That is the promise of this technology so you can treat both problems together. So what is this scheme? This is just an acute diagram from a scientific American mind article I wrote a couple years ago.
Sort idea is simple. You see something here that looks like kind of like a cochlear implant. That's because it basically is.
There's an implanted receiver stimulator. Just like a cochlear implant except that some of the stimulating arrays -- these down here, go into the vestibular system. The device has an external behind-the-ear processor which is basically the same as the behind-the-ear processor of a cochlear implant. It can process sound information and send that then to the stimulator, the implanted simulator, just like a cochlear implant. It also has, however, another thing about the same size as an Andes Thin Mint. The reason I use that as an analogy is because I happen to like them. It's small and it sits right next to the behind-the-ear implant. And it contains gyroscopes and a processor and it converts motion information into something that looks kind of like sound information to the cochlear implant processor.
So the cochlear implant processor is processing sound and it's also getting these other signals which are related to motion, which look kind of like sound, and processes those and frequencies well above the normal frequencies for hearing and sends those to the vestibular system instead of sending them to the cochlea. So the

device actually provides you with balance information and also with information to help you hear.
So what was our road to human trials? First, we designed a device that would help us to stimulate vestibular afferent fibers. Leveraged a highly developed existing technology. Cochlear implants. We modified the software and hardware. We did that along with cochlear limited. We created a minimally invasive electrotechnology. We create the appropriate -- we partnered with Cochlear Limited to make this go. We developed a simple surgical approach with the right target and those are those three semicircular canals. We constructed prototype devices but those identical to the very devices we were seeking clinical approval for so it was ultimately the same device we were going to go to the FDA and say this is what we want to put in patients to help make them better.
We then evaluated these devices in an animal model. We implanted Rhesus monkeys with these devices. Didn't hurt the monkeys. If the monkeys lost vestibular function, then the device would restore it. We evaluated the risk and efficacy long term so before we implanted these devices in people we knew they were safe and we news they would work at least in animals. We then sought FDA approval and obtained it for a test of these devices in human patients. We tested these devices first in Meniere's disease patients. And the reason for this is that Meniere's disease patients have a procedure, if they've had longstanding Meniere's, where the surgeon goes in and kills the ear to save the patient, to help the patient. So the FDA said Okay. If you're replacing a procedure that's destructive, then you can try this device. You can try to restore function and help these patients who would ordinarily get standard of care therapy that would destroy their ear. Otherwise, too risky. And we used this to prove that the device is safe and that it works.
We then modified our devices -- so this trial is ongoing. We modified the devices to create a combined cochlear and vestibular prostheses, which I've shown you. We tested this device in Rhesus monkeys. We're doing this right now. The new device is being tested. There are two monkeys here at my lab in University of Washington who are walking around with these devices. Then we modified our existing approval from the FDA to test patients with hearing and vestibular loss with the new combined implant and we're expecting to hear from the FDA in two weeks as to our request to do this. So we're hoping that by the fall we'll be starting ray new trial and that new trial can include patients who have Usher's syndrome.
But also it can include patients in general who have both hearing loss and vestibular loss and the plan then is to test this new device in human patients with combined hearing and vestibular loss.
So it's an idea. And I just want to show you it's an idea that I think has some merit. We put the device in -- there are very, very small arrays that we slide in next to the vestibular end organ so we can activate the vestibular nerve. When we turn the device on, the electrical stimulation produces eye movement just like the eye movements that stabilized your eye when you turned your head. It produces body sway. When we turn on the device and we provide a stimulus that says your head is moving, your body sways in the opposite direction. That suggests that we're informing your brain about the movement of your head. It produces a sensation of

motion. Effective vestibular stimulation does not produce nausea. That's a big concern. We could make people sick with this. It doesn't produce pain. It doesn't produce sound sensation when we activate the vestibular part of it. It does when we activate the hearing part. It doesn't produce facial nerve activation so your face doesn't twitch when we do this. That's another concern the FDA had.
So when you turn on this device, and you're not moving, your brain thinks that you're moving. If it's constantly active, your brain things you're moving, constantly turning in a specific direction and it generates eye movements and those eye movements indicate that your brain thinks you're moving. If you turn it on and you move a stimulus, your eye turns back and forth. That's basically what this is showing.
If you put in short pulses, little trains of stimuli, you produce eye movements. The eye drifts in one direction and jumps back. Drifts in one direction and jumps back. That's exactly what your eye does when you're turning and that happens the same whether it's in a monkey subject or in a hike who is implanted with the device.
Not only that but when we stimulate the canal that tells you that you're turning horizontally, when we increase the frequency of simulation or increasing the current level of stimulation, so this is the current level here, this is the speed of the eye. The eye moves faster so we can parametrically control the stimulation that's coming in. We can inform the brain in a way that makes sense. We can calibrate this so we know what's going on. Want to change? Go ahead. We're going to change interpreters now.
And in the four human subjects? The four patients who have been implanted so far, the device works in the semicircular canals that have been implanted. Not only that, but their eyes don't just move the way they ought to. But they perceive motion as they should. So when you stimulate the part of the inner ear that tells you you're turning that way, you feel like you are even if you're not. When patients are turning in a chair, they think the chair is turning. The chair can turn, they can't tell the difference. And finally, when people are stimulated with this device, we can cause them to sway in the appropriate suggestion suggesting that the device is providing information that their brain can use to maintain their balance. And if you turn the entire device on, to help them maintain balance and help them move their eyes, to help them feel their sense of where they are in the world, these patients claim that they have benefit.
So in conclusion, we know that a vestibular implant works. It may not -- we don't know that it's going to work forever and we're studying that to make sure that's true before this becomes a readily available clinical tool. We have tested this device in humans and in animals. We have existing approval to test these devices in patients. We built a combined cochlear and vestibular implant specifically to address the problems that are faced by patients with Usher's syndrome. We're currently testing the device in monkeys and we're working with the FDA to modify our existing human trial to test this new device in patients with combined hearing and vestibular loss. The most important thing I'm telling you is we're not the only people doing this. Just in this initial study with four patients and a lot of preliminary work in animals both by us and guys at Harvard and people at Johns Hopkins, the Johns Hopkins group now has a straight vestibular implant and they're starting

clinical trials with their device too. So these tools are on the horizon and may be available soon to benefit people who have these problems. [Applause.]

>> MARK DUNNING: Thank you, Dr. Philips, it has been fascinating to watch the eight years or so to see the progression with these implants from an idea all the way through to the point now where they are helping patients specifically. So it's very exciting to see that happening.

Our next speaker is Dr. Kathleen Sie who is going to speak about hearing and Usher syndrome and diagnosis and management of hearing loss and people about Usher syndrome. So just also wanted to point out that we will have a panel of all of the researchers so you'll have an opportunity to talk to all of them. But we are also having many breaks over the course of the day. And we encourage you to corner these guys and ask any questions you want. That's why they're here. So Dr. Sie.

>> Dr. Kathleen Sie: Good morning, I am thankful to the organizers, Chris that has been fabulous, Mark and the McKittricks of course who have been fabulous hosts. I want to congratulate people for coming and pulling together as a community. I think this type of activity is really what's going to help improve awareness and help us make progress in making opportunities available for people with Usher syndrome. So I'm going to talk about hearing loss and first, let's see, just to give you an overview of what I'd like to talk to you about today, first all talk about childhood hearing loss. I am a pediatric ear nose and throat doctor at Children's Hospital and I see a lot of kids. It's one of the most exciting areas of otolaryngology of what I do because of all the changes that have happened really in the past three to four decades and go over that a little bit. We'll talk about how we measure hearing and how that's changed. So let's see. And then talk about Usher syndrome more specifically in the second half of the talk.
So you've all seen this diagram and Jim alluded to this. We think about the outer ear. This is a diagram of the ear as if I took a slice through my ear canal. This is the outside and when we look in we see the eardrum. The eardrum is connected to one of the hearing bones and there are three little hearing bones, the smallest bones of the body. And when the eardrum moves, these little bones move and stimulate the cochlea. And so the inner ear has two parts. One part for hearing and one part -- and the semicircular canal is for balance. And they are connected as Jim talked about. So the work he's doing is incredibly exciting but this is just the input system. What happens is the nerve get stimulated and the brain sorts out what all that means. I think one of the exciting parts of working with kids with Usher syndrome is that cognitively they're normal, right? And so there's a lot of potential that we can unlock for kids as we help them with their sensory input.
So this diagram is kind of what we explained in clinic but it's just the surface and that's a cool thing about medicine is that we're learning so much. And so what we're going to do now is talk the cochlear which is the inner ear part and if we take a slice like this through that bony channel, we'll see the inside of the cochlea and the very complicated structure that is set up to allow us to sense sound. And so we have

these three compartments in the inner ear and this very specialized structure called the basilar membrane on which the hair cells that Jim was talking about live. And then we can get even deeper, this is a scan being electron microscope image of this structure here. So this is a cartoon and if we take this and really magnify this, this is actually a section from an animal that shows this very complicated system.
And then we -- if we take a shot like from an airplane, aerial view of this structure, we see hair cells and they're very, very organized. And so these are the out hair cells, three rose and a single row of inner hair cells. So we can get deeper and deeper and that's the interesting thing is we've learned more and more about how these structures work.
And so, if we take these hair cells then, these outer hair cells and inner hair cells, this is a cartoon then of these hair cells. So this is the outer hair cell and this is a cartoon of the inner hair cell. So the hair cells are at the top of these, the little purple area at the very top of the cell. But then there's the body of the cell that does all the work. Or does a lot of the metabolic work of these cells. What we've learned -- this is a cartoon. You don't need to see all the little details here but we're learning more and more about how these cells function at a molecular level and that is going to be really important in how we manage patients moving forward.
And then this is -- if we take then the blowup of the hair cell part of the cilia of these cells, then we know more and more about how those -- that part of the hair cell works and that's going to be really important in understanding the molecular differences between different types of hearing loss and even different types of Usher syndrome. And that will ultimately have an impact on what we can do for these conditions. So just to give you a history of hearing loss, you know, we talk about hearing loss and it seems like it might be a static thing. But in reality, our ability to test hearing has changed dramatically in the past 50 years.
And that's really started with the development of auditory brain -- our understanding of auditory brain stem responses to sound stimuli and then we went for several decades kind of refining that and putting that system to use. And then in the 1980s, pretty recently, we had systems for automated testing. And evoked auto acoustic emissions were described and that allowed us to diagnose hearing loss in kids before they were able to developmentally participate in normal audiograms. So that really serves -- so everything -- there are all these building blocks, right? So those things had to happen for us to be able to start newborn hearing screening which is totally changing the face of hearing loss for children.
And so in the 1999, there was federal legislation that legislated newborn hearing screening. And that system was really focused on hearing screening but what we've learned, what the community has learned is that screening doesn't do you any good unless you go on to diagnose the hearing loss and offer interventions for these kids. So now the term that we use is called EHDI, Early Hearing Loss Detection and Intervention.
So we have to make sure that we have the follow through for those kids after they've had their screening. So just to talk about the physiologic test briefly and show you what these responses look like. We divide these tests into what we call -- we divide test of hearing into physiologic tests, which means that we're just testing the system's response to sound and we don't need the kids to cooperate. Or we don't

need people to cooperate. These tests are also done in adults and so here is a baby at newborn and they can have their own hearing tested by putting a probe on their ear and electrodes on their head. We could commit -- we introduce a sound into the ear canal and then we measure the brainwaves in response to that. And on the far panel, far right panel is the output for evolved otoacoustic emissions and that's a fascinating technology or response where we put in sound to the ear and there's something called the cochlear many amplifier. So the inner ear makes additional sound initialing than what we put in. The evoked otoacoustic emissions is measuring the sound that the inner ear creates in response to sound stimuli.

And so those are the tests that we use for newborn hearing screening. But what we hang our hats on is behavioral testing. There are different types of behavioral testing and we use the different types of testing based on how developmentally advanced the kids are. So we have something called visual reinforcement audiometry for the very young kids. Conditioned play audiometry for kids who are a little older, toddler age where they want to play a game so they get to do something when they hear a sound, they get to put a block in a box. And then conventional audiometry, which is what adults do. The audiologist presents a sound and you raise your hand when you hear a sound. So those are the different types of behavioral hearing tests and that requires that the child be able to sit up in the booth and participate in that testing. But it turns out that, by and large, the physiologic testing is completely related to the behavioral responses. So we can use that information together to characterize a baby's hearing and predict how they'll respond to sound. So the way we present behavioral audiological testing is on an audiogram. And this is what we call the audiogram of familiar sounds. So as we come across in this direction the sounds is getting higher pitched and from left to right it's getting higher pitched and from 0-120, the sound is getting louder. So we can characterize how much hearing someone has and the audiologists have pretty strict definitions of what's normal hearing, mild hearing loss, moderate, severe and profound hearing losses.
So we use that description, that terminology to describe how much hearing a child or person has.
So once a person has hearing loss, when they come to clinic, we approach these kids in a very organized way and so we get a history, which means we talk today parents about what they notice about their child's hearing. We get a history about the pregnancy, and then the early neonatal period, the early infancy and the hearing screening. We also get a family history, which is very important and we do a physical examination looking for other things that might be associated with hearing loss. We work with the audiologists very carefully to understand what kind of hearing loss the kids have because kids with Usher syndrome have sensorineural hearing loss and not some of the other causes of hearing loss. We will get imaging studies but more and more, the imaging studies are coming later. We used to do the imaging studies fairly early. But now we're concerned about the effects of radiation on young children. We'll have an interpreter switch now.
So the way we approach evaluation of new diagnosis of hearing loss is really changing in part related to the technologies we have available but also our emerging

concerns about certain types of testing. And so we're often times reserving CT scans for later in the evaluation.
One of the things that we've become aware of is cytomegalovirus. And cytomegalovirus is the most common viral cause of hearing loss. It's called CMV. Cytomegalovirus.
Waiting for the interpreters. And that has replaced rubella as the most common cause of hearing loss in children. This is an exciting area because the kids who have CMV loss are at increased risk for progressive hearing loss and now there is an anti viral treatment to try to prevent the progression of that type of hearing loss. You can have CMV and genetic causes of hearing loss. And so, if we can identify this virus in babies with hearing loss, the infectious disease doctors will offer anti-viral treatment to at least delay the progression of that hearing loss. And then genetic testing has played and increased role in evaluation of kids with hearing loss. And so what I like to tell our residents and people who visit our hearing loss clinic is that hearing loss used to be diagnosis. Kids would come in with speech delay and we diagnose the hearing loss and we'd say your child has a hearing loss. That's a diagnosis. But now 98% of babies born in Washington State and in the country have their hearing screened when they're born before they leave the hospital. And so now hearing loss is a symptom and it's our job as professionals to help understand why they have the hearing loss. So the whole mindset has shifted another level, higher or lower or more detailed. So there are other tests we do once we do the first screening and we're not going to talk about these in detail but certainly an important thing that we consider is balanced testing so I work closely with Jim Philips to do this testing. He has some of the most sophisticated balance testing for children in the country and we're so happy to be able to collaborate. We do send kids for ophthalmology assessments, ERGs that that are helpful for diagnosing Usher syndrome and then other tests we do not really relevant to kids with Usher syndrome. That's how we approach the workup. I wanted to show you CT scans, some CAT scans because you hear about CAT scans and I just want you to kind of know what they look like. This is a CAT scan and CAT scans are layered pictures through the ear and they show us bone, air, and soft tissue. And so this is a normal CAT scan through the cochlea or the inner ear. Here. And this shows a different patient, the same level and it just shows that the inner ear is not normally formed. So instead of having two 1/2 turns, this patient has just one -- a little over one turn of the cochlear and that is called a Mondini malformation, this is a normal image through a different part of the inner ear through the semicircular canals. Sorry.
And in this patient you can see that there's an area here that's different than up here and it's -- that's an enlarged vestibular aqueduct. Those are common things we look for on CAT scans. Most of the time people with Usher syndrome have normally formed inner ear and semicircular canals on CAT scan. So we talked about this. The CMV testing is something we do routinely now for infants. And we won't go into a lot of detail. People have 3-day conferences on CMV hearing loss. And then genetic testing. That's changed dramatically even in the past five years. So we used to do what we call single mutation analysis. So we would start with connexin testing, get that test, and then if it's negative go on to request other specific tests.

But next gen sequencing allows us to test with a single test for 90+ different mutations and so that is revolutionizing how we can -- how well we can make a diagnosis of what causes hearing loss.
As far as management of kids with hearing loss, it's all about exposure to language. Right? We want kids to be exposed to language. If it's sign language or spoken language, we need these kids to get consistent, accessible exposure. And that's often through early interprograms. 90% of children with hearing loss are born to parents with normal hearing. Their parents need to change how they make language accessible. Amplification can be very important for kids to access spoken language. If families -- some families choose not to use spoken language, those kids don't need amplification. They just need consistent exposure to language. But amplification can include hearing aids and cochlear implants and other assistive listening devices and then school accommodations. And so I put school accommodations on the list because families really need to start to become advocates for their kids and the kids become advocates for themselves, which is the really cool thing about watching these kids over time over the years as they grow and be able to -- and become self-advocates. Now we're going move on to the Usher syndrome part of the talk and this is the classic table we learn about in medical school. Talks about the incidence of prelingual deafness in children about 1 in a thousand probably a little bit more than that. But this number is really probably refers to kids with severe to profound hearing loss. The number of kids affected with any degree of hearing loss is probably four or five times that number. And then we think idiopathic which means we don't know the cause. Non-jet incompetent and thin genetic causes account for at least 50% of hearing loss and then we divide the genetic causes into non-syndromic and syndromic and so the syndromic kids are really that group includes the Usher syndrome.
So childhood hearing loss, 1 to 3 in a thousand newborns have severe to profound hearing loss. More will have lesser degrees of hearing loss. And, again, most of these kids are born to families with formal hearing. So what that means is that the language of the home is typically a spoken language. As far as Usher syndrome goes, the numbers are about 1 in 25,000 in the United States and accounts for 3 to 6% of children with hearing loss. And -- but half of people who have dual sensory impairment have Usher syndrome. These numbers may not be terribly accurate and people say that some of the numbers are 3-6% of children with hearing loss. Those numbers are derived from deaf and hard of hearing programs, schools for the deaf and so that number probably represents the kids with more severe hearing loss which means usher type 1. If you include the usher type 2 and 3, for people who may have milder degrees of hearing loss and may be in mainstream settings, or may develop hearing loss later in life, those people aren't necessarily counted in those numbers Usher syndrome is probably more common than we usually think. It's important for us as physicians because we need to keep track of these patients, right? Just because usher type 1 often times gets a lot of the attention because those kids are born with profound hearing loss. Really, the kids who have progressive hearing loss later in life or adults, they may be -- they may be people that we should be thinking about making the diagnosis of Usher syndrome.
So the family history is very important. The congenital bilateral profound hearing

loss and bilateral areflexia, those are the group where we think of Usher's syndrome for diagnosis.
But I will say that not all kids with bilateral profound hearing loss and vestibular areflexia have Usher syndrome. That's not enough to make the diagnosis, to confirm the diagnosis. But a family history of blindness or dual sensory impairment can really help support the diagnosis of Usher syndrome. The finding of retinitis pigmentosa can be very helpful. Those are the pigment changes in the retina. But there are also -- there's a differential diagnosis of things that can cause retinitis pigmentosa. Those include things like paroxysomal disorders, edema locos dystrophy, Refsom disease, those are conditions that can cause the same two things but those kids are people that usually have developmental delays. So the kids with Usher syndrome are otherwise typically developing with the exception of their gross motor milestones. So we take all that information into consideration when we're trying to actually confirm the diagnosis of Usher syndrome.
And so the genetic testing is available -- there are actually several different tests, we tend to use the testing at University of Iowa. The testing is constantly changing so you have to keep up with what genes are included on this test and the great thing about it is unlike most things in medicine, the cost of the testing is continually going down. So nowadays you can get the otoscope testing for about $1,500, which is very comprehensive.
The Usher syndrome is divided into three types and type I, type II and type III and they are distinguished by the on set of the hearing loss and the degree of hearing loss. The balance involvement, vision issues and then they're associated with the different genetic causes, that is going to help us provide molecular therapies in the future. But interestingly all these genes, mutations in all these genes have also been associated with non-syndromic hearing loss. So you really have to have a team of professionals to put the pieces of the puzzle together for you because just because you have one of these mutations doesn't mean you have Usher syndrome. But, if you have the hearing loss retinitis, pigmentosa and mutation you can be certain that you have that diagnosis. So again when we diagnose Usher syndrome, we really, again, emphasize very similar things, right? Exposure to language, early intervention, support for vision impairment. That is really important for families. And starting to work with those kids before they have the on set of their visual impairment is important. We're ready for a switch. The other thing that's so important for families is psychosocial support and, as Mark alluded to, it's so important for families and children to have peers and people to help them through the process.
So cochlear implementation you guys know what cochlear implants are, they are FDA approved for children as young as 12 months of age. Absence of medical contraindications. There are more and more implanting kids at younger ages with lesser degrees of hearing loss. And we've -- as a community cochlear implant community really working on ways to preserve any residual hearing with cochlear implant surgery. So these are just audiograms of the degree of hearing loss, profound hearing loss, what they might get with hearing aids and what cochlear implants can do as far as access to sound.
So basically, for hearing loss, management of hearing loss, we don't yet have

genetic therapies as ophthalmologists have for people with hearing loss. But understanding mechanisms for hearing loss is going to pave the way. On the horizon last month in nature chemical biopsy a group from Case Western published and article about identifying a molecule that would stabilize the hearing in mice with usher type 3 and that's based on knowing the molecule, the Clarin1 mutation is associated with usher 3 so they've developed a molecule that may help prevent progression of the vision and the hearing loss in these mice. So I think there are exciting things on the horizon.
So we want to work together with our hearing health team to diagnosis Usher syndrome. It gets complicated but we do work as a team. We wanted to really diagnose Usher syndrome early so we can implement early intervention for these kids and treatment options will improve with our understanding of the molecular mechanisms. Thank you.
[Applause.]

>> MARK DUNNING: Thank you, Kathy. So I think just about everything in this room who dealt with Usher syndrome, one of the great concerns we all have is around the vision loss and that tends to be the focus. But the diagnosis of Usher syndrome starts with people like Kathy. So it's very important that we have them and it's terrific to have her as part of this Usher syndrome community because that's where a lot of the understanding of the -- of the certain diagnosis starts right there with the otolaryngologist.
So this morning we spent some time talking about the vestibular function and the hearing loss function. Later on today we'll talk a lot about the vision loss part of it. Want to make sure everybody has a full understanding of the -- of what's going on with all the research on the Usher syndrome side of things.
So we are going to take a break right now. We're running a little bit behind schedule, which is pretty typical for us.
So we're going to take about a 20 minute break if that's okay for everyone and we'll try to get back at 10:20. In the room where there was food previously there is food again.
There's chips and popcorn and there's drinks in there if you want to grab anything. And of course remember the bathrooms are down the hall. And please use this as an opportunity to connect with Kathy and Jim and with each other. This is a great chance to meet people. Thanks. Talk to you in 20 minutes.
(A break was taken.)

>> MARK DUNNING: Hello, everyone. We're going to get -- if I could ask people to start trying to head back toward their seats, we're going to get started in about five minutes.
So, if I could ask everyone to please take their seats, we're going to get started again. Can I ask for a wave from the interpreters to tell me they're all set? I'm seeing no waving so I'm assuming they're not ready.
You're good? Okay. Thank you, everybody.
We're going to get started again. And it's great to see so many people networking. And enjoying themselves.

But to try and stay on schedule, we're going to get going. And I will go over and deal with that rowdy crew over on the right in just a minute.
I'd like to introduce our next speaker who is one of my best friends in the Usher syndrome worlds. Dr. Jennifer Philips who is going to come up here and talk about the genetics of Usher syndrome and her favorite topic in the world zebrafish.
So Jen.

>> JENNIFER PHILLIPS: Thank you, Mark and hello, everyone. I'm honored to be talking here today and I this is I believe my 4th Usher syndrome family conference I've attended and it's fantastic to see the community growing and becoming so much more vibrant at every iteration. So let's keep it going.
I am a scientist. I do research at the University of Oregon. And I'm not going to give you a science talk today. I give a lot of science talks to other scientists and clinicians but this talk is not for them. This talk is for the families. So I'm going to put things in very general terms. I've tried to pull out the jargon as much as possible. Sometimes it's unavoidable. But I really hope it will be accessible to you and if it isn't, then I certainly want to hear afterward any questions you may have. Also if there are people who want to take a deeper dive into the technical things, I'm happy to talk to you at the breaks or the Q&A about that as well.
So in my laboratory at the University of Oregon we one on Usher syndrome models using zebrafish for about the past dozen years or so and we are particularly working on understanding the molecular basis of Usher syndrome for starters. In terms of how that applies to humans, we're trying very hard to work toward a cure for the vision loss. I'm going to tell you today about some of the projects we've begun with that. So when I was trying to think about how to broadly summarize our goals for non-scientific audience, I came up with in a nutshell our goal is to giver you the stars.

And I mean that in a literal sense, because I know that night vision loss has a lot of consequences to daily living but also nightly living. I know that a lot of you have not seen the stars in a while. And I wanted -- I also mean that in a metaphorical sense. This is a lofty goal. It's challenging and takes a lot of effort and science and hard work. But it's reachable. So our method of doing that and achieving that lofty goal is to study retinal degeneration that we have and trying to figure out exactly what's going wrong and how we can fix it. I'm referral several times already to animal models. Let's advance this. Oops.
So animal models, why do we need them? That's not clear to a lot of people. Basically, a disease model is a necessary prerequisite to developing treatments that are going to be used in humans. You need to be able to show safety above all. You to be able to show that actually works. (Brief break in captioning)

Okay. So as regarding animal models, a lot of different ones have pros and cons, there's a bit of a -- I have a pointer. A sort of spectrum of add man models up on the screen here and you know, on the similar to humans all the way down to very different from humans we have a subset of all the animal models that are in use right now.

You know, obviously the advantage to being more similar to humans is that you can make more direct applications so what happens in a non-human subject. However, these models tend to be quite expensive, they have a very slow generation and growth time. They don't make very many babies and that makes genetics challenging. That makes sample sizes harder to come by when you're trying to do statistics. They're genetically fairly variable and that sometimes makes studying genetic disease harder. And there's a lot of ethical controversy that goes along with things especially furry things. When you get back to the other end of the spectrum these animals are very inexpensive to maintain and study the super fast generation time compared to anything approaching this, many offspring very well understood genetics and nobody really worries too much about how many worms are sacrificed in the name of understanding genetics.

So you know, there's a balance to be found and if you notice, not by accident, I have a zebrafish right in the middle of this scale because we believe that zebrafish give us kind of the best of both ends of the spectrum. For the rest of the talk I'll talk about inner fish as a model for Usher syndrome and I didn't make that up. This is a wonderful book by sorry, I keep advancing, by Neil Shubin if you ever wondered why you're so similar to fish this book will tell you that and more. So I highly recommend that. In a basic sense we have, you know, zebrafish are closely related to us that they pretty much have all the same parts. Brains, hearts, guts, importantly for Usher syndrome eyes and ears that function very much like human eyes and ears do. They're human-like enough that we can get good experimental read outs from those tissues and then they make loads and loads of offspring. We have very large sample sizes and we can get information is a single experiment with so many offspring that we can look at. Too far. Okay. Just to briefly touch on the relationship between genetics and disease, this is something that we understand better by virtue of studying animal models. Genes create the template for life. They can read the genetic code like an instruction manual and establish proteins based on the information that's on there. So, if you ever put together a horrifically complicated Ikea cabinet, there's a big instruction boom but, if you were to summarize that, you could say something like assemble items 1-2000 and then you're done. And in the cellular protein sense of it, if you follow those instructions, you get a nice long protein with lots of different parts that does an important thing. However, if the DNA code has changed and this is what we call mutation, then the message in the manual changes and the instructions can be wrong. So instead of making out that full following the instructions all the way to the end you get erroneous instruction like assemble items 1 through 244. Instead of a long protein you get a much shorter and clearly much less operable protein and this is the result of the genetic problem. But that is the basis of disease when you have these non-functional proteins because the code is bad. So for studying Usher's in zebrafish, screen is frozen. Trying to follow it so I can see it and not crick my neck and now I've gone too far. We're building -- we've studied Usher syndrome for about 12 years and zebrafish have all the usher genes that humans have plus a few extra in fact. And we have now or at one time in the past 12 years had active projects on all the Usher syndrome genes that we know about currently.

We have quite a few of them still ongoing today but because of time I'm going to talk

about just two of our projects in brief. One of them is about Ush 1F. You'll see this is one example where zebrafish have two genes as opposed to the single one that humans have. And also USH2A I'm told this first family conference where Ush 1F has been discussed and I have to tell you how incredibly privileged I am to be the one to tell you about that. Because it's an exciting day. So the other cooler Dr. Philips and also Dr. Sie did a really nice job of showing you what a hair cell looks like. I'm going to talk a little bit about those and I have a very rudimentary cartoon to show you of about what a hair cell looks like and the parts that I'm going to be talking about briefly. So here's the hair cell. It has these projections that are the things that contact the fluid matrix or the gelatinous matrix that Dr. Philips talked about and respond to movement or to soundwaves moving through that fluid. At the tips if you can see of those individual projections there are these little links that combine and those links plus the things that are inside those projections anchoring them are all made of different you proteins. In the blown up thing on the slide here you can see this one here is the USH1F protein. This other one is the USH1D protein and they're reaching across this gap. And holding on to each other what we actually call a molecular handshake. So that's creating a physical link between those two projections and that's important to the function of those cells as well as to the very shape of those cells. We also see similar types of cooperation in this other cell type I'm going to talk about, the photo receptor that's found in the retina. There are similar distributions of various usher proteins that work together and have those molecular handshakes and are partners in making normal vision and hearing work. When you have mutations in usher genes that scripts these cells because protein partners aren't there to shake hands or are not shaped in the proper way to make a good connection.

In terms of USH1F, a common mutation in many patients that have this, which we call R245x creates an error in that instruction manual that results in a short protein that doesn't function properly. So instead of again the long multi domain version, you get a very short non-functional type of protein. And our lab question that we're working on with zebrafish is what can we do to compensate for situations where you have that guy. In order to answer those questions we made zebrafish models that make the same type of wrong protein as what is to Deuced in R245x Ush1F patients and we made two models in parallel affecting one of the genes in each of the lines of zebrafish so we now have two models we have double the opportunity to understand what's going on.

And our study has shown in fact that in zine both of the zines are really important for hearing and vision so it just gives us another to be able to understand what's going wrong and figure out how to fix it.

We consider that a feature, not a bug.

Okay. So what does Usher syndrome 1F look like in a zebrafish? I'm showing you here my little cartoon of the hair cell next to some actual zebrafish hair cells that are highly magnified and these projections in my cartoon are colored green in the slide that you see here. Because these are so very tiny, you can't actually see the individual projections and because the links at the tips of these guys are working really nicely, you can't -- you also can't see the individual ones, it just looks like a nice tight cone of green or a little Christmas tree or something like that. And so in

the normal circumstance, the zebrafish that has hair cell parts that look like this has excellent hearing and good normal balance.
However, in the model that we made of the aging and zebrafish, we have those structures are highly disturbed. They're not held together very well because they're -- the protein is affected and is not able to make that molecular handshake so you see little whispy parts that are much thinner, they're not functioning well because of that structure. Knees fish have severe hearing loss and very poor balance.
When we make a similar mutation in the other zebrafish gene, it doesn't look exactly the same. But it's still impaired and this one, although it still has some hearing relative to this one, it's not normal and it also has much poorer balance than a normal zebrafish.
We're going to do an interpreter switch. So when we look in the eyes of these models that we have of USH1F -- I'm showing you the cartoon of my photo receptor cell next to zebrafish photo receptors again highly magnified and labeled with this green marker and just to notice how they're nice and long, they're nicely organized all in a row, and this shape and organization gives you normal visual function and it's very unusual to see cells in a group like that that are unhealthy or dying. When we look in the USH1F zebrafish mutants, we see a different story and it's interesting because with respect to the hearing and balance problems, the aging was far worse than the A gene problems and in the eye that's opposite. So you can see here we have slight problems in the A model. The cells don't look exactly as normal as they do over here, we don't see very much cell degeneration. However, it's very impaired in the v mute and here where you have shorter disorganized cells and we do see a high level of very abnormal level of cell degeneration in that so this is modeling the visual defects again in a very young age just as we see in USH1F patients.
So we now we have great models to test things on. What's the next thing that we can do to move toward a therapy? We have a couple different approaches that were taking to try to work around that misprint in the instruction manual that this particular group of patients has. So the first thing that we have attempted is a process called Exxon skipping and that's if we take the manual and just sort of rip a couple pages out, that contain that misprint, maybe the cell can just sort of skip over that part and continue the rest of the assembly instructions. So the part that is in the red box here is what we would be looking to delete so then you would have, instead of assemble items 1-2000, you'd have assemble items 1-2000, but clip out items 241 to 290 or so. So then the big question is that protein that's slightly shorter slightly modified missing a few parts going to be better than nothing? Is that going to be better than the very short protein that the R245x patients already make?
On our other approach is to use another drug therapy that is coming online in other systems and with other disease models, shall called nonsense read through. With respect to my instruction manual analogy, can you convince the cell to ignore the stock message that comes too early and just turn the page and just keep going and building the rest of it? So we have the models to be able to test these things now. And we have a number of different tools at that time our disposal. So we have these genetic mutations that I've described to you that cause the early termination of that protein, of early discontinuation of the instructions. With those models we can

ask what's the role of this protein in the eyes and ears? And what goes wrong when you have this R245X mutation or other mutations in usher 1F we have models that skip that region that delete the part that contains the error message at R245X but then the surrounding information is intact.
So, if then we're asking is that skipped posser important? Can we do without it? Can that protein that's missing that still make a molecular handshake?
And then this is very important to know before we proceed with trying that out in people.
And then finally we have a third model of this disease that basically has transplanted a small portion of the human DNA sequence that contains that R245X region into the zebrafish gene and this is what's necessary to test that second therapy which is the read-through drug because we want to have the exact human sequence to test the drug on. We want to know if it's going to work on the human patients. So we need to have human DNA at our disposal to test that in a living system like the zebrafish. So being able to ask that question in zebrafish models saves a lot of money and time and preserves resources for being able to go to the point where we're ready for clinical trial with just our best shot, our moon shot, the one that's most likely to succeed. We can work a lot of that out in the animal model before we get to that point. So that's a valuable contributor.
I'm going to switch gears and talks about USH2A, the most common form of Usher syndrome. Part of the reason is this is an extremely large gene and you might think because it's as common as it is, it would be the one that most people work on and the one that the vast -- you know part of the usher research community is trying to solve. But because of its large size it's actually really challenging to work on. So our question in the lab is how do we overcome those difficulties? How can we really still do some meaningful analysis on such a large gene? And look at different mutations that cause Usher syndrome and different new mutation that's come up because we're not really sure they cause Usher syndrome in that USH2A gene.
So another part of that challenge is that because it's so large and has, as you can see, just depicted in the stick figure many different parts, we don't actually know what a lot of those parts do at the molecular level. At the very end there's a little blob down there we know that's really important as far as interacting with other Usher proteins. Remember I told you they all kind of come together and do that molecular hand jive, and that part is important for making those connections. This part down here is important for interacting with the membranes of the cells that this protein is expressed in. But beyond that we're not sure if there is any particular importance in this part of the protein other than the fact that it gives the protein a certain size and shape.
You know, that in and of itself is certainly important. But in terms of other unique interactive capacity, that's kind of a black box. So another great reason to study it in an animal model.
Okay. So as I mentioned earlier in the talk, many of the Usher proteins reside in a particular part of the photoreceptor and physically interact with each other. Here I'm showing you my little cartoon. I don't know if the light bright be too bright for you to see much on that slide. But you can see I have a little red -- on the cartoon there's a little red blob and green stalk and on the tissue there's a zebrafish retina. You can

see the part of the photoreceptor cell. The little red blob is the USH2A that's in that exact zebrafish location. The handshakes, my little cartoon here, this part is the membrane the long red sticks here are the USH2A protein and the little yellow circles are another protein it's interacting with. So this, again, is the joining teamwork kind of operation that the proteins do there.
So now that we have a number of models of USH2A in zebrafish, we can understand what those phenotypes look like in those animals. What we see again is very consistent to what we see in human USH2A patients and that the hearing deficit, the hair cells of the ear are not as perturbed in these animals as they are in the type 1, the Usher type 1 fish models that we have. We also see that when we raise fish in a normal daylight levels, they have retinal degeneration, it looks like RP. But the USH2A patients also suffer. When we raise them in low light condition which is the normal condition for zebrafish housing facility, they have very light levels in there they don't show retinal degeneration so we're seeing a difference in light exposure in these animals. The third thing we can see from studying these models is that the other Usher type 2 proteins, not USH2A but other ones on the type 2 list are not localizing properly. The little yellow circles aren't getting to the right spot when you take away the USH2A protein. That's could be further that molecular interactions are important from both directions. So what can these models do for USH2A patients is a question that's probably on a lot of your minds. Now that we know what it looks like we have a lot of symptoms to test future therapies on. We can test that same read-through drug that I spoke about with the USHF1 project on USH2A models if they have the right type of mutation and for different types of mutations that drug doesn't work for all types of mutations but for different types we can test other therapies, there are other drugs, other interventions we can start developing because we have such good read out of what the problems are. We'll be able to do really robust testing of are there things that improve them or make them go away? Which is our hope. And furthermore, given the really strong information that we have from seeing what happens to retinal cells in different light levels, we have an experiment planned where we're going to use light filters to filter out different wavelengths of light and see is it just a quantity of light in totality? Or are there particular wavelengths, parts of the light spectrum that are more or less damaging to those photo receptor cells and I hope that will have some clinical importance going forward as well.
So in general what can zebrafish models of any type do for the community? If I didn't talk about your gene today, I did mention we have a lot of other ones that I just didn't have time to go into today. In general it's very important to be able to get more information about how the proteins work in a normal situation and what goes wrong when the instruction manual has misprints in it. It's also important to be able to have a system with good read out of all these symptoms that we have developed and all the different tests that we can now do on the fish models when new variants come along. When you have genotype information that comes from a patient and it's a must mutation that no one has ever seen before. Sometimes when you're screening through a lot of DNA, there are lots of differences that may or may not be problem causing. It's difficult to tell sometimes just from looking at the sequence on a piece of paper on a computer screen. Sometimes you have to recreate it in an

animal model and see if it is a disease causing kind or not. That's what we can do now with fish models and of course being able to have a model that has proven symptoms and testable features. We now have lots of different capacity for testing new treatments, some of which probably haven't been invented yet but people are working on it somewhere in the world. I'm going to stop there and keep within my time limit. I want to say thank you to the organizers for inviting me to speak to you today. I'm very grateful to our hosts and all the efforts that they do for the community. My lab at the University of Oregon, Monty Westerfield and technical staff that helps me with the fish and molecular aspect of this are indispensable and I owe them a great debt of thanks as well. I also want to mention that much of the work that I talked to you about today was funded by the Usher 1F collaborative. We also have very generous contributions from the Megan foundation and Vision for a Cure and we are supported by the National Institutes of Health. So thank you. [Applause.]

>> MARK DUNNING: We're going to do an interpreter switch.
So thank you Jen. Not many of you expected your life to be so tied to zebrafish going forward.
But this is a good point -- good place to point out that you can -- I mentioned earlier that we're trying to identify every individual in the world who has Usher syndrome and get them into the -- to register with the Ush trust. Jen mentioned about the number of different mutations and the differences in those mutations and how they can impact how the disease progresses. So we're trying to make sure that we can get everyone into the Ush trust and get everyone genetically tested so we better understand what those mutations are that we should be developing in animal models so we can then develop treatments for those. Nancy O'Donnell, our registry director is here today. And she's in the lobby. So any time over the course of the day if you're not in the Ush trust and you'd like to join, Nancy can help you. She's in the lobby. No she's not. She's over to my right. So don't listen to me but do listen to me. She's over there jumping up and down. Very excited for you to come over and meet her.
Also over there as you can see there's a number of vendor tables so you can go over to the vendor tables and visit with them as well during the breaks. Please do so.
And I did see a number of people go and get their pictures taken so you can still get your pictures taken on the various breaks as well. So please take the opportunity to do that.
We're going to talk a little bit more about the genetics of Usher's syndrome coming up with one of our board members. Karmen Trzupek. So she's going to come up and talk about unraveling Usher syndrome which I just mentioned a bit earlier and the role of genetic testing in Usher syndrome. And Karmen was really instrumental in putting together the Unraveling Ush program that we have with the University of Iowa. Karmen, would you like to come up and speak? There you are. Good, I was worried you weren't here.

>> KARMEN TRZUPEK: I'm a lot shorter than Mark.
So thank you both to Mark and Krista for inviting me. And allowing me to be part of not only today. But, as Krista eloquently put it, being part of this broader community and part of the broader family that's become part of my extended family over time. I think I'm going to bring it down a little bit from Jen Philips who is so brilliant and make this a little easier.
So for those of you who were a tiny bit overwhelmed by some of the brilliance this morning, I'm going to make this easier. It's going to come down just a little bit for those of you who know a lot about genetics, I'm sorry, take a nap for five minutes and hopefully I'll bring something of interest to you. I'm going to do the same as Jim did and try to use this one instead of craning my neck but that means, Jim, I have to do both. Advance it here and here, yes? Okay. So why genetic testing? I'm going to talk about genetic testing. And I thought it's -- I thought it would be worthwhile talking about why. Why do we feel that genetic testing is so important. One reason genetic testing is so important for this disease is to clarify an uncertain diagnosis. I spent time talking yesterday with a couple of fellow board members who have children with Usher syndrome where it took a very, very long time to get an accurate diagnosis.
And I expect that happened to many of you or your children here. That it takes a very long time. Sometimes to get an accurate diagnosis and we want to change that.
So genetic testing is a big component of that and we're trying to do genetic testing earlier in the disease course to get people accurate diagnoses early.
We can sometimes predict some degree of disease progression.
Certainly there are certain genes that are associated with Usher syndrome type 1 versus type 2 versus type 3. There's also emerging data on some modifiers that can influence the progression of disease. So sometimes we can use genetic testing to really help prepare families. Increasingly people, families are getting interested in genetic testing to determine whether they would qualify for a clinical trial. As Mark mentioned that's important not just for what's available today but really in preparing the entire community, the entire Usher family for up coming clinical trials to really prepare a group of individuals who are ready and waiting in the wings for the next trials.
Genetic testing can enable testing of other family members whether those family members might also be affected or whether they're trying to determine whether or not they're carriers. And importantly, aid in the research and I'll talk about that at at very end how that aids in the research. I'm going to take a step back so everybody starts on the same level so we all know what genetic testing is and what we're looking for. So our genes, we have about 22,000 genes. We all have the exact same number of genes and number with the exception of the genes on the X and Y chromosome, which make us fundamentally male or female. We're not talking about those. Those are not involved in the Usher syndrome. When we talk about Usher syndrome genes, it is the same number, same type of genes. When we do genetic testing we're not looking for a gene that causes Usher syndrome. Right? All of the genes involved in Usher syndrome are genes that we all have and they in fact are very important normal functioning genes. So the problem becomes if you

have an error or genetic mutation in a gene that should do a normal function.
So we have chromosomes, in fact, if you look here this is kind of old-fashioned picture of chromosomes laid out. You look at this and all you know is that this is a normal chromosome study of a female, two X chromosomes. That's really all this tells you. Within those every single chromosome has anywhere between several hundred and several thousand genes that you can't see at this level. if you stretch that that long, each stretch is broken out into individual genes and if you break that out you'll see the individual sequence or lettering of each gene.
Each gene is made of up a specific genetic sequence, made up of only four letters, chemical waist pairs represented by four letters, A, T, G and C, that's it. A genetic mutation can be anything different than that normal sort of expected perfect sequence so it could be as simple as one single letter changed or there should be an A instead of T or it could be something larger than that. It could be a deletion of one or three of those individual base pairs or letters or it could be a deletion of the entire gene.
Any of those things we would call a genetic mutation. And Jen pointed out that would be like you're no longer putting together your entire protein. It gets cut off early.
So Usher syndrome -- mine doesn't want to advance. I'm doing it both ways. Okay. Sorry.
Usher syndrome is, as probably almost all of you know, a recessive genetic condition. So in recessive genetic condition, we typically see no family history of the condition in previous generations. Both the mother and father are carriers carrying a genetic mutation and it's only when a child inherent two genetic mutations in the same gene that they would be affected. This is like inherenting blue eyes if neither parent had blue eyes or red hair those are recessive traits so Usher syndrome acts as a recessive trait.
And so when we do a family history in clinic, this is what it might look like. Squares are male, circles are female. If it's filled in that person is affected. So what we typically see is we only see one person in a family affected or we might see siblings affected. Occasionally you'll see more family members beyond that. But this is the most common thing that we see in families. Either only one person affected or siblings. I already told you that. So the Usher syndrome genes, this is kind of interesting. So this graphic shows all inherited retinal disease genes. This particular one is -- this particular slide is a couple years old. But you can see the progression of the identification of genes associated with inherited retinal diseases including Usher syndrome. Now, the total number of genes you would think would be pretty simple. Right? Everybody should know how many genes are associated with Usher syndrome and yet on Jen's slide there were 10. Some people talk about 11. Some people say 13. So I have -- how many genes are there actually, are there 12 or 13 now? And it's not quite as simple as you might think. So there are 11 that we absolutely would say are Usher syndrome genes and I'm going to talk about this sort of possible and 13 in a little bit. Here's Usher syndrome type 1 and genes we know to be associated with Usher syndrome type 1. Those in 7A is often called Ush 1 -- is responsible for 50-60% of all cases of Usher syndrome type 1, USH1C,USHD and USH1F make up the vast majority of the rest of Usher syndrome

type 1. In Usher syndrome type 2 we have these 4 known genes, USH2A makes up the vast majority of Usher syndrome type 2 at least 80% and then GPR98 or what's called VLRG1 and WHRN make up most of the rest. Usher syndrome type 3 we thought there was only one gene, there is a second gene HARS that was discovered two or three years ago that appears to be quite rare.
Somebody's going to tell me when we have to switch, yes? Okay.
So for a long time we at the Usher Syndrome Coalition board have been talking about how do we make genetic testing more accessible? We want more people to be able to get genetic testing when they want it. You often hear from people well, I would get tested but I don't know how. I've talked to my doctor before it, my doctor said I think that's a great idea, but he doesn't really know how. Or I tried to get tested and my insurance company denied it and it's really expensive and I can't afford it. Or I was part of a research study a long time ago and I thought I was going to get results and three years have gone by and I never heard anything. So it was negative. How do we enable people to get genetic testing and get past those barriers? So that was the task in front of us and this is what we've done. We have put together a program that we call Unraveling USH. This is a genetic testing initiative to provide guidance and affordable testing to individuals and families who have never been tested or who didn't get successful positive genetic testing in the past either due to financial access or financial barriers, to try to get past all of those challenges. This is a collaborative effort that we're doing in combination with the University of Washington and the Wynn Institute for Vision Research with the lofty goal of identifying everyone with Usher syndrome worldwide. Eventually.
I'm going to pause for an interpreter switch.
Good. Okay. So at a high level, there are three steps to participating in this program. Number one would be to meet with a physician or a genetic counselor and ask them to order the test.
Now, some physicians are going to be supportive of genetic testing but not feel confident ordering it or not have the time or resources to know how to go about that. So we've put in place some mechanism for help. There's an information sheet on the Usher syndrome coalition Web site. About the genetic testing initiative with step-by-step instructions for the physician. So, if a physician is supportive and wants to do it and needs some help, you can print them out and take it with you to your appointment. If a physician is supportive but doesn't feel confident doing it themselves, you can ask for a referral to a genetic counselor or geneticist. I'll talk about that in a bit. Step 2 is to work with provider to try to provide insurance coverage for testing. We don't want to put in place a financial support system that tells insurance companies you don't have to pay for the testing any more, we'll take care of it. That's not good for us as a community. This testing is important. It should be part of the standard practice of care and we're going to try to get insurance to cover it every time.
Every time. Plaintiff.
If they don't, we're going to put in place financial support. So we have information about that as well. We have a letter available on the Web site to use to submit to your insurance company to support the medical necessity of this testing. Why is it important? So that's the second part and then testing goes off. Right? Your

sample goes off for testing. You get test results back and then the third component is to add your genetic test results to the Usher syndrome registry which -- where did Mark go. They have a new name for it. What am I supposed to call that? Ush trust. Brand new to me.
So the Steve Wynn institute for vision research who we're partnering with through the University of Iowa, they have information about this program on their Web site as well. They lift five goals for this project. To provide hope for families by helping to identify the underlying cause of disease and therefore, layout a path toward treatment. To provide accurate information to individuals and families to find the remaining genes, currently, over all in Usher's syndrome we find that genetic cause in 80+ percent of cases so that's not everybody. That tells us there are other genes yet to be discovered. To find cures and make genetic testing available to all.
Okay. I am advancing on mine and not yours.
Okay. Here we go.
So this is a little bit -- oh. Did that get cut off? Here's the pipeline of what the actual testing looks like. So genetic or a blood sample gets sent into the laboratory. And the first tier testing, so the way that the laboratory is doing this and the way they're keeping costs down which is a big component of us being able to do this. They have to keep costs down to the extent possible. So the first step, the first tier of testing is to do was called targeted testing of common mutations.
So when somebody asks you do you know mutation that's technically different than knowing your gene. So one person can have Usher syndrome type 2 as a result of a genetic mutation in the gene USH2A and another person can have Ush 2 as a result of husband but those mutations may be different and the genetic mutation is just where along that sequence of the gene that error lies.
Right? So in this first tier 1 test what they're going to do is test for the most common known mutations. That, as it turns out is a pretty simple, relatively cheap test to do. So by doing that test first, what necessity do is look for the most common known mutations and the most common genes and if you go down the first column here, that is -- that we expect to get results back in fact we have a guarantee to get results back in under four months. And in 50% of the cases, done. We will find two mutations with that first tier test.
That test is about -- I don't remember the exact -- I should but I don't remember. It's right about $500.
As genetic testing goes it's incredibly cheap. So 50% of the time we're going to be done with that test. If that identifies one genetic mutation but not 2 because this is a recessive disease, right? We expect to find two genetic mutations one inherited from each parent. So, if we find one genetic mutation, the vast majority of the time what that tells us is that now we've identified the gene so let's go back to our example. Let's say now we've identified the gene and it's USH2A and let's say we find the most common genetic mutation in all of Usher syndrome. 2299LG which is I a mutation that deletes one single G in the hh gene so they find that but not a second what that tells is that USH2A is almost certainly the cause of disease, but that the second mutation isn't one of the really common ones.
So now what we're going to do is go back to only USH2A to only that gene and we're going to test the whole gene. Right? You don't have to test all 11 or 12 or 13,

whatever your count is, genes because now you've pinpointed which one and you go looking for the second mutation.
That could take up to a year, probably won't but it could.
So in an extra 20% of cases, that's going to identify it.
So now we're up to 70% of all individuals with Usher syndrome who go through this program at that point have positive results for two genetic mutations. If a second mutation is not identified in that gene, then that tells us that one of two things is going on. Either that second mutation is a very, very difficult to detect mutation and maybe that's in what's called an intron which is technically a non-coding portion of the gene that we actually know mutations can occur in, or maybe it's a large deletion that didn't get picked up that we need to do additional type of testing for. So maybe it's a hard to find second mutation.
Or maybe it was a red herring. Maybe it wasn't USH2A at all. And maybe that was just a throwing us off course and maybe it's a different gene and we need to keep looking. In any case what's going to happen then if a second mutation is not found, the lab is going to go on to something called whole exome sequencing. Whole exome means they're going to at all the coding regions of every single gene you have. We all have about 22,000 genes. We're no longer talking about testing 11. We're talking about testing 22,000. That seems like a huge jump. We went from targeted testing to do doing that. The reason they're doing it is we can have all that data with the whole exome sequencing and analyze the part related to Usher syndrome and then if they find a result you're done. If they don't, all that data that came from those 22,000 genes is now part of our effort to search for novel genes. So you're doing two things at once. You're continuing to try to test for that patient, you're also wading in the discovery of -- aiding in the discovery of new genes.
Let's say you walk out here and say I want to do this. What's the best way? You talk to your doctor. Doctor doesn't feel super confident knowing how to do this or importantly, how to interpret the test results. Some doctors would be happy to order the test but don't want to have to interpret the test results and help you understand the implications of that. So genetic counseling and genetic test coordination is something that's available in all the inherited retinol clinics so there are a list of those clinics, the specialty clinics at the Usher Syndrome Coalition Web site as well as the foundation fighting blindness Web site. You can also go to the NSGC, the National Society of Genetic Counselors and search for someone in your area locally. You can do it by phone. As a total disclaimer, I am a genetic counselor. I do telephone-based genetic counseling. So that's a little disclaimer about where I've come from and I've done that by phone for a number of people in this room to help them get genetic testing and help get it covered through insurance and then your local physician, if they feel confident can do that with resources we've made available on the Web site.
So who will benefit? With we think about clinical trials a lot of people think about genetic testing because of clinical trials. Who will really benefit. Clinical trials there's a current Phase II clinical trials of Ush stat at the KCI institute. Not even everybody who has clear known myosin 7A mutation is going to be the perfect candidate for that study. There are other up coming clinical trials that we think are going to become available nor some of the other Usher syndrome genes where

researchers are actively working on that in addition to the ones that I've listed here. Jen just talked about Ush 1F. Is genetic testing necessary for clinical trials that are not gene-based? We see this in other retinal diseases and the answer is sometimes yes. Sometimes understanding the underlying genetic mechanism kl lead to treatments that aren't necessarily gene therapy but are still dependent on knowing the specific genetics of type of disease. So genetic testing is going important for many types even if not gene therapy.
Are you standing to tell me I need to wrap up? I'm not paying attention. Probably yes. Okay. I have two minutes.
So what can genetic testing research teach us? There are underlying shared pathways. There's something frequently called the Usher syndrome frequent ak only where the proteins made from these genes all interact together and genetic testing has taught us a lot about those individual proteins and how they interact. That gives us insights for treatment. I already talked to about how genetic testing can fuel the discovery of novel genes. Genetic testing can teach us about modifiers of disease. This PDZD7 is what I might call gene number 12. This isn't a gene considered to be a classic Usher syndrome gene because we don't know of anybody who has two clear mutations in PDZD7 and Usher syndrome as a result. But it may modify disease and make it more severe if they have for example two GPR98 mutations mostly sunny skies one in PDZD7. That's an area we're learning a lot about. Jen was on that paper. What else is genetic testing teaching us? There's another gene called ABHD12 which is sometimes considered an Usher syndrome gene but it also includes a neurologic disease, poly neuropathy and ataxia. And so, if that also challenges our definition, right? What defines Usher syndrome? Is Usher syndrome only RP+ hearing loss plus or minus vestibular areflexia in patients who have mutations in one of the genes in Usher syndrome if you have other symptoms does that mean it's not Usher syndrome? What about people who clearly have Usher syndrome from one of the known Usher syndrome genes and they have other symptoms? So Mark has talked about how there's this emerging data that maybe some subtype of patients might have irritable bowel syndrome or Crohn's disease. We don't say they don't have Usher syndrome. Part of genetic testing is what would we call an Usher syndrome gene and what wouldn't we?
And I think I will end there.
Thank you.

>> MARK DUNNING: Thank you very much, Karmen. We're going to break for lunch. The lunch is in the same room as the food has been and you're welcome to bring it back to your table. It's buffet style.
And we're going to start up again at 1:00. Please take the opportunity to introduce yourself to other people around here. That's the whole point of this is to try to network and meet other people with Usher's syndrome and you can talk to Jen and Karmen and Jim and Kathy who have already spoken.
And of course you can visit the vendor tables that we have over on my right. And you can he -- vendor -- and you can be sure to join the USH Trust if you get the opportunity. Hopefully Karmen helped to convince you on that. And of course if you

want to have your picture taken, Evan is still here taking pictures and he's right by where the food is. So look forward to talking to you all again in about an hour and 15 minutes or so. Thanks. (Lunch break.)

>> MARK DUNNING: If we could get everyone to take their seats, we're going to get started again.
So we'll give everyone a minute to grab their seats. I think we're just about ready to get started. So I hope everyone had a good lunch. Hope you didn't eat too much so you don't fall asleep this afternoon.
I know I saw a number of people over signing up for the USH Trust. That's great. Continue to do that. I saw a long line at the pictures, which was terrific. We'd like to try and get pictures of everyone who has Usher syndrome as part of our Usher syndrome awareness. This morning we heard about some new treatments coming for the vestibular. We heard about identification of people with Usher syndrome through the otolaryngology. We talked about fish, which I bet you doesn't expect to talk about today. And we also talked about genetic testing and how important that is. All of this leads to some of the newer treatments that are coming for vision loss. And we're very fortunate today to have Dr. Jennifer Chao here today to talk about advancements of retinal disease there's is cool fascinating stuff. I will apologize for advance for Jennifer, she is dealing with a very sore back. So my apologies for turning the platform towards the screen but she's having a hard time turning at this point. So she's not trying to be rude and turn her back to you guys. She just can't move very well. So Jennifer, it's all yours.

>> Great, thank you so much. I'd like to thank the Usher Syndrome Coalition for the invitation to speak to you all today. It truly is an honor and pleasure. So today the topic will be advances in stem cell research for treatment of retinal degenerative diseases.
So I'd like to start with a patient saw a few years ago or almost a decade ago when I first started training who had a big impact on my decision to practice in retina. So this patient was a 57-year-old gentleman who came to see me in clinic and he noticed that he recently decreased -- had some decrease in peripheral vision and he was having difficulty driving at night. But when we checked his vision, it was about 20/30 in the right eye, 20/40 in the left. Not too bad. But when we checked her peripheral vision whereabouts we could see in normal peripheral vision it was wide and large and normal, had his visual field was restricted to about five degrees in the center, somewhat akin to looking through the end of a toilet paper roll. And then when we looked at electrophysiology testing to see the electrical responses of the cells in his eye, instead of seeing the usual wave forms, his was entirely flat.
So in order to understand what was happening in his retina, I wanted to sort of review the anatomy of the human eye. I know we talked about fish earlier. We're going to talk about the human eye.
And here we go.
So an often used analogy for the human eye is a camera.
And it's actually quite appropriate. Because the front of the eye has the cornea which is sort of the clear glass in the front of the eye. And then we have an aperture

in our eye as well. It's the pupil. Much like what the iris makes and then just like a camera we have a lens. And in the back of the eye is the wallpaper of the eye. That's all the retina. And that's much like the film in a camera, it detects the light coming in through the eye. So our entire visual world what we see is distilled and perfectly focused on to the back of the eye or the retina.
The retina has a very personal part of it called the macula. The macula is this maybe just 10% of the retina. But it's absolutely like the Park Avenue real estate of the retina. It's responsible for our central vision in terms of reading and driving vision, color vision, our ability to recognize faces. That is the primo area. So everything is focused on to that spot.
Now once you get there, what is the retina?
Well, the retina is made up of multiple layers of cells. So, if you were to make a cross section across it, it basically looks like layers in the layer cake.
You've got the most -- and what happens is light actually travels through the entire extent of the retina and it activates these cells called photoreceptors.
Photoreceptors are the light sensing cells in the eye. They sense color, they sense light and what happens after that is that they send the signals back up through the retina and these very last cells called ganglion cells extend axons all the way throughout the eye and it forms essentially a cord which is the optic nerve in the cable that then connects your eye to the brain.
And essentially how we see.
Really importantly these photoreceptors also have support cells. And these are called retina pigment epithelial cells and these cells help support the photoreceptors and you essentially can't have one without the other. They both need to be there and functioning for us to see well.
So this first patient that I saw had retinitis pigmentosa. A disease very similar to Usher's syndrome as you all know. And one in 3,000 people are affected. And as the symptoms are night blindness, early peripheral vision loss and central vision loss.
The cells that are affected in this disease are the photoreceptor cells.
And these no longer function.
A disease that I'm sure you've heard of called age-related macular degeneration is exactly the opposite. Instead of losing peripheral vision first you lose central vision. This is a more common disease, 1 in 80 people are affected by it over the age of 40 and by the year 2020 it's estimated that 3 million people will be visually impaired in some way due to macular degeneration. In this situation the photo receptor cells are damaged as are the support cells.
So what do these diseases have in common? RP, Usher's and AMD. All three diseases have photo receptor cell loss. Now unlike cells in our skin for instance if we cut it, they divide and things you know get better.
The problem is photo receptors don't divide and they can't be released. And so the one question that is -- replaced. One question come to the forefront is how can we replace these cells? Can we do this through stem CAL therapy? So before we get started into the therapy, I just want to do a quick review of what a stem cell is. I know we hear about it all the time from the news but I think it would be useful to review it. So at its earliest stages fertilized egg divides and becomes a blastocyte.

And inside those are cells that are grow in culture indefinitely. And what's amazing about these cells is they're essentially pluripotent. That means it can become any cell in the human body. It can be your muscle cell, heart cell, brain cell skin cell, it's essentially in kindergarten. It hasn't decided whether it's going to be a lawyer yet or an endocrine specialist or whatever. They're undifferentiated is what we call them. And I've got a cartoon here that says what is a stem cell. So here are two snowmen looking up at snowflakes coming down, saying look stem cells! and then there's a guy here sitting with his professor saying why do I have to decide on a major? Why can't I just stay a stem cell? and then there's stem cells in a Petri dish that says stem cell parental advice: you can be anything you want to be when you grow up! And that's the point.

So I'm going to divide my talk into two parts. Because there are really two different applications for stem cells at this point. There's the traditional what we think of in terms of cell replacement that we're talking about. And the second one is using stem cells to improve cell survival. So cell replacement is good for when you've lost your vision, improving cell survival is great for while you still have some and stem cells can help with both.

So we'll talk about cell replacement first.

So this whole technology of stem cells is really only useful if we actually know how to make a retina from stem cells. And I'm sort of proud to say that the Reh lab at the University of Washington was the first lab in the country to be able to do this. So back in 2009, they took some stem cells and then figured out which signals to give them to tell them to become all the different types of cells in the retina.

They can make ganglion cells, the cells that are affected in glaucoma, they can make photoreceptors with the cells that are affected in macular degeneration, RP, Usher's and then the support cells that are affected in AMD and closely related disease called Sorsby. So that's great. That's sort of ground breaking at the time. And the question was well, okay. It's great that you can make it in a dish. But can they actually do anything if you -- can they integrate? And that was the next step. That's what they did next. They took stem cells. They made them into photoreceptors, keeping in mind that these are now human stem cell derived photoreceptors, these light sensing cells. And they injected them and labeled them green and injected them in the back of a mouse eye. Remarkably these cells knew exactly where to go. In all the layers of the eye that there could be, they went to exactly the right layer. Okay. So that's pretty amazing.

But then can they actually work like regular cells? These are human photoreceptors in a mouse eye. Do they actually work? What they did to test that was they took a blind mouse that has a genetic mutation that basically did not allow it to have any photoreceptors. And put in these human photo receptors and they could show that these cells could integrate and it's kind of difficult to ask a mouse if it could see so they did electrophysiology testing and showed there's some restoration of light signal. Actual vision was difficult to assess. At that point everybody sort of questioned that's great. It kind of works in a mouse but really, what we need to do is to test it its safety in a larger animal model because mice don't have maculas. Their eyes are a little different to ours. So there was a request that the study be done in a non-human primate. So at this point these cells were injected into two separate

squirrel monkeys, non-human primates. The monkeys were not immunosuppressed at all and followed weekly to assess for transplant survival. Immune rejection and whether or not when we're working with stem cells we always worry about tumor formation. And remarkably at one month we could see that the cells were -- the cells were in green. They sort of coalesced. They were surviving just fine. Eye was fine. There was no inflammation of any sort. But remarkably at about two months, not only did they continue to survive but they were starting to extend axons and into -- in a pattern similar to what the host retina would look like. So they were starting to look like they were trying to integrate and then by about three months the effects were pretty striking. So one thing we did see in our study is that these human embryonic stem cell derived retinal cells could survive in a non-human primate host retina after transplantation and they could grow axons and dendritic processes that extended into the optic nerve. And there was no rejection in the transplanted animal even though we had no immunosuppression. And there was zero evidence of tumor formation. Since that time I sort of simplified the history of it. But since the first time that Tom Reh's lab had developed this. Multiple labs around the country and world had worked on figuring out how to differentiate human embryonic stem cells into photo receptors in a very efficient way and at this point you can grow a 3D retina in a dish and the results are pretty amazing what's happening now.

So I think what everybody wants to know is how do we get this to patients and how does this work? So I'm going to talk about this for just a second. How the FDA process works in the U.S. anyway. So the first step are these preclinical studies that I've been talking to you about today. The most important things that we need to know are whether or not what we're trying is safe. So long term safety studies are done and the second question is this effective longterm efficacy studies. The next step involves humans, phase 1. Phase 1 trials are 100% involved in figuring out -- sure. We're going to take a break for just a second. Interpreter switch.

The next phase is phase 1. That's when humans are involved. There are just about 3 or 5 patients allowed to be enrolled at this point and really, it's all about safety. Studies to make sure that the same treatment that was safe in animals is safe in humans and then dose ranging. Really how many cells do we need? What's the minimum amount? What's the maximum amount? That's sort of being worked out in phase 1. If that works out we move on to Phase II. Phase II is Okay. Now we've done this. We've proven its safe. Now we want to know is it working? Is it efficacious at all? That's the main criteria for a Phase II trial. And also if it's working, what's the minimum dose? What's the maximum dose? We need to figure that out. If everything is looking good at the end of Phase II, we're off to the races, it's phase 3, you can start your multi center clinical trials and do treatment anywhere you want while pending FDA approval.

So excitingly, there are two companies that took up a lot of interest in this. They're probably interested in it for multiple diseases including macular degeneration. But there are two specific companies that have spent millions of dollars now on getting FDA approval to do the first trials. So jCyte is holding their study at UC Irvine and also on retina private practice group down in Los Angeles and they're injecting human embryonic stem cell receptors just like the ones we talked about earlier and

injecting it into the vitreous space of patients with retinitis pigmentosa. Last I checked they were currently enrolling but they've already done four transplants to date at a minimum. Re Neuron is a second company doing this. Their approach is different. Instead of injecting into vitreous space which is the center cavity of the eye they're injecting it as we did and many other studies did at exactly the space we want them to be which is under the retina and my colleague who is actually doing the transplants indicated to me that they've already done two and they have multiple coming down the pipeline patients that are enrolled and I think that they are approved for maximum of 15 patients.

Both of these trials are phase 1, Phase II, which means that if everything is safe, they're allowed to look at the efficacy of as well. This is exciting. This is the sort of thing we weren't sure we were going to have as of a couple years ago in terms of venture capital interest and just industry interest in it. Because these trials are really quite expensive.

So let's just talk about the summary for the first part of the talk. So human stem cells can be differentiated into retinal cells that are affected by macular degeneration, affected in RP and Usher's syndrome and glaucoma. We know that retinal cells can integrate. They can form communication synapses and they can restore function, visual function in mouse and in a separate that I didn't show you primate model.

There are current multiple ongoing and future stem cell trials aimed at cell replacement and photoreceptors.

Moving on to the second part of the talk: understanding how to improve cell survival. You can think well, how could that really be -- why is this a stem cell issue. Is this not looking at a drug or something else. And really, you know, besides replacing lost cells, stem cell technology can be used to better understand how these diseases work and prevent cells from dying at a first place and try to slow degeneration. One of the main advantages in understanding retinal diseases is understand you ho to look under the hood. Imagine it's like having a broken car by the side of the road and you're allowed to look at it and you know it's broken and like when I'm looking at a patient's eye I can see that things aren't working but at a cellular level I can't understand what's going on in there unless I can really understand it in a dish.

So most people are still pretty attached to their eyes. So that's understandable. But being able to pop the hood and look under the engine and tinker with it and try different things is something that we just haven't been able to do in the past. And it's been really a disadvantage in terms of holding us back for trying to find new treatments. But a recent advance in stem cell technology changed our ability to be able to understand the disease in a dish. And this was the advent of something called induced pleasure I potent stem cells. These two guys are pretty amazing. They were separated by about 50 years but got the Nobel prize at the same time. This guy on the right is John Gurdon. He's English. And way back when he figured out that he could make a frog intestinal cell from the gut into a tadpole with the right DNA. I mean you could basically reprogram a cell from the gut of one animal and make it -- or the -- you know a frog and make it back into a tadpole.

And it's kind of like turning back the clock. And then Yamanaka in about 2009 I

think, yeah, he figured out I can do one better. I can do that from a skin cell in a mouse and then I can do it in a human. So that's essentially what he did. He as able to show that just by taking some skin cells from someone he could reeducate the cells and say you know what? You're not a lawyer any more. You're not an endocrinologist. You're back in kindergarten and then we're going to reteach you into becoming something else. So basically turning back the clock and usually the Nobel committee makes people wait for a long time. This guy got it in five years because this was just a mind boggling and field changing sort of discovery. So induced pluripotent stem cells are not much different from embryonic stem cells. Besides the ethical differences this is completely the same in the sense that you have an adult human being and you could take their skin fiberglass little skin biopsy, take their cells and reprogram them with just four genes and make them into any cell you want. Just like human embryonic stem cell. You want cardiac muscle cell, anything you want.

Now, how is that really useful to us? Something that came up really early that people were interested in is something that goes along like this. Imagine a patient comes to you and they say you know I have AMD, I have Usher syndrome, I have RP. And now actually we can do this and I do this in -- I've been doing this in my clinic. But instead of a -- instead of a skin biopsy, all we need is two vials of blood and from your blood cells we reprogram cells into individual stem cells so we have patient specific, disease specific stem cells and now we make them into your retinal cells. So for the first time essentially your exact retinal cells are available for me and other scientists to study in a dish. In a way we've never been able to do before. And at this point you know, perhaps we could treat the cells and it goes back into the patient or perhaps we could treat the cells and figure out how the cells -- we can slow cell death that's the idea. In terms of our particular study, this is going around nationwide we've enrolled a lot of patients with Sorsby muscular dystrophy and Stargardt's disease and Usher syndrome. I'm just going to provide one example of a disease where we've used this technology to help try to find a therapy. And this is a little different from Usher's - it's similar to macular degeneration. Its advantage is it has a genetic component and patients so they are affected at an early age and lose center of vision usually in their 20s. We had a family re-enrolled and made their cells and studied them in a dish and what we found is that they're more susceptible to oxidative stress among other things and we could actually rescue them from cell death with this metabolite that's commonly found. So it's just one way for us to sort of give you an example of the ways we can use these models to study disease. Here's a list of the recent publications of disease that's have been studied in this way including RP, Usher's LCH guy rate. I'm going to talk about the Usher paper. We're going to take another interpreter switch break. Usher syndrome type 1 is studied. They took a patient with USH2A mutation and made their retinal cells in a dish and studied them. One of the things they found is a protein they didn't know about earlier was misfolded and so that was sort of an interesting finding. And a potential target for gene therapy in the future. More importantly or more interestingly, they also made progenitor cells which are retinal cells from the patient stem cells and transplanted them into a mouse and sort of remarkably found that these cells worked just great in a mouse. Which kind of told them that you know

what? It's probably such that these cells aren't affected by the mutation until later and certainly not in development. Which means theoretically if it could be transplanted back into the patient perhaps it would buy more time before the cells degenerated. A lot of things needed to be worked out in this technology before we get there. But that's the next idea that next big idea which is the next-generation of stem cells, which is not stem cells that are embryonic stem cells derived but patient specific and disease specific. We haven't gotten to a point where people are doing patient specific photo receptor transplantation in humans yet but there's a group in Japan that are using patient specific stem cells to transplant the support cells that we talked about earlier. So at the RIKEN institute in Japan there's a 70-year-old woman blind from macular degeneration, they took a skin biopsy from her and made it into support cells and then they took the support cells and they put them back into her eye and they did that in September of 2015. Made big news and at this point there are no serious adverse effects to date. They have a different sort of approval process than we do at the FDA. But they met the criteria for that. They enrolled their second patient and unfortunately detected mutations in the patient's stem cells that were not from the patient. Non-of the mutations were deleterious. Not harmful but it gave everybody the heebee jeebies enough that basically that trial was -- and that part of the trial was stopped. And all subsequent patients will be receiving cells from an adult patient that's been screened before. But it's not necessarily from that same individual.

They might still have immune rejection. It's something that we need to talk about. It's interesting because if your own cells are reprogrammed and put back, we don't have a whole lot of experience as to whether or not there will be immune rejection. Certainly we don't think it would be.

And NEI and NIH are at this point in this country we're working on the preclinical studies on this one in terms of working out safety issues.

So in summary we can also use stem cells to understand disease better.

This is a new avenue that is not available to us previously. We know that patient specific and stem cells can be generated from our patient blood samples and a fast and efficient manner. We know that patient specific cells like photoreceptors and RP cells which can be generated from personalized stem cells and that this type of technology has really allowed us to better understand the disease by being able to model it in a dish so that we can poke at it and prod and figure out what's going on. And that currently there is interest and at least one trial out there where they're using a patient's own stem cells to give them their own retinal cells back.

That's the end of my talk but I'd like to acknowledge all the people in my lab, collaborators, along with my funding sources including the NIH. Hear See Hope and the Bill and Melinda Gates Foundation. Thank you. [Applause.]

>> MARK DUNNING: Thank you so I'd like to invite Dr.S, Philips, Jen and Jim along with Karmen and -- to come up front -- and Dr. See, is she still here to come up front. We're going to do a Q&A session. This is your opportunity to ask these guys any questions that you have about anything that they've spoken about. You've heard a lot of great things from the retinal -- from excuse me, from the vestibular implant to stem cells to the genetics, the animal models that are happening, the new

things that are happening around hearing loss. And these guys are here to answer any questions that you may have. Ricky, do we have a microphone, a pass mic that we can use? Yep. Okay. We do. I'm going to grab the pass mic and if you guys want to raise your hands we'll have you ask your questions.
Thank you. So does anybody have any questions?

>> Dale Kosier: Thank you. Yeah. My name is Dale. I'm from the Seattle area. And I can't recall maybe late '80s or early '90s, I had DNA testing on my -- I've been identified with Usher type 2 back at that time. And my question is -- and they were done by Boyd town research, Dr. Kimberly. Do you guys collaborate with each other? I'm sure he's retired now. But do you have that resource information as well to share? Or do I have to go through testing again to help you guys out?
>> KARMEN TRZUPEK: So there's a couple questions embedded in there whether you know it or not.
Yes, sorry. Karmen Trzupek. So there are a couple questions in that. One is for people who have research testing. And your question and I don't need to know that to answer but may be related to the fact that you got results or it might be related to the fact that you does not get results. There are almost certainly people in this room in each of those categories.
So anyone who participated in genetic research-based testing particularly if it was 10 or more years ago, when I used to enroll patients in genetic research testing I will tell them they are making a contribution to research. Right? With no expectation that we get a result. We can hope for it. But really they're making a contribution to the research. And that's fundamentally different than what we do today when we talk about genetic testing. So today when we do genetic testing we can doing a clinical test a test that your doctor can order for specific known genes looking for defects within those genes. So past of your question which maybe you weren't asking is between those two things. If you participated in the genetic research in the past and you never got a result, that's not because the lab didn't do any work or because they were lazy or because they lost your sample or something. It's because that was a research effort. So, if you never got a result, now is a great time to revisit testing.
The other part of your question is about whether or not that got shared.
Dr. Kimberling at boyd town research hospital had the greatest collection of patient samples with Usher syndrome in the world.
He -- somewhere in the range of 5-8 years ago moved up to the University of Iowa where Dr. Ed stone is and all of that data went there and is actively being used as part of our body of knowledge about Usher syndrome. So you contributed to that and it's still there.

>> MARK DUNNING: Just to add on to that. This is Mark. Dr. Kimberling was a member of the board of directors of the Usher Syndrome Coalition but he's been sick for a number of years and has not been actively participating. I did see him about a year ago when the University of Iowa dedicated the first Usher syndrome focused laboratory in the world and named it after Bill. So it's the William Kimberling

Usher syndrome laboratory at the University of Iowa and University of Iowa has all of his records. But to Karmen's point if you didn't get anything back from him the information is there as part of a previous study but the best thing for you is to get retested genetically. Ramona, did you have a question?

>> RAMONA RICE: Hi, this is Ramona Rice. I think I have a question for Dr. James Philips. I have Usher's type 2a. You mentioned Usher's 2 do not have a balance issue but for me to lose my vision, I feel like I am losing my balance more and more. Before having my dog, I found myself having a hard time with my white cane until I had my dog and now I'm able to steady myself because of him.
So do we lose our balance as we get older or lose our vision as type 2? Or is it a vestibular issue.

>> JAMES PHILIPS: Yeah, Jim Philips. I think it's fair to say that all -- everyone in this room --
>> Could you repeat the question?
>> JAMES PHILIPS: Oh, repeat the question. Can you hear me now? Okay. Great.
So the question was I had mentioned that Usher's type 2 is not thought to be associated with vestibular loss. And yet several people actually have come to me here at this conference to tell me of the fact that they feel as though they've been losing balance as they lost vision.
And the fact is that all of us actually lose balance from the inner ear as we age. And ordinarily what we do is we compensate for that loss of balance by utilizing other sensory inputting. And that compensation process is so complete and so effective that we're unaware of the fact that our ear is providing us with less and less balance information over time.
So, if you have at the same time as this normal aging process takes place, if you also lose information from other sensory systems, then that adaptation is not as effective and you feel as though you're losing balance because you are. Because your inner ear is providing less information. Someone with someone with that kind of loss is not really a target for the kind of therapy was talking about today with a combined cochlear vestibular implant.
But I think it's fair to say that yeah, your loss of balance could be directly related to the fact you're losing other sensory information that you would ordinarily use to compensated for the national -- just as they get something called presbycusis they also get loss of balance from the ear as you get older.

>> RAMONA RICE: He said I could ask another question for the cochlear implant. I'm all for the Usher's 1 or for the intervention, early intervention for the Usher's one so they can hear at an early age. So let's just say for example if one person has Usher's syndrome, 1, did not get cochlear implants at early age but let's say at age 30, and gets the cochlear implant, would that be successful if he'd never heard the sounds earlier? Can he be successful with the cochlear implant later in life?

>> JAMES PHILIPS: So the question is would a cochlear implant be successful if you were implanted later as opposed to being implanted later in life. This is Jim Philips again and I'm going to refer to Dr. Sie on that.
>> Hi, I'm Kathy Sie, I'm the ear nose and throat doctor on the panel. It is true that if someone has congenital deafness so born without hearing and they go for many years without access to sound, the cochlear implant, although it would reliably provide sound information would not -- we would not expect that the patient would be able to communicate with spoken intelligible speech at that point. If they're 30 years old and they've never had any access to sound.
But it would potentially make them aware of sound. Although we don't typically offer cochlear implants for congenitally deaf adults, for people with Usher's syndrome who have dual sensory impairment, it is something to think about for sound awareness and just connection to their environment. But it -- but we're trying to be very careful with the expectation, what is the definition of success. So for kids who are typically wanting them to communicate in the hearing world with spoken language, that would not be a realistic expectation for that patient.
>> So we're going to do an interpreter switch. I'll ask interpreters to change.
I have several people on the left and several people on the right but I'm going to go to Dorothy and head to the left and come back this way.

>> Good afternoon, this is Dorothy Walt speaking from Washington. Do you know if the doctors are still supporting vitamin A as a therapy for slowing down the progression of RP?

>> JENNIFER CHAO: So the question was -- I understand the question to mean are doctors still supporting high dose vitamin A for the treatment of RP? I think that's very doctor specific. There's evidence that goes both ways as to whether or not it's actually helpful or not. Anything in a high enough dose could be considered a drug so I think we try to be careful about prescribing things that aren't 100% proven. There is a retinal degenerative disease called Stargardts that some people can confuse in diagnosis with RP and high dose vitamin A for patients with Stargardt is harmful. I think we need to be careful about that. Up to doctor's discretion after genetic testing to make sure the patient does not have Stargardt's.
>> I think Mark had a question over here. Can we get an ASL interpreter.

>> AUDIENCE MEMBER: Hi, I have actually two questions. One is a question about vestibular implant and the use of that for people with balance issues. Do you recommend that for younger people rather than waiting until older or what's the impact or effect if you were to get one when you were older? My second question is about Vancouver British Columbia, the well spring, RP treatment. I'm wondering if any of you have been heard about that and how that works exactly. I think they're using acupuncture and some other natural techniques and I'd like to hear your opinions on those things. And that's a general question for whoever would like to

answer.

>> JAMES PHILIPS: I'll take the vestibular question.
That -- excuse me. The currently there are four people in the world implanted -- oh, the question was do you recommend vestibular implantation for children as opposed to adults. In other words, might it be more effective for -- might be it more effective for a younger patient than for and older patient or someone who had Usher syndrome. And the answer is currently there are four people in the world that have been implanted with this device. So it would be very premature for me to make any kind of recommendation in that regard. But I think that for this clinical trial, this technology will be tested in adults long before it's tested in children. And there may be benefit associated with implantation in adults that will be demonstrated before it's demonstrated that it's much more effective in children. If that's reasonable to say.
>> Would you like to take the well spring question Jen?
>> Which Jen are you talking to?
>> MARK DUNNING: You.

>> JENNIFER CHAO: Hi. This is Jennifer Chao. I think I'm answering a question as to whether or not acupuncture is helpful for RP. I guess I have a personal story to share about that. I found myself for the first time or second time now on an acupuncture table not long ago because I just had a slipped disk that I think was alluded to earlier and when the acupuncture, I hadn't even heard about this but when the acupuncturist found out that I work in retina, she handed me a brochure and had a number of treatments I think that she offered for RP and Stargardt and all sorts of things and she does visual fields before and after the acupuncture treatment. I had no idea it was so well laid out. But that was -- you know, I don't know of any large controlled studies that show that it's effective or maybe that it's not effective. In general, the way I approach it with my patients is if you think it's helpful and we've decided it's not harmful or if you'd just like to try it, there's no harm in doing it. As long as you know we've actually determined that there's no harm in it. And I think that that's sort of how I approach things. But I don't usually offer it as a recommendation because unless something has been sort of proven in a clinical trial, I generally don't offer that as a therapy.

>> MARK DUNNING: I know John Natasha. I'll get to you. I have a couple questions over here. Karen?

>> AUDIENCE MEMBER: Hi, everyone. My name is Karen. And I have Usher syndrome. I have a question about the genetic testing. Now, I know that there's one B, 2A, that has been tested. But I believe H through Z has not been fully researched yet. And I know there's additional subtypes that are being found and I'm just curious to know in the future, do you expect to find more subtypes for types C, D, E, et~cetera?

>> KARMEN TRZUPEK: This is Karmen Trzupek. So the naming convention confuses people a little bit. So when we say U1B, Ush 1C, Ush 1D, that is not to suggest that there are actually 26. A through Z. It's just the order in which those genes were first identified. In fact, not even really when they were first identified but when the location of each of those genes was first found.
So sometimes you'll hear that there is a locus which just means location for a gene known but the gene itself is not known. Sometimes that can persist for many years, we know there is a gene there but hasn't been characterized. Fully understood. Today when we do genetic testing for all the known Usher syndrome genes we get a clear result back in at least 80% of the cases. So are there other genes. Yes, there are other genes associated with Usher syndrome that we do not yet know. And that's part of why when we developed this genetic testing initiative, it was important to us to not only provide testing based on what's known and available today, but to put behind that a research initiative. So that anyone who falls in that 20% is contributing to our growing understanding of these genes.

>> MARK DUNNING: There's another question over here.
>> Hi, my name is Jackie and I'm also from Seattle and I have a question about your database. The USH Trust. I don't know whether this is happening now through the University of Iowa. But my question is what about people with Usher's that have other disabilities like MS or diabetes or other syndromes perhaps syndromic issues that are associated with Usher? And are you able to help us connect with other people in that database if they have similar issues? I myself have some other disabilities besides Usher and you know, I certainly would like to be able to communicate with other people who have the same issues as I do.
And it could be very challenging. I have some issues with neuropathy so I'm having difficulty now using an iPad and being able to actually get sensation through my fingers, I'm using tactile sign which makes it more challenging. I'd love to talk to other people with the same issues so we can share ideas and troubleshoot. Okay.

>>So this is Mark. I'll answer that question. About the USH Trust and I'll answer it with a bit of a story. So Bella, my daughter, has Crohn's. She was diagnosed a couple years ago with Crohn's. And I was talking with the doctor at Mass general hospital. A guy named Chris Moran. And he told me that there was 130 something genes that are associated with Crohn's and irritable bowel disease. Knowing Bella had Usher syndrome my thought was is there a connection between the genes that cause irritable bowel the genes that cause Usher syndrome and there was not at the time. I happened to write a blog post about this. And I got a whole bunch of people who e-mailed me and said they had irritable bow el disease of some form. Next time I saw Chris I said what is the incident rate of irritable bowel disease related to the general population? And he said it was 7 in a thousand people. And I said well, I don't know a thousand people with Usher syndrome personally at this point. And I know I have more than 7 responses about people having irritable bowel disease. To Chris's credit, he used the Usher syndrome registry. Actually it was funny. He didn't know who he was related to Usher syndrome. So he looked up on the Internet the leading Usher's syndrome in the world and he e-mailed Krista and asked her if she

has the ability to contact any people with Usher syndrome. So through Krista, we sent out a questionnaire to people in the industry and we got several hundred responses from people and it appears as if there is a much higher incidence rate in irritable bowel disease in people who have Usher syndrome. This is very, very preliminary information. But to your point this is the real power in that USH Trust is if we had everyone in that fry and we could get everyone to respond to these questions, you'd have real data that was actionable data that would tell you whether or not these diseases, these other things are part of Usher syndrome and I think Karmen was saying earlier we're trying to define what is the syndrome in Usher syndrome. A syndrome is having multiple issues associated with a particular disease. You've heard non-syndromic hearing loss. Those are people who have a particular mutation and have just hearing loss and nothing else. You have a syndrome, moat many issues that are associated with it. We know there are hearing issues, we know there are vision issues, we know there are vestibular issues but we don't know what other things are common in people with Usher syndrome. And that's where the power of USH Trust comes because that's our pool of people 20 decide whether or not that's worth fur pursuing so as a follow-up to that IPD question, Chris is going to continue to look into this but we just randomly quat a call from a researcher down in Vanderbilt who said he had been researching a connection between the Usher one C gene and irritable bowel disease that he independently sort of ferreted out. He had his grant through the NIH function that pursues research on bowel diseases. So he wasn't looking at it from the vision or hearing side. So we've been able to put you in touch with Chris Roman and they're collaborating on that to see if there is a connection there. I can't say there is but I can't say if you get involved in the USH Trust we have a great opportunity to gain a lot of information and knowledge about the disease. We're going to do an interpreter switch at this point. I see you waving on the right. I have three people on the left that I'm going to hit up first. I'm going to start with you, John.

>> I'm from Seattle Washington. 8 blocks away. A question for you. My support service provider informed me that the Usher one group, 1A that is, has some information that is incorrect on the Internet. They told me that apparently Usher group 1A is no longer in existence and it's been replaced with Usher one, B, C, D, et~cetera. Because I'm a little perplexed about this. I thought I was told I was Usher 1A but is that no longer just simply a single group?

>> JENNIFER PHILLIPS: That's a very good question. As Karmen said earlier the naming convention came with when the loci were discovered. 1A was the first loci that the researchers thought they identified. However, there weren't very many patients who fell into that category. And I think over time those patients that were originally placed in 1a some of them were re-evaluated and they found there were errors made in the original mapping of where the defect was because they were able with better techniques, they were able to go back and reassign people who were originally called 1A into their proper genetic categories. So I expect that will -- if you were able to get retested, you would be assigned to a more appropriate group

of Usher.

>> Hi, this is Natasha. I have a question specifically regarding the phenotypical variance within Usher syndrome. So just anecdotally, I've met other families whose children were diagnosed with the same type of Usher that my child had, uber type Ush 1B. Yet effects they were experiencing seemed to be more pronounced in some cases versus others. Can you talk about that variance or if there's any research going on in that particular area.

>> I think as the genetic revolution has hit medicine that link between genotype and phenotype has become less clear than we had originally thought it would because many of the genotypes were associated with the most severe phenotypes. As we've been able to better test we learned that the phenotypic variability is almost always for any condition greater than the condition that was originally described. And so it's not unique to Usher syndrome. It's really a common phenomenon. And I think there's a lot -- we're understanding more and more about some of the non-genetic factors in phenotypic expression.

>> KARMEN TRZUPEK: I'd add for retinal disease. So any inherited disease has some degree of genetic predetermination. Right? You inherit a genetic mutation or in the case of Usher syndrome, 2, and you are predetermined to develop symptoms associated with that disease. And yet there is variability in some cases there's a lot of variability and that has different underlying factors. So some of those are genetic meaning that -- and I alluded to one of these when I was talking. So there's some early data and I suspect we're going to have a lot more ha shows us that patients may have one sort of primary genetic dice sis so you could have two genetic mutations in A 2A or GP or myosin serve and and these are gene names, they have associated locus names like Ush 1B and Ush 2A.
So you may have a primary genetic diagnosis of two genetic mutations but it may turn out that people with more severe disease have a third genetic mutation in a related gain that acts in that same pathway. We have some evidence for that. In retinal disease as a whole, we have some evidence of the opposite where there's one form of retinitis pigmentosa that we know can sometimes skip generations and we now know there's a protective genetic modifier that people can inherit that protects them from generating RP which explains how to treat. If you can inherent something that protects you from developing it we should learn from that. Beyond that there are non-genetic. We know patients who smoke who have muscular dystrophy have more severe disease than those who don't. So there are clear genetic modifiers. We don't know what all of them.

>> MARK DUNNING: Mitch, did you have a question on your right-hand side.

>> AUDIENCE MEMBER: Hi, this is Mitch Turbin from Portland, Oregon and I have Ush 3. I always wondered about the parallels between retinitis pigmentosa and

sensorineural hearing loss. In one case you have photoreceptors and support cells. In the other you have hair cells and also support cells. I'm wondering -- we talk so much about looking at treatments entirely separately between the two systems. I'm wondering if for example, stem cell research and intervention, if there might be a good reason or even a key to trying to look at stem cells for example and stem cell intervention that's might have some kind of treatment effect in both the retina and the cochlea.

>> JENNIFER CHAO: I'll address the retina part and let somebody else take over the cochlear stem cell research. So the parallels between the retina and the inner ear cells and other sensory cells is that they're called actually celiopathy, it's like a protrusion from the cell body. The ear cells have the same and a lot of Usher genes that are associated with the disease affect transport of proteins to and from the protrusions or cilia. So it's really not by extent that there necessarily affecting both. It sort of makes sense. I don't know maybe a comment about the stem cell work which I know exists but –

>> This is Kathy Sie: I think the issue with the stem cells, stem cell treatments are that the stem cells have to be --
>> AUDIENCE MEMBER: Can you get closer to the microphone.

>> The issue with the stem cell perhaps is that the stem cells have to be delivered to the Oregon but your question is a great question and that's why this work from the group at Case Western was so interesting. They were taking a different approach to try to protect the protein and the status of the protein in the cell membrane. It depends on whether the protein is affected on whether the condition is eligible for stem cell types of therapies or protein based therapies. So and so there are different differences and part of it is related to the specific condition and the proteins affected. But that's why stem cell therapy is not just kind of infusion of stem cells and then it happens everywhere. You have to put the stem cells in the Oregon at least the way it is now. So we're not there for hearing for a number of different reasons. But for the Ush 3 work that's being done right now, they're looking at a more systemic approach.

>> MARK DUNNING: I am way over to the speaker's right.
>> Hello, I'm Ingrid from Seattle with Usher's 2A, a couple -- not really a question. For example, I take some supplements not vitamin A actually, but in hopes of slowing the progression so when treatment does become available, I would maybe -- it would be good for me. I notice there's a lot of research on treatment but there's a little discussion on how we can slow our progression. Because it could be 10 or 20 or 30 years before we're ready before there is a treatment.
So a lot of supplements I would take hems many other health issues, you know, that prevents oxidative stress and cell death, who would one talk to. I don't want to give advice to other people on what supplements they can take. A lot of doctors don't

like to bring it up.
And also if one takes supplements, let's say alpha acid, are we going to not be attractive to some clinical trials?

>> JENNIFER CHAO: So I get that question a lot from my patients. I think this was a little of something I was alluding to in my talk. Up until recently and I would say in the last couple years we really have not had any idea about how to study, how to slow the disease down but really hoping to make that progress now since we have cells in a dish that we can actually sort of focus on and study. And clinical -- there haven't been any sort of clinical trials specifically for Usher's in terms of understanding specific nutritional supplements. I think it's probably not a bad idea to take supplements that might be in general sort of eye healthy or behavioral things that are eye healthy like wearing sunglasses and stuff. But there's not the data out there so it's difficult to recommend which is often why you don't hear a doctor bringing it up. But certainly the idea is that we can have something as we have these cells in a dish to study now.

>> JENNIFER PHILLIPS: I just wanted to add regarding research about maintaining cell viability before a treatment is ready. We didn't discuss that today and there indeed is no treatment out there that can do that in a pharmacological kind of way. But it is being actively heavily researched by a number of different groups both in the U.S. and abroad. I've heard a lot of talks at the revision research meetings where people are looking at different families that maintain cell health and cell growth and looking at different ways to do a time release in the receipt tissue to preserve cells and have them as personally to leave enough tissue there that can to be treated at a later time point. It is something that's focus of research I hope that's somewhat encouraging. (off mic).

>> JENNIFER CHAO: I think you make the right point. All the advice we give patients now is based on studies for macular degeneration. That's where the data. So when we talk about eye healthy supplements, it comes from the vague rant study.
>> MARK DUNNING: We're going to do an interpreter switch and David I'll get us to in just one second.

For the panel, I'm going to be in the cheap seats over to the right.
>> I'm Errin from Louisiana. My daughter has Ush 1C. My question is for Dr. Chao. In regards to the induced pluripotent stem cells for someone who has Usher's is that a possibility because wouldn't those stem cells also have stem cells also have Usher syndrome. Could we create retina cells from stem cells but wouldn't those retinal cells still have Usher syndrome? The mutation, yeah.

>> JENNIFER CHAO: Absolutely, that is for sure something that we talk about. So the first step is if you were to make induced pluripotent stem cells with someone

with already identified mutation you can study them and understand how they work in a dish. In terms of transplanting it back, I think that's why that study I showed earlier from 2013 is that the cells they transplanted back into a mouse eye, these were made from a patient with Usher's is they developed fairly normally and they looked as though they were normal and sort of had outer segments and that was very interesting because the question is whether or not these photo receptors have a time clock on them. In other words, can you buy five years or 10 years out of it. That's one thought. That's if you didn't alter it genetically in any way. But that brings up the third possibility which is if you know the gene mutation and it's something you can fix in a dish then poke it back in the eye that is the goal. It's hard off now but that's the idea because menu imagine you wouldn't have an issue are reject and it would be sort of your fixed cell back in your eye.

>> My name is David Alexander, I'm from Oakland, California. Two things: One, I won't talk about it my daughter at least had experience with memory loss is a whole other issue.
[Laughter]
In any event, has had acupuncture and I know others. I'm happy to chat with anybody about it. It's not inconsistent with that Dr. Chao said but there's some additional information I can provide.
My question is could the appropriate persons up there comment on the application of opto genetics or the development of opto genetics and I may have missed it if I did or forgotten it. Or secondly, Chris% which is what I understand is underlying what Dr. Stone and Dr. Sie are doing.

>> JENNIFER PHILLIPS: I can field those for you. With respect to opto generic, this is a field in which proteins that are very similar to the visual molecules in our photo receptors have been identified in other species. And because those monthly molecules can be isolated they perceive different light lengths just like our eyes, different colors, different levels of light and the idea with that is this would be a potential therapy, it's not near to being a therapy. But people are actively researching this as well. If you take those and put them in a cell that is not a toto receptor cell, you can give light sensing ability to that other soul. So Usher send him a lot of requests with WP, other cells in the retina remain. So, if you have no photoreceptors to work with, gene chap is kind of off the table. You can't fix what isn't there any more. But, if there are other cells that exist in the retina you could give them at built to sense light and restore some level of light sensing vision to a person who previously would have none.

>> AUDIENCE MEMBER: Are the ganglion cells among those.
>> Yes, the ganglion cells would be monk those par gets. As of crisper that's what we're using to make zebrafish models and I can speak to that. That's the primary effort being made towards repairing the IPSEs in the dish and Ed Tucker d stone's lab this is the best way we know at the present time to be able to modify genes in the cell and still have the cell functions what we wanted it do. That's the main effort.

That's this time. Technology is moving very fast. It may well be superceded by something even cooler and better. Next year but -- it's a great tool and being widely used for these and other purposes.
>> I'll just add a quick comment, you mentioned Steve Sheng. He's used the -- and I think that's where the food is going, either fixing it or introducing a genetic mutation on a normal cell line to have good control and know what you're studying. But I think that is another possibility that relates to the earlier bet about whether the patient IPS correctioners would have the same genetic mutation. That's certainly a form of quote, unquote gene therapy that people are looking into as well PIC technology using other forms out there to fix the mutation and then differentiate at cells and then consider transplantation.
>> My daughter is in the same --

>> MARK DUNNING: So for the panel I'm now well over to your left.
>> My name is Lori. I'm no Scottsdale, Arizona. I have a daughter with Usher's 1F who received a cochlear implant when she was 3 and then many years later got a second implant in her left ear. The question is for Dr. Jim Philips. My daughter has not benefited very much from that second implant. My question is if the development of this kind v and cochlear implant shows Great Western get going forward, is there thought so many children and young adults are received bilateral implants to potentially ex planter one of the crick implants and replace that with this combined implant technology.

>> JAMES PHILIPS: Thank you for that question. Our studies are so early that it's hard to say but I would think that if they had -- if this shows great promise and so on, if it was demonstrated that this technology was effective and it was effective long term and you had a non-working implant or an implant that you derive a little benefit from and you're thinking of ex planting that and replace it, yes. That would be a very reasonable alternative. But as I say, there's a lot ways to go before we've demonstrated this is an effective therapy for this problem.

>> AUDIENCE MEMBER: Hi, I'm Moira Shea from I'm from Washington, D.C., and I wanted to comment on the issue of acupuncture. About three years ago I about acupuncture protocol that was for the retina at Johns Hopkins university.
And it was 10 days, one hour. And about 4 needles inserted from my toes to my capacity scalp and then there was a micro current to do little vibrations to simulate. I experienced a significant improvement in my night vision. I was able to see better at night when driving in a car. Not that I drive but someone else, the color red came back very, very well. I could see in the Metro with where I couldn't see before in contrast -- my contrast was much better. This is knowing that acupuncture I think helps the rods. It simulates the rod. I don't think it does anything for the cone. This benefit probably lasted for about four months. Do it over the summer and I think by December all the improvements had made. At Hopkins their -- she had done a feasibility study and out of that -- a number of individuals may impede and improvement it was tested, it was a contrast test before and and counselor, based

on that she got a $250,000 from NEI to do a clinical trial. She moved to southern Florida and conducted a clinical trial down there. And that study has the -- the result of that study has been released and I believe it shows positive results. However, I don't think this is sustainable. I am not feeling as though I need to go back and get acupuncture because it just didn't last long enough. Not endorsing acupuncture and I'm not condemning it. I'm just telling you my history. No ream scientific background. But, if you do acupuncture -- like I did do a follow-up. The study, the protocol was released in the clinical trial publication. It was published?

A.Not the clinical, the feasibility study. In there it tells the acupuncturist and once the protocol was released another woman and I worked with an acupuncturist in Washington C.D. and both she and I had no results and I discussed this with Dr.-- and she said the real training process and need, you just couldn't go to the publication and follow it. But I'd be happy to talk to anybody about it. But I don't think you can go to any acupuncture and get it done. It's really a very defined setting. Thank you.

>> MARK DUNNING: I think we have time for one last question. I've been directed that way. Give me a minute to make my way over there.

>> AUDIENCE MEMBER: Hi, it's nice to be here in America and from Seattle. I come from Finland and this is my sign name. If you can see. Like this. I'm signing in Finnish and my transferer is going to do American Sign Language because in Finland I've been in many similar conference and legislatures about Usher types same as here. But here it feels -- it's very interesting it's interesting to hear how you explain about these issues. You have 1A, 1 -- you have like the categories a little bit different. And it feels -- it's like 80% of the Usher syndrome patients here in America have USH2A right? When -- the most of the Usher syndrome patients have type 3 like me. I've been born deaf and it was discovered when I got to an older age when I was 40 years old it was discovered that I have Usher syndrome 3.
And in Finland the majority of Usher syndrome patients have type 3. So I was wondering why is it so that here in America the majority you have type 2A and Finland type 3 of the.

>> KARMEN TRZUPEK: This is Karmen Trzupek. So this actually happens with genetic diseases all over the world. In Usher syndrome there are certain types of Usher syndrome that are more common to certain ethnic populations. Particularly in certain geographically somewhat isolated populations.
And in fact, in Finland, Usher syndrome type 3 is the most common type of Usher syndrome in Finland. It turns out actually that Usher syndrome type 3 is also more common in the as can ash I Jewish population most who live in the United States. Most who live in the United States are not Finnish but of ashkanazi. There aren't in the world who are one of the two. In the United States there are little ethnic populations where you see different genetic mutations more commonly in the Acadian population in Louisiana there are two mutations which are common there which leads to Usher syndrome type 1 and one leads to a subtype of type 2. This is

something we see in all genetic diseases throughout the world. Usher syndrome is pan ethnic meaning that affects people of all ethnicities everywhere in the world but the underlying genetic cause differs substantially based on it hold on to that?

>> MARK DUNNING: Thank you to everyone on the panel. If you do have additional questions or comments, I believe that most of these folks will stick around and take any questions that you want. We're going to take about a half hour break so that's a great opportunity for you to touch base with these guys we're going to pick up again at 3:00. We have all of the kids have returned from the Experience Music Project. And so they're kicking around here someplace. So, if you do have kids who are here you may want to touch base with them and figure out where they would like to spend the next little bit.
And when we get back, we'll have our family panel which is usually one of the most popular points that we have.
So thank you.
(A break was taken.)
Test.

>> MARK DUNNING: If I could ask everyone to take their seats, we've gotten the family panel organized up here.
And we're going to start in just a second. I see there's -- you know, we always have a long line over at the USH Trust which is a good thing.
So I'm going to -- the -- our moderator for this is Moira Shea who is the vice chair of the Usher Syndrome Coalition. And she's going to rub the show. And Moira, I'm just going to hand it off to you.
>> MOIRA SHEA: I don't need the microphone.
>> MARK DUNNING: You're on but get real close to it.
>> MOIRA SHEA: Hello. Are we having a good time out there? Are we learning a lot.
Okay.
We're going to rock and roll.
My name is Moira. I'm here with my guide dog Finnegan who is always up to a lot of shenanigans. This is a great hotel. I went to take a shower this morning and I'm like oh no and I went back in the bedroom and I said to my husband, I don't know -- I don't know how to get the shower to work.
The oddest shower I've seen. And so he goes in the bathroom and a minute later he goes this is what you do. I'm like I married a genius. I goes he goes no. I just read the instructions. But it's a very challenging shower.
Anyway. It's my privilege to be here today to moderate this panel. And it's my honor to be here today with you. I'm 60 years old and I found out when I was 15 that I have Usher's 2A. I was living overseas and there was no information. I can't tell you how many years it was before I met another person with Usher's. Probably 7-8 years. I remember people going to England to get bee stings in their neck convinced that it was a cure. Convinced if they got 25-30 bee stings by a quack, they were going to get their vision back. I remember hearing stories of people going

to Russia, people like Gordon Gunn who is the chair of the foundation fighting blindness who went to Russia and spent a few months in Kiev and his wife went to pick him up. He was a different person. He lost vision. People were convinced if they got this injection in their eye that was going to help their vision. And the needle was used over and over. And it got to the point where the needle was so blunt that it was painful to get whatever you were getting into your eye. It was all psychological in seeing better and I'm here today and I was there in the beginning. You know, looking for the needle in the haystack. No genetics. No genetics. It was slow going. We had nothing to say. Today we can't keep up with it. And today the closer we get to treatment, it's going to be more exponential. In the beginning we had no resources. We had to he create the first lab. The Gunn lab at Boston and there was nobody wanted to research RP it wasn't sex I and now we have so many investigators, so many publications, so many genes, so many -- so much opportunities, so much potential, so much hope.

With that, I want to get this panel going. And I thought we would start out by everybody going a self-introduction and I don't want to put anybody on the spot. But I've not met Ramona Rice and I had the same question she had earlier today. Ramona, would you mind introducing yourself and telling us a little bit about yourself and what your hopes are and what you do and let's get to know you.

>> RAMONA RICE: Thank you. Well, to start with, I'm a rebel with a very soft voice. Okay? I'm from Ogden, Utah. And I do have Usher syndrome type 2A. Wasn't diagnosed until I was 38. And then Usher was at age 42.

I have two children in their 30s and they're not affected by it.

And their children aren't either. So I hate to say it but I'm really blessed by that. What I have been doing is I noticed Utah there was a lot of struggle for a deaf-blind community. So I decided make a difference I guess to create a collaborative partnership for people with vision and/or hearing loss. And that is by partnering up a lot of facility and agencies who would help us in the deaf-blind world. Not world, community with communication access. Whether it's interpreters or devices, CART, job employment, training. And I also got Brian Ogland from Helen Keller national center to get involved. And he had done a wonderful job this past year. I found that the more I got into it -- and to be honest, I thought I was the only Usher person in Utah until I started reaching out and we had over 20 right now that I found this year alone.

And we got this new deaf-blind specialist who is doing an absolute amazing job. We created a newsletter, we started ASL tactile classes for the deaf-blind and I also just started a book for 28 writers who are affected by Usher syndrome that's going to be published this summer and it's called "walk in my shoes."

And it's all about all of us have a similar walk in life experiences. But we all had a different challenges like being misdiagnosed or how to have that independent living skill. The parents of children with Usher or the children with parents who have Usher's.

It's a really good book and I hope you look for it because I've been hitting every library in the United States to get them into the e-book, the audio book and the Braille for anybody who would like to read about the deaf-blind -- excuse me not

deaf-blind but people who are affected by Usher syndrome. This is the very first book in the United States that I know of that's going to be created like this. All the proceeds is going to go to the Usher Syndrome Coalition to help with the scholarship and awareness as well. So that is something that we all wanted to do for more of our friends who have Usher syndrome.
I think that's what you want me to do. Moira. Is there anything I'm missing that you want to remind me.

>> MOIRA SHEA: No. We're going to do the self-introduction and then after 45 minutes we're going to open the floor up for question and answer. So Clare, do you want to talk a little bit about yourself?

>> CLARE WEIGEL: Hi. I'm Clare Weigel and I'm from Tampa, Florida. I'm only 18. Oops, my bad.
I've never spoken on a microphone before.
I was diagnosed with Usher syndrome when I was 15. It hit me on a really rough time because I was planning on getting my learners permit the next day. So what happened was that I went to the appointment and they told me there was something funny going on with my eyes.
And several appointments later and several painful tests and evaluations they found out that I was diagnosed with Usher syndrome type 1B.
And that was only three years ago.
A lot has happened to me in the three years since then.
I have gone through many personal -- I was ready for this. Everyone goes through a time in their life where they're going to have something that's either going to crush them, break them, or completely tear them down or they can grow and develop from it.
I went through a year of denial. And then I went through a really long two years of depression from Usher syndrome after my diagnosis.
I nearly went through an eating disorder because I was so obsessed with how my body wasn't working for me. And I have so many wonderful things in front of me and I just couldn't see it when I had Usher syndrome because every waking day I thought I can't see, I can't hear. Nothing's going well for me. It was so funny because at the same time I didn't realize all the wonderful people I had around me who just wanted to help and just be there for me.
And I struggled. Just trying to be social. It was hard. There were days I just didn't even want to leave the house. It was difficulty because sometimes people don't realize when you go through depression, it's not something that completely is visible. Sometimes it's hidden and I hid it even from my own family for about a year. And it took me a really long time to start talking about it. Well, last summer before my senior year, I finally broke through it and last year has just been absolutely wonderful. I have been a cheerleader ever since I was 11. And I cheered all four years of varsity and now captain the past year with only 30 degrees of vision and not even some of the girls in my own squad new about it until much later and they were absolutely amazed that could even just do the cheer or stand in formation

without falling over my feet. I did get tackled by a football player one time though. [Laughter]
It was very interesting.
But you know, it's been a very short three years for me but I can honestly say it has absolutely changed me for the better. Now I just wake up every day and don't even think about the dark years I went through and now I just focus on what I have before me. I just graduated from high school in May and I'm leaving for Samford University in Alabama in the fall and I'm excited because I get to go on and have a new journey and be able to share my story with other people my age. And when I found the coalition two years ago, it was of all my so-called suffering that I went through in my own mind. And I watched so many amazing people and I thought I'm not alone. There are other people would have been through this really, really dark stuff. But they don't let it tear them down. They just break through. And they let themselves shine through the darkest moments of their lives. Even when you can't even see or you can't even hear anything.
But I'm so fortunate just to have my little 30 degrees of vision even though I trip every day.
And I'm just thankful for my cochlear implants which allow me to hear and speak. So I'm just thankful for what I do have. [Applause.]

>> MOIRA SHEA: Thank you, Clare, for sharing that. You're a very brave young lady. I can empathize with a lot of your feelings and I would just like to share that I lost my final vision in 2011. And I was depressed and I was like very anxious. And scared. And I've had some time to adjust to it. And I am on antidepressants. And I did a blog recently because I've had an aha moment. And I am no longer scared of blindness because I'm blind. I don't have to adapt to changes. I don't have to adapt to the constant declining vision. And I don't have to -- you know, constantly make changes from the cane to the dog to print to audio to screen reader to JAWS to make -- you know, I'm in a final place until there's a cure. So someone tweeted after my blog was posted "What is scarier the journey or the destination?" And I think for my personal experience, the journey is far scarier than the destination.
So let's go on to John.

>> A moment for the interpreting process. We can switch interpreters in this moment.
John Romish.

>> John Romish: What specifically would you like me to say in the introduction? A little bit about my background. Will that work? A little bit about my background in the introduction. Will that work?
>> MOIRA SHEA: Yes, that would be perfect.

>> John Romish: Good afternoon, my name is John Romish and I live here in Seattle. as I said earlier, eight blocks away from here. And I've been in Seattle for

19 years 8 months. I was born in June of '63 and I grew up not using sign language but using lipreading and using my voice. I didn't know sign language until I was -- well until about '75.
So between my birth to 1980, I really didn't have any sign language. And I -- well, for example, my brother would throw a ball to me, this red softball and I was supposed to hit it you know as kids do. We play. And I could hear the ball being hit by the bat but I couldn't find it.
And I would look and look and look and that was the first indication that I had something going on with my eyes.
And what's it between '75 and '80 that I started to notice there was something going on with my eyes. We went to a variety of doctors in Boston, Massachusetts, and none of them could really diagnose me. And I was at a loss.
Later my father was working in Portland, Oregon -- I'm from Boston. But moved to the west coast to Portland later on. And there was one hard of hearing person that I was the only hard of hearing person in a mainstream school. I didn't go to a deaf residential school. I went to a mainstream school.
And the teacher would say did you see me? Could you see what I'm writing on the board? And later I realized that I really couldn't see a lot. And my parents and my self with my hard of hearing teacher and one of the supervisors who is working in the public school for -- but with a deaf program let me know that they're suspecting something is going on beyond my hearing loss. So I went to Oregon Health Sciences University.
And Richard G.Wilbur was there and I met him when I was 16 years old. And he said you have something called Usher syndrome.
And I had no idea what he was talking about. And of course, mind you, I'm a 16-year-old boy. I didn't readily take that information.
I was graduating high school in '83 and I was at a loss for what I was going to do. I planned on going to college all my life.
In '84 was the first time they had the American Association of deaf-blind conference here at the University of Washington. And there I got a sense of what this Usher syndrome thing is. Prior to that I met very few people with experience like mine. There I met hard of hearing people, I met people whose vision was changing and I found my support. And that was in '84. The summer of 84, I had my parents come and I explained what was going on. And it was the first time I was able to accept myself for who I am. And I had some pretty blurry vision at that time. There was no SSPs available to me at that time. I was fortunate I had a community but I rally grew when I found -- really grew when I found that community of people with Usher.
I got a college certificate. And I started working. And the job that I was first in in '88 wasn't really working for me. So I lost that job and I said -- you know, it's time for me to do my mission. With my church.
So I did that for two years. In '89 to '91, and I came back home after my church mission and start the looking for work again. That journey of searching was five years.
And I tried to be optimistic about it. And then I found the Lighthouse for the Blind and they hired me. And I've been working there for 19 years. And 7 months. Time really does fly. But the Lighthouse has several people with Usher's syndrome there

and a few people who are deaf-blind from other causes. But now I'm really focused on practicing with pro tactile communication with the deaf-blind community. So people can let me know what's going on in my visual world around me, not just my auditory world behind me. It's really helpful for me getting a sense of everything that's going on. But really excited to be here this afternoon. Thank you for your time. [Applause.]

>> Moira Shea: Thank you, John.
We're going to do an interpreter switch now.
In the Usher's community we try to have diversity. So we have someone -- an individual who is totally deaf and we have a young lady and we have Ramona Rice and now I'm going to introduce you to a parent of the individual with Usher syndrome. John.
Take it away.

>> Hello. I'm David Hebert, I'm from Louisiana. I have three children. Oldest is Catherine. She was diagnosed at birth with a profound hearing loss and man, we got a lot, lot of, lot of information, a lot of help quick and a lot of resources pretty fast.
So it did hit us kind of hard because there's no history of deafness in our family. So we were kind of confused. Didn't know where to go, what to do. But in the turn we had a lot of resources available to us at the time. We had early steps, parent pupil educate tore, Baton Rouge hearing, all that LSD, all that Louisiana School for the Deaf. So -- not the drug. Just letting y'all know. I know I'm from da bayou, nothing like that.
[Laughter]
We get this help and learning sign language and they're telling us about the cochlear implants. We wasn't really, really really sure from day one that we wanted the implant because it's our first child, kind of protected, didn't want to put it -- head for sure. After probably months of discussion, going back and forth, we figured it will be best for our family to go ahead and give her that option. We felt that if we got her implanted and once she grew up and became an adult and she wanted to embrace her deafness, she could take off the implants and put them in a drawer and just be deaf. So that's why we got that. So we're doing good. Going -- get all this help. Speech is coming around. And at the time we decided to get implanted. She was going to get first, didn't do bilateral back then. She was going to do one implant and she was going to get it in 2005. And the only thing that implanted in Louisiana we had to go through New Orleans and of course y'all know because Katrina came through that year and that kind of put a damper on that. So in 2006, about April, she got her first implant. Got turned on a month later. Going through like I said, LSD and Baton Rouge speech and hearing a lot of lot of resources and then about 2009 rolls around and she gets her second one. And she really, really takes off doing well. So we decided to pull her out of the Louisiana School for the Deaf. Not LSD. And go ahead and put in mainstream school and she did very well for the first couple years. And then all of a sudden she started getting real clumsy at night. Get

all very scared, very all this and we're like -- we thought she was just -- you know, making excuses. Wasn't really taking her sincere. And so we, like, what's going on? So my wife made an appointment to the eye doctor and just average eye doctor, no specialist and they did an opti map on her retina and she seen some spots and she said something's going on here. So they sent us to a retina specialist and he kind of set kind of looks like RP. We're like what's RP? Never heard of this. Like retinitis pigmentosa. I'm like all right. Never heard of that before. So we even scared even more like Okay. What to do. And through all these years through all these systems and stuff, that one time daughter was born deaf maybe we should look into Usher syndrome but this is the first time in 2011 that we're hearing that this syndrome exists. So you know, do like any other parent do, get home, start researching and start reading definitions, start seeing all the different types, all this. Happened to be the coalition Web site. Google, sitting down looking at her, I see that Mark is the chairman and all this contact information is on it. Sitting there looking at it. So I go ahead and sent an email and I want to say within the day got email back. I'm like well, that's pretty good. He had -- answered my questions and gave me some direction where to go. And for once started feeling a little bitter. Until we get research yet went through the University of Tulane and genetics and stuff and got to pinpoint she has Usher's type 1B and just like I said, went through a lot and don't really see too much where I'm from. Finding this Web site and this community made us feel like we belong. We had a community of people that we can talk to you know because when we're dealing with this, we also have life, we have every day challenges on top of this so just to give people advice or just help or direction and which way to go, it's very helpful. So that's where we are right now. [Applause.]

>>So I'm going to ask the panel a question or just ask them to elaborate on something. And if someone doesn't pick up the microphone within 15 seconds then I'm going to call on someone.
So what I learned is that when you have a combination of deafness and blindness you face also discrimination -- deafness and deafness and blindness, you face discrimination and when I worked on Capitol Hill 20 years ago it's common for someone to go to the floor with the Senator when they're introducing legislation that the staff person has been key on it.
And when the Senator asked for me to be able to go on the Senate floor it was refused. It was very unusual. And so I knew this was going to happen. And Senator Biden from Oregon we were able to -- we had done the evening networks and all the international papers and next day I got on the floor and I had to stand up for my civil rights. And I didn't grow up in an era of self-advocacy, advocating for my rights. I think as I became older I learned to do it. But I think today I know today that younger people with Usher's are learning to be self-advocates. So I would like to ask someone on the panel to share advocacy and education or transportation or -- in the supermarket or you know just for other people to learn how to become better advocates and fight the face of discrimination.

>> DAVID HEBERT: I'll take it. I found myself when I go out in public or we're at a

cam will ground or normal every -- campground or normal every day places like Al 0'Riley's shop I noticed she had cochlear implant and I introduced myself and started talking to her and let me know what kind of options there out there because in Baton Rouge the Chesney Center is very, very top notch speech therapist out there. And I just wanted to know she knew about it and she didn't so we got talking and I was trying to see if she had any eyesight problem just in case nobody told her that hey, you got this hearing problem, you might have this vision problem too. So you know, you might want to look in to, you know, maybe Usher's or something like that. I don't want you to walk in like a brick wall one day you find out all of a sudden you have vision problems associated with this learning problem so we became pretty close friends. Every time we go into O'Reilly's we talk and check on herself. She kinds of lets me know how she's doing but she's going through some therapies and stuff and it's like what I do.
Great.
Ramona, you seem like you might know a lot about self-advocacy.

>> RAMONA RICE: Well, like I said, you know, is it on. Like I said two years ago when I created that Web page the Facebook collaborative partnership. Once I start to meet people and tell them what my goals are to help the deaf-blind community, and the importance of it, once you make an appointment with them and sit them down for more than five minutes they'll listen to you and they want to participate. So for instance like a disability law center and Utah transportation authority.
I saw a lot of problems that we have in the community. So I joined their board just so they can be educated. Not in a bad way because they don't know what it is that we struggle with. Smallest things. You know, like let's say the train comes by they're supposed to the in the ADA session to sit down in a disability section and then to help you get off at the appropriate platform. But, if they walk away and don't think about it, they're really not doing their job to help us. And then we feel discriminated against. And for whatever reason. So that is where I felt that I have to step up to educate the staff and the facility. The importance of it. It's about not just appropriate training for -- to serve us but it's also to help us traffic safely and how we can get on and off safely and how we can cross the street and little things like that makes a big difference for us. We didn't ask to have Usher syndrome but we're doing the best we can with what's given to us and same thing with communication access. I've been really hitting hard in Utah about you know we're being deprived of having communication access through the Web site because they don't have it where we can call in. So we want them to modify their Web site so we can type it in and ask for online chat line so we can communicate with them. That would be great for Usher syndrome or deaf-blind people especially for speech impaired. Just the little things that you can think that would make a big difference but it doesn't work overnight. You just got to work with them time after time and it does take a while for them to change the program or their software. But I think once you get them committed, that really helps. And so that's what's working for me in Utah.

>> Thank you, Ramona.

Clare, do you want to talk a little bit about advocacy or what you've done in school to get accommodation or -- you want to share a little bit about that with us?
>> CLARE WEIGEL: Well, I'm going to college in the fall –

>> MOIRA SHEA: Excuse me, Clare, I'm sorry. We need an interpreter break. Time is going fast.
>> CLARE WEIGEL: Oops sorry. I'm going to college in the fall and the year began to come to a close my mom and I were talking and we realized that you know, the college I'm going to has a lot of random steps because it's a very hilly campus and the last two times I've been there I tripped. On the stairs. So we got around to talking to the disability advisors and they've been fantastic. I was very adamant about how I wanted to have orientation of mobility training at school even though I already do have current O&M training at home in Tampa. I love my girl she's awesome.
And you know gradually it took me a while to get used to the cane. At first it was like some mythical object. I was terrified to touch it. And then I got used to it and oh, it's basically an extension of my center so I got used to it. It's really nice when you're out in public and you're using it. People move for you like the Red Sea, it's awesome. I love it personally. I don't have to worry about running into people. It's pretty nice.
[Laughter]
But at school I'm going to have O&M training and I already have priority seating when is awesome because I cannot see far distances like fine print so that will be awesome for me to be able to see what the teachers have on the screen for PowerPoint and that way I'll be up close so I can hear them. I also have a CART system for my classes, which will be fantastic especially for long lectures, I'll be able to see what my professors are saying. So I have to really talk about what I wanted and whether it was too much or not enough for me so I have to learn to get adjusted to that. However, when I was younger, I was going through 12 years of speech therapy and I absolutely hated it. I felt like I was different than all the other kids because the teachers could never understand me in elementary school. They'd stoop down to my ears and I hated it. I felt so different. So I was channeled toward speech therapy. I hope y'all can understand me. I talk fast when I'm nervous. But I had to gradually get used to accommodations, I carried around a huge speaker box when I was in elementary school. it was on my shoulders, it was really heavy. I carried it around. People -- this is the worst part people in my class would use it to spy on teachers when they walked out of the classroom when they went to the bathroom. I listened to my teachers going to the bathroom when they were still wearing the headset. And my classmates would turn up the volume. You could hear the toilet flush, the sink, everything.
[Laughter]

They would walk back in -- and the teacher would walk back in and like what are

y'all laughing at? That was my accommodation during elementary school. I didn't like it. Once again I hated it because I felt like people were laughing at my expense because it was something supposed to help me, not to laugh.
But so as I've gotten older, I've had to get used to advocating for myself. So I've gotten used to that and I will continue to get better at it. There are times I'm a little too quiet and times I'm a little too bold about it. So I notice that a lot of you are parents of young children who have cochlear implants. Look, I'm just going to tell you this. They're great and they're going to learn how to adapt to being in school, to being around normal hearing children.
It won't be easy sometimes. Sometimes they're going to feel like a little set apart. But sometimes they're going to feel like the coolest people in the world because kids are going to ask them hey, what's that. And it could be cool and they can tell them things about themselves that's completely different. And you know, being different is not a bad thing. You're advocating for yourself being different in a positive way. There's really what I learned from my own experience.

>> MOIRA SHEA: I know Clare is a tough act to follow but on the other hand let's have a parent talk about advocacy I don't know if you have a story to share about school or whatever. Appreciate hearing from you.
Who did not speak. John, please speak. I'm sorry, I missed you. I'm sure you have a lot to share.

>> JOHN ROMISH: Yeah, thank you, no problem. I do want to back up and say that while I was in college I majored in graphic production. So it was for print.
And I used cameras for making print and I learned a lot about that for three years. I was doing graphics and I got my certificate and then later after I graduated college, I was looking for a job. Of course, something that related to that. And I found a job with a federal government in Salem, Oregon, doing print making. And I was there for three months and that's when I lost my job. Said I wasn't able to keep up with the pace of the workplace and the graphics I was producing weren't centered or were at an angle and they needed to be exactly the layout needed to be exactly perfect. And so you know, I wasn't using enough ink or I was using too much ink or not enough water or too much water and I lost my job as a result of that. I mean, after only 90 days.
And my father then suggested that I do something quite different, that I drop the degree, my major all together, and open my mind and try to do something else. Pursuing the same career wasn't going to be beneficial to myself or anyone else. And I know that sometimes when you're through getting through your college years and lifelong dreams, this Usher's thing can really throw a wrench in things and you have to be amiable. You have to be flexible to switch gears midstream. And it can be frustrating at times. A friend of mine joined my church and I went on my mission and that's when I let go of the idea I was going on a print maker or work in graphics and I went something different and I met other people like me who were deaf or had Usher syndrome and that was helpful. For me to gain the skills to advocate for myself. I did that for two years. Came back. Came back to Portland. And was at a

crossroads. My father suggested I do something different as I mentioned before. So I was looking for something different and I wanted to try to work perhaps in production. I liked working with my hands. I liked working on machines. And I'm a very assertive person. I didn't want to go through DVR. I wanted to do it myself and after about four months I went on eight job interviews and about 30-40 different places that I applied for -- this is in '91 and I finally got that job at the Lighthouse. And I'm working quite different work right now. I'm -- I've learned hinge strips and different sorts of production materials. And I started to lose my vision more and more. And I was -- you know, expected to do certain things in the warehouse where they were driving forklifts and they didn't necessarily have lights on the forklifts. They had horns. And that wasn't good for me. So they had to accommodate me and I had to ask for those accommodations. And sometimes I wasn't -- I was a little paranoid to ask for the accommodations, I'd just come from a job that they fired me from. And so I wanted to be able to advocate for myself but walk that fine line of keeping everyone happy.

And I quit that job because I knew that it wasn't going to be right for me. The situation was too dangerous. And it was quite frustrating. So I'm -- I have to think about my safety. And I was the only deaf-blind person, really the only deaf person there. Everybody else was sighted in that door hinge job. And I lost my job there. And I was thinking Okay. I can use all of this information to inform my next decision. And that's when I went to the American Association of deaf-blind AADB conference. And that's when I saw first hand the Lighthouse for the Blind had a booth there. And I said this is a place that I need to keep in mind. I didn't go just then. I was thinking about college. My degree that I had. I was thinking about my experience. But in 94, July of '94, so that was quite sometime after I met the folks at the lighthouse and their booth at AADB, I went and I said I can work with my hands. I might not have clear vision, but I can work with my hands and they said that's fine. We have people who are running machines that are fully blind. We have machinists who can see some. We have somewhere peripheral vision, some without. And I thought well, I'll have to be really careful. I have to at my workplace every day I'm pushing carts full of materials through aisle ways and I have to be real careful about where I'm going and what I'm doing. And so I tried -- I applied to the Seattle Lighthouse for the Blind after I had that initial intake. Sent the application and thought I'll just give it a shot. And they called me up for job training. I had 12 hours of job training. At that point I did have a case with DVR.

And I think it was a few days later they hired me. And then I had cataract surgery to remove cataracts in my left eye. It was -- I was experiencing pretty blurry vision. My right eye was pretty okay. But my left eye was pretty blurry. So I had that surgery and then moved to Seattle. And about you know two or three years later I'm still at the job at the lighthouse. And now at the blink of an eye I'm at 19 years, seven months. I learned a lot not just for myself and experience advocating for myself but also my co-workers, I have to advocate for even Braille. When I'm working on a specific type of machine I work on a machine called a Nokuma, a computer numeric controlled machine. I was trained to do that job by another deaf-blind man who also has Usher syndrome. So not just how to be safe but how to advocate for yourself and how to advocate for your safety and your promotions

and your next possible job. So I have to say I really relish that job. It's good for me. There's a critical mass of people who have deaf-blind there who use American Sign Language as well and I'd like to stay there until I retire. This is by the way the third time I've been at this meeting and I appreciate you hosting these meetings, thank you. [Applause.]

>> MOIRA SHEA: Thanks for sharing that. I think it's important to learn and become advocates in both employment and education arena because those are the two most critical parts of our lives. Quality of lives. I we're doing an interpreter switch.
I would just like to tell a quick story about two years ago I wanted to join a new gym and they were putting me off, putting me off, putting me off.
And I think it's really important to really know the significance of title 3 of the ADA because in there it -- in very specific about public places making accommodation for vision and hearing. So in this gym I take yoga classes, I take other classes. And they're very accommodating in providing excellent verbal cues and making sure that I can hear them. Title 3 of ADA is probably one of the most important resources we have.
We're past the 45 minutes so now I'd like to open the floor to Q&A. Questions? Comments?

>> MARK DUNNING: Does anyone have questions.
>> MOIRA SHEA: I can't believe this.
>> MARK DUNNING: No, we have questions. Just a second.
>> MOIRA SHEA: Okay.

>> AUDIENCE MEMBER: Hmm. I don't know if this is really a question actually. But as a person who grew up deaf, deaf-blind, really, I have two brothers that are deaf-blind. My parents can hear and they're also sighted. They also have two brothers that are sighted. One thing that I want to share especially for those who have cochlear implants -- I'm not criticizing the cochlear implants at all. I support speech and language absolutely. But you could consider ASL as well. Suppose you have a cochlear implant that isn't working or your hearing deteriorates over time or your vision deteriorates over time. Communication with my father and mother unfortunately because they never learned ASL is not available perhaps. Or if you don't have communication through ASL with your children. So it's kind of a backup communication system. That's one thing that I wanted to share with you all. ASL is also a viable option.
>> MARK DUNNING: Thank you. We have another question. Thank you for that.

>> AUDIENCE MEMBER: My name is Jody Reeves and I'm here with my family from Pittsburgh Pennsylvania my daughter has Usher's one, she could not join us today because she's doing training at Helen Keller National Center right now. My daughter actually joined our family from China at 11 years old. And so there was no

language stimulation for the first 11 years of her life.
She was in an orphanage. She is not a candidate for an implant. So I concur with the recent speaker. We are an ASL family, all of her siblings are deaf. Now in our state, I'm aware of the national deaf-blind funding that comes through Helen Keller National Center and it goes out through different states. In our state yearly we have a deaf-blind conference. The challenge that we found is when we've gone, there's about 50 families that attend and not any of them sign.
And so I'm wondering about the support for people with Usher syndrome that do not wear implants that are part of the Deaf community that are signing when we go to these places to get support and where there's national funding, I'm wondering why we're not including people who are part of the ASL community. It's hard for me to understand how we could go to a conference where there's 50 families and none of them are signing except for my family. I'm wondering if anyone could respond to that.

>> MOIRA SHEA: I don't know if anybody on the panel can respond to that. Anybody on the panel?

>> RAMONA RICE: I understand about lack of support and families not knowing ASL. But to go to a function thing not getting additional support, it can be really hurtful for those who want to have that communication access to be part of a team or part of the group. It's really important. I think it really should start with you to make that awareness. Given the fact that not everybody can be extrovert or introvert. But, if you find as a passion to help your family, you know, your daughter or anybody else, I think it should start with you. Because, like, I have a 60-year-old autistic grandson and we fight for him. 16 years old. We fought for him because he wasn't going to the right school. He didn't make it in a mainstream school. We had fight and get a doctor. We had no knock on doors because we love him that much because we want him to be successful when he grows up. He needed to be in that program. That's what we did. I felt my parents should have fought for me but they didn't because they were in denial about me being deaf or hard of hearing. So I didn't speak at all until I was in 8th grade and just like Clare, that speech therapy it was brutal. It was embarrassing. It was demeaning to me. And it took me a long long time to get where I'm at. And I was quiet as a mouse, believe it or not. But I learned to open my mouth and speak up and so I started to educate people a lot about the Usher syndrome. Like if I go to a restaurant, I would tell the server I'm deaf-blind believe it or not so, if you bring something to the table let me know you brought it I'm not going to hear it, I'm going to make a mess and you're going to clean it up. So I learned educating them is the best way. They don't know what we're going through. They think it's a small thing that can be overcome but it's not. It's a big thing. Start with you, you don't have to start big, just little things. Okay? I think that's the best way to go unless somebody wants to --

>> DAVID HEBERT: I can add from our perspective.
We weren't an ASL family from the beginning. Once she got implanted, therapists

were like stop stop stop. No, that's her first language. We stayed with sign once she got implanted and once we got to the main steam schools, early steps, parent educator, we wasn't at LSD no more and getting that sign every day. And just over time we stayed with it and just one morning we woke up and we wasn't signing any more. It was just kind of -- it wasn't like we just turned it off. It just kind of just ran its course. And then I guess, just as Catherine got older and more dependent on hearing, she started using it less. And I guess as parents we sit there fighting we're going through the therapies and all this other humbug we've got to go deal with, we just didn't realize that she was using it less. We was using it less. Like I said over time, it just was a gradual decline and now like I said we barely use it. I wish -- I really do looking back I wish we would have stayed with it. So maybe if you can get something going in that way families got another resource, you know, and -- just keep it going like I said, I regret us letting it go.

>> JOHN ROMISH: This is John, a moment for the interpreting process. Yeah, first I'd like to say with regard to Deborah's comment about cochlear implants, you know, some parents if they have a child and they're diagnosed with Usher syndrome, I think the parents need to make that decision whether or not to implant their children. I noticed that many of the Usher children who do have implants the parents made that decision and they don't allow sign language. I think you really have to consider all of your options. You know, just want to warn you that there are a lot of people in the world and it really different to hear through a hearing aid versus a cochlear implant. It's quite different. You have to go through training, speech therapy, you have to do sound training. So I think -- you know, yeah, sign language is one possibility, one viable option. But it's really there's a lot of options out there and you have to measure your comfort level and what's best for your family. But what's new is I bought these hearing aids that I'm using right now at the Hearing, Speech and Deafness Center in Seattle. and they were $4,000. That's better for me and my age. I can hear a little better and my mother said my voice was a little too high. With these hearing aids I can modulate my own voice and sure they're able to hear me. My family is used to listening with my voice and other families have a variety of other things going on. When I talk with Mark dunning for example, I know that I can understand his voice. If I were to just try to concentrate on his voice using my hearing aids. So it really depends on the individual and what they're using for amplification. Good luck, Deborah.
>> Clare, did you want to add something.

>> CLARE WEIGEL: Thinking from the perspective of someone who does have cochlear implants, I know personally it was a hard choice for my parents when they found out I was completely deaf. So as you were saying that, you do have to make the ultimate decision for your child. You have to think about everything. And I am just so thankful for the ability to hear and speak. When you do have cochlear implants you do have to go through sound therapy and training and finding courage because they want the child to be determined to speak as a first language and not to sign. And so I've been speaking my entire life and I tried to learn sign language. One time. And you know it's kind of hard for me because I can't quite see. I just

wish that I would have -- if I was to start learning when I was younger, I would be able to communicate with everyone I encounter with sign language. So I think you have to look at it from your own personal perspective and I do wish more people out there did know ASL that way communication could be deeper and more meaningful and speaking of someone who would love to know how to sign, believe me, I've tried so many times it's so difficult for me with my vision to read the sign language. And I would just say that you know you have to think about it's hard decision in the first place to get cochlear implants and there's a lot that comes with it. So I can understand the frustration of not having enough ASL. Or something more people join the conference with ASL, you can bring your friend and families with you. Bring more people.
You know? Bring the whole parade of them. Encouragement.
Look for friends and family for support. I can honestly say that's the best thing you can do.

>> MARK DUNNING: Thank you, Clare, we're going to have an interpreter change. And then I think David has a question.
>> This is David Alexander, I asked a question earlier. But I don't think this is an either/or. ASL or cochlear implant by any means. My daughter has a cochlear implant. She knows ASL and she knows tactile signing. Keep in mind that your affected child or yourself are going to be dealing with people who don't have cochlear implants and the only way they can communicate effectively is through ASL or in the instance of deaf-blind tactile signing. So I don't view this was one or the other. Rebecca is very much involved in the Deaf community even though she has a cochlear implant and is part of her psychotherapy practice she treats patients who don't have cochlear implants but are deaf. So she needs to be able to do ASL. So you know, I -- it's individual, it's personal. But you're going to encounter a lot of people hopefully in the deaf-blind community or in the -- in the deaf community and you need to be able to communicate with them. It will empower you. Thank you.

>> MARK DUNNING: I'd like to ask the next question if that's okay.
We've had a bunch of questions about hearing loss. I want to ask everyone on the panel which is worse, the hearing loss or the vision loss?
>> RAMONA RICE: Vision.
>> Vision.
>> Vision.
>> Vision.
>> So why?
>> RAMONA RICE: I think it's because I was born with hearing loss so I'm used to and then later in life at age 42 you kind of notice your vision going bad and you can't fathom an idea of losing what you've been seeing all your life. I think my biggest scare at first when I was diagnosed is losing sight of my children's face or grandchildren or how am I going to function as a deaf-blind later on? I think no matter how prepared you're going to be I'm somehow not ever going to be ready for it. But with all the education that coalition has given us and what we can do by self-advocating, I think we can be ready. It's not going to be easy. So vision is the

one that's brutal for me to lose.

>> MARK DUNNING: David did you have something to add to that?
>> DAVID HEBERT: It's just hard. Catherine was born deaf. That's when from the beginning. But when you see vision loss, you see running into big objects and hurting herself, it kind of hurts you as a parent and makes you feel like what am I doing wrong? I need to help my daughter and you really don't know what to do.

>> John Romish: This is John. I would like to add here I think as I mentioned I was born hard of hearing and kind of learned how to lipread and that sort of thing. But as I lost my vision, it became more and more challenging. And just relying on hearing aids, the misunderstanding and the communication itself just becomes an obstacle and you just misunderstand each other over and over again. So I would definitely say the vision. Sure I'm not going to advocate for my one method but, if you're raising your kid to lipread and the kid is going to lose their vision over time you might want to add sign language for communication, for example. My ex-wife in bed every once in a while she could tap my shoulder and I would put my hands on top of her hands. We didn't even need to use light. I could feel her signs, there was no voice happening. There was no light in the room and we were still able to communicate as though I were fully blind. Having all of those options available to you is really great. Do what you need to do but it can be as simple as that.

>> MOIRA SHEA: I can definitely relate. I wear two hearing aids and when I lost my final vision I lost my ability to read lips. And it was not something I ever thought about. In all my planning, I never realized how much I depended on reading lips. And nowadays I just have a difficult time hearing people. Especially a conversation going on between different people. And I'm like is it my vision loss or is it the digital hearing aids or I need to get them reprogrammed? But it is very frustrating, really terrible.

>> John Romish: This is John. I'll just say one more -- just to add to that. When I take off my hearing aids at night, I am fully, fully deaf. And so you know just having that stimulation.

>> CLARE WEIGEL: Excuse me. I do want to add that you don't have to determine all of us agree it's vision between vision and hearing, but it's amazing how you can kind of simultaneously lose both of them. But you can still use what you have remaining. The vision I have left is not perfect at all. I constantly have floaters. Like once in a while there will be one float are I have I'll just chase around with my eyes and people think I'm crazy because my eyes are moving in every direction. And you know, there are times in different environments I will crash into people. I've literally broken glasses in restaurants before. But I do read lips a lot of times. That way I can ensure that I'm doing everything in accommodation because my hearing is not perfect. Even though I do have cochlear implants. I have tried to learn how to

read Braille and it's fascinating to me how just the little bumps in the paper can just tell awesome things. I started to learn it's not perfect. I only know 18 letters of the alphabet by the way. But I just love being able to experience everything about it and there's just so many options you can have to cope it with it is all I wanted to add.

>> MOIRA SHEA: I'd like to ask the panel in terms of my vision loss, I have not had the temptation to learn Braille. I find information so accessible on the iPhone and you know in different programs and apps and the only time I think I would use Braille would be to be able to find the button on.

>> I use it on the keyboard of the Braille keyboard. It's so much, much more defined and I was able to read it. I don't know why there's a difference between the keyboard and papers. But I find my body or myself I'm more receptive to that keyboard because it's much more defined from a computer. So that's kind of interesting right there.

>> AUDIENCE MEMBER: My name is Steven. I'm from the Long Beach peninsula recently having moved there. I guess I have Usher's 2 that's what I've been told but it hasn't been verified. I grew up hard of hearing, mainstreamed for the most part. And it wasn't until 1974 when I was 24 that I was diagnosed with RP. And part of what happened after that is that I went in to a 10 year denial process which ended the day I gave up driving and I wonder if anyone on the panel or anybody else here has gone through that sort of process of the denial of the blindness mostly and finally realized well, I need to move on. That's really all I wanted to ask and comment on.

>> MOIRA SHEA: I can say that I learned that I probably would lose my vision when I was 15. So I deliberately made a point of leaving in the city with public transportation -- living in the city with public transportation and I never learned to drive because I thought it would be too difficult to give it up and I could never forgive myself if I ever hurt someone. But that's you how I dealt with it. So Ramona.

>> RAMONA RICE: I don't think anybody would jump up and down when they're diagnosed with deaf-blindness and they have to hang up the key. I remember when I hung up my key because I almost hit the light pole in the parking lot. Because it wasn't there. But I think that -- you know, there's five stages of grieving. And you should have to go through it in order to make it through it. I was in denial for about two years, actually, I was really angry. I bawled all the time. But then I decided to stop it because had to do it for my children and show them how strong I could be and I owe it to them. It's always about them to show or at least lead by example. So I think -- anybody else.

>> CLARE WEIGEL: I don't drive. We don't have a lot of transportation options in Florida but we have buses. We don't have trains or subway although I wish we had like a T or like a monorail I really wish we had some. Like my parents drive me places out of the goodness of their hearts even though I might ask a little too often.

But I have friends I can ask to drive or other family members. And it's really difficult because I never know the sweet freedom of just being able to go for a drive by myself. If I could have any wish in the world just even like 10 minutes I'd love to drive along a woodland path or something, I'd love that so much. But for someone who has driven, people who have driven and had to hang up the keys, I do not know how to relate to that. Although I can add I would really love to know how to relate to that because I'd have loved to be able to drive just one time.
>> A moment for the interpreting process. John has a hand up.

>> JOHN ROMISH: This is John. Yeah, I was in denial for a good four years and you know, I didn't real eye understand that denial in the that AADB conference that American Association of deaf-blind conference. And I met some friends and colleagues that really helped me with that acceptance so I'd say at least four and a half years of denial and I think that's a common thing for people with Usher syndrome to go through.

>> DAVID HEBERT: We didn't have denial with vision, we had denial with hearing loss. You know, how it goes. First hearing test failed at hospital. Oh, that's common, fluid on the ears, second and third one and failed and you start getting a little nervous and of course you go do the big test and it comes back and is deaf and then you sit back maybe they got it wrong but it took us a few months to really swallow that pill. Once we did that and started moving forward, once we found out about the RP, we just didn't want to waste no time on really being in denial because we didn't like I said know what it was. So we just wanted to educate ourself and just start moving forward.

>> MARK DUNNING: Are there other questions out here for the panel? Moira, do you have any other questions you'd like to ask the panel. We're going to do an interpreter switch.

>> AUDIENCE MEMBER: This is Mitch. Very good. Thank you, Mark. This is Mitch again from Portland with Usher's 3.
And I wanted to return a little -- a few minutes ago to that question of which of the senses is -- has been more -- it's been more difficult to deal with the loss of. Because with Usher's 3 I've had my whole life experiencing declines in both hearing and vision.
And I've gone through different stages and different plateaus. I can honestly say that from the time I was diagnosed in my 20s until I was about 50 and got my cochlear implant losing hearing was more difficult for me. I agree with Helen Keller who said vision problems separated me from things and from some activities. But the progressive hearing loss made it more and more difficult for me to communicate with people. And that was much more painful.
Then I got the cochlear implant and it was like a miracle. It really turned my life around. It made it so much easier for me to participate in many social activities. In the last few years, my vision is much worse, I probably don't have a whole lot more time left. As a person with very individual you'll vision. I probably -- residual vision.

I probably will lose the rest of am I vision sometime in the next few years and that certainly is scary. But as a matter of fact in the last year I've gotten involved in the Northwest association of blind athletes. I've been going hiking and tandem biking and kayaking with them. I'm the only one with hearing loss in the group but many of these other are blind people, some of them are totally blind. Obviously they all have some degree of severe vision loss. And it's been quite encouraging for me to be around people for whom it's only vision loss that they're dealing with. And for the most part they were all doing pretty well.
So scary though vision loss is, I think it's something that can be manageable.
And last thing I'll say about that is when I was a counselor, voc rehab counselor for people who are blind and low vision, we used to say that vision loss is almost never the primary disability that people have. The primary disability that people have would be whatever difficulties they had adjusting to their vision loss. And that actually vision loss can be quite manageable. So I guess I wanted to just share those things. And I don't know if anyone has any comment or my comment.

>> MOIRA SHEA: No, I'm just very glad you spoke up because as we were answering the question of vision loss I wished we had someone with Usher 3 because they're the ones that can really speak to it. So thank you very much.
>> AUDIENCE MEMBER: You're welcome, Moira.

>> RAMONA RICE: Thank you for sharing that. I just met with my really, really good audiologist and I was telling him I just got off chemotherapy and it affected my vision a lot and I couldn't figure out why I wasn't hearing as well. You know, then what he was just saying because of your hearing and vision and lipreading or looking at people and working together but when your vision is being clouded or you've got the blindfold on it's auditory process that's not working properly for you to hear anything. So I kind of want to let you know if your vision is going and you feel like you're not hearing it, just kind of remember according to what he told me, they both work together and if I feel like you're losing your vision not able to read lips or anything you feel like you're losing your hearing as well, I think that's normal. You're not losing your hearing it's just that process is not getting to your brain. And so I kind of wanted to share that.

>> MOIRA SHEA: Thank you. John is going to say something, but I just want you to know that the dialogue today is not going to end. Because Usher syndrome coalition has made a blue book like a list serve and the forum will be saved and archive comments so, if you have questions about other syndromes or cochlear implants, share that with the forum, the blue book forum and all of us will respond as much as we can. This is a brand new resource for you and it has a lot of potential and I hope we can continue that dialogue with the blue book and maybe Nancy can say a few words about it later but I want you to know this is another resource the coalition has brought to you. So John, you want to speak?

>> JOHN ROMISH: Yeah, this is John. Just related to Mitch's comment. I definitely understand when you talk about your eyes -- I think we're all going through

the same process because it's a dual sensory progression. And there's nothing wrong with that at all. In my own research, 36 years experiencing Usher syndrome, you know, as I -- as my vision changes, as I get older, I mean I can imagine I'll be fully blind. And fully deaf. And by the time -- by the age of 60, we might all be. But I mean, will a cure help. I don't know. We've spent the whole day talking about what might be coming down the pike in the long term.
So I just think you know relish today and accept what's going on. And learn from what's going on. But really be in the now, be in the day. And think about your life. Your mind is functioning and you have the resources available to you and use them.

>> MOIRA SHEA: Thank you. We're reaching the end of our panel. The takeaway that I have that I've gotten through my life experiences is -- Darwin is wrong. It's not survival of the fittest. It's the survival of the most adaptive. And I think all of the panel and all the people that I met with Usher's have shown great capacity to adaptive and that's what we do and that's what makes us strong. So with that, we're going to -- I'd like to thank the panel for sharing. It's been really, really great. And we're going to -- we're not going to have a break but we're going to go right into the closing session. So would you please help me thank the panel. [Applause.]
If you have any questions for them they'll be here throughout the remainder of the day. Thank you (A.

>> MARK DUNNING: Do we want to do an interpreter switch or are you guys good to go? We're good to go. Okay.
So we just a couple more things before we go, we have for the last several years we've done an ward called the foresight award for which we have given to an organization or an individual that has really helped a lot with the cause of Usher syndrome and has helped people with Usher syndrome tremendously. Our award winners this year are people who could not attend. They live in Washington, D.C. but it's actually and organization called Hill+Knowlton, a public relations firm that donated time to Usher Syndrome Coalition for the last several years and have been instrumental in helping us craft our message on Capitol Hill. And it's a big reason we've been so successful in talking with the senators and the folks there. I think you heard it mentioned earlier they were helpful in the own the equinox event and helping us promote that. They've been tremendously helpful. They give us time every week to help us out. But they could not attend for us to give them the award. But Moira lives in Washington, D.C., and went there yesterday and took a video of them and we're going to play that now. My apologies, it's not captioned because it was taken yesterday but we will have the captioning up here as well.

>> I'm Moira Shea and I have the honor of serving as vice chair of the Usher Syndrome Coalition and I'm here today at the Washington Office of Hill+ Knowlton strategy and they've been generous with their support for the coalition the past few years. They've done rebranding for us and done the logo and Web site and helped us to develop our message. We wouldn't be here today without them.
And I'd like to introduce you to Jordan and Lauren and I would also like to add that the exercise of the heart is when -- and I thank them both.

>> Thank you. We have not opened this yet so we are really excited so we'll kind of -- thank you.
Okay.
Oh, wow.
On behalf of H+ K, we want to say thank you. This is a really amazing things to be a part of and your community is really beautiful (voice breaking) so thank you so much for this.
This is a very, very special thing. And have a wonderful time at the conference.

>> I have to say having -- for the last two years that I've been with H+ K, I came in and almost immediately started working with the coalition and to be able to grow with them and have the opportunity to work with such amazing people has been an incredible experience and thank you so much for the opportunity to work together for this amazing award. And we look forward to doing more amazing things together.

>> Yes?
>> MOIRA SHEA: I have to add if it wasn't for Hill+ Knowlton we wouldn't have the people to make us a success so we'll have to do it again very soon.
>> MOIRA SHEA: They are so great and they are so compassionate and we're so lucky. We are working with such a great team with such a phenomenal global public relations firm. I'm sorry Mark.

>> MARK DUNNING: I was going to read the email they sent me when we told them that we were going to give them this award because I think they kind of sum up the Usher Syndrome Coalition and our relationship with them very well. So bear with me as I read on my iPhone with my bad eyes.
Over the last 3 years we've been in awe of the Usher Syndrome Coalition team, a group that simultaneously raises funds, educates doctors, works alongside researchers, supports families makes life changing connections and constantly reminds those with Usher that they have both hope and the entire Ush family in their corner. There is no job too big or too small for your attention and for that we've been lucky enough to watch you become the leading organization on a global scale. You have given us the opportunity to play a small role in the remarkably impactful work you conduct day in and day out and for that we are so grateful. As you head into this year's family conference, we hope you take the time to step back and enjoy the community your team has both connected and supported. Your work has a profound impact and serves as a constant reminder for all of us at Hill+ Knowlton of the life changing impact a few can have on many. I don't think I can summarize this conference and the impact that you guys have on me any better than those words there."

So thank you very much very much for coming today. If anyone is here who would like to go and have their picture taken, there's still time to have that done. I'd also like to ask Jan if she could come up here and say a couple words about her experiences today with people coming in to get their pictures taken and the artwork

that was done.
You got to see the beginning. Here's the end.

>> Jan: Thank you.
It's honestly hard for me to put into words what we've experienced here today. It's been such an impactful day and I think we said at the very beginning of the morning, it's -- it's really taking a back seat with this idea we have for this campaign. And it's all of you who are going to be the face and the ones who make a difference. And we've been just completely moved first by the art party and watched the kids. I want to give a huge thanks to Melissa and Clare and Bella who basically took over for me.
And I was giving the kids suggestions about what they could draw and they all jumped in and gave much better advice than I did. The children were remarkable and I think what moved Nancy and I the most is the siblings and how they drew and talked about their siblings who had Usher syndrome. It was really touching. And I think again it's just such a -- we were just floored not only by the feelings and the love in that room but also by the amazing drawings we got. Even from some of the really young ones so we're going to the home we're going to scan all the artwork in and we'll have it up on our Web site and the Usher coalition Web site. We also have brought some incredible portraits today. So for all of you who were brave enough to sit in front of that camera, thank you. I think in addition to the portraits, the stories that you've shared with us -- we're just so full of admiration and for those of you in the room who we didn't get to photograph we have the same sort of feeling. So at the end of this day, we're filled up with complete passion and determination to take this campaign and really spread it worldwide.
And I think today is the sort of first day and we'll keep everyone informed. We're about to redo our Web site and we'll be sharing links on both Web sites and we'll keep you right up to date about what will be happening with the portraits, the artwork and the stories. For those of you who had your portraits taken Evan will send a low res. We have all your emails so you'll get something from him so you can see yourself. It's just a huge thank you from us. And I hope that the next family conference we're light years ahead of where we stand today and we can look back and say ah we remember this very first art party and the very first day of portraits and have a lot of progress to report back to you. So thank you very much.
[Applause.]

>> MARK DUNNING: So this has been a wildly successful conference. And we have multiple people to thank for. But I know Krista would like to come up here and say a few thank yous.

>> KRISTA VASI: I won't take too much of your time. It's been a long day. Thank you all for coming. I know a lot of you traveled very far to get here and we so appreciate having you all in this space with us sharing this day with us.
But as many of you likely know, you probably communicated with her, someone who's behind all of this and making this a success today is Julia Dunning. So I want everyone to give her a round of applause. [Applause.]

Thank you, Julia. Curtsy, kisses, yes.
And thank you so much to our interpreters. You've been amazing. Our SSPs, our CART provider, all of this makes this event accessible today. And we couldn't do it without you. We appreciate it so much. And thank you to our speakers. You were phenomenal as always and we love you and we can't wait to do this again next year in Chicago. So we hope to see you there. July 15th.
I think, I hope I've covered it. Thank you, Mark for everything. And we want to invite you all to join us at our evening social just down the road, rock bottom brewery on 5th after. Ave. It's a quick walk away. We hope to see you there around 6:00. So thank you.
[Applause.]