Dorie and Laurie Shapiro

Dorie's Mother's Journey

By Laurie Shapiro

I'll never forget the day we learned our daughter, Dorie, was diagnosed with profound hearing loss. It was March 24, 1989. My husband suspected something was amiss but I thought he was needlessly worrying. We were devastated to learn that his fears were correct. How would she learn to talk and communicate? I grew up in a home that constantly played music. Would our baby ever hear Bizet's Carmen? A friend shared a column reprinted by Dear Abby that comforted parents learning that their child may have a disability by drawing a metaphorical reference. "It was like planning a trip to Italy and expecting to see the gondolas in Venice and the Coliseum in Rome and then finding yourself in Holland with tulips and windmills." We were lucky in many ways because with the advent of cochlear implants and superb auditory training, Dorie learned to listen and speak and was leading a pretty full life. Then fourteen years later, our travel plans changed again, and we learned that her hearing loss was related to a rare disease that was robbing her of sight as well, Usher Syndrome 1F. So now we were off to China to seek the Great Wall and Buddhas. This journey though, is fraught with obstacles that have been much harder to overcome. The rareness of this disease and the intricacies to treat it have proved to be very challenging. Meanwhile, with each passing day my daughter's vision is diminishing and her world grows darker. Her plucky demeanor and confidence have been shaken as well. Like any parent, we hope to prepare our children to take on the challenges and obstacles that life may throw at them. Few of us expect our children to face those challenges without the benefit of sound or sight. So to revisit the travel analogy, how do we navigate these travels without maps or modes of transportation? Funding the promising research to find a cure for this terrible disease will help Dorie and others (and the future children who may inherit Usher 1F) to continue to see and live the promising lives they deserve. I hope we can count on your generous support. ◆

Ebba

Usher 1F in Sweden – Ebba's Story

By Larsola Bromell and Stina Hoglund

Early in January 2018, this adorable little kid was born. For sure - we're biased though seriously don't you agree? Ebba is the happiest, most curious, stubborn, contact-seeking and kind kid we've ever met. Always a smile on her face, always these wide open eyes, never missing out on a thing.

Ebba was born profoundly deaf and... that was hard to grasp at first. Though with early use of sign language, and from 9 months of age bilateral cochlear implants, our communication has never really been limited. She's 22-months-old now, sings "Twinkle Twinkle Little Star," and tells us what she'd like to have on her sandwich. We are really amazed by the progress.

But... oh why is there always a but?... in June this summer we were called to a meeting with Ebba's consultant at the University Hospital in Lund, Sweden. We had participated in a new study with genetic screening of babies born deaf, and we were given the results. That Ebba has Usher Syndrome 1F really came as a shock to us. We had fought and struggled for 1.5 years to give her the best possible start in communicating, and now you say she will gradually lose her vision too? The cruelty of her being deprived of another sense is just impossible to take in.

So - another race has begun. The one against time.

There is progress being made. Just not fast enough! It is so insanely frustrating that research funding can be the single one factor determining if Ebba will be able to have a life with or without her eyesight. Keeping Ebba's vision would mean the world to our family.

Of all this, little Ebba knows nothing. Please help us in this race, finding a cure so that we won't have to tell her - until after we've won. ◆

USHER 1F COLLABORATIVE

NEWSLETTER

December 2019

Sight.Sound.Sweat, Dorie Shapiro front row center

My World Is Darkening

By Dorie Shapiro

I never knew why I was born deaf. Until receiving my first cochlear implant at age 3, all I knew was silence. I never experienced the sense of loss of my hearing. When I was fifteen years old, I found out that I had Usher Syndrome Type 1F. It explained why, for years, I was struggling to see in dark places and straining to see peripherally. It also meant that my vision would get worse. I initially feared that I would be denied the life of a normal teenager. Did this mean that I would not get to have a driver's license and drive around like I had planned? Learning this was earth shattering. I was angry and resentful. I felt that I had worked hard to learn how to speak and listen. I rely on lip reading and listening skills to understand conversations. Would this mean I would no longer be able to see faces and read lips...so vital to my communication skills? Many questions went through my mind without clear answers. Thankfully, I had supportive parents who trusted me to share with them my feelings and the true state of my vision.

I made the tough decision halfway through my senior of college to give up driving altogether. I asked my Dad to sell the car during winter break so I would be spared seeing the car leave, taking my independence with it.

Initially, I felt shame for having Usher 1F. I didn't want my friends to feel burdened to guide me and shield me in dark settings. I worried needlessly since my college friends welcomed the opportunity to help and automatically took my arm to ensure I didn't trip or bump into things. *(cont'd)*

> *I became part of this amazing community at a gym earlier this year, Project 13. When I told them about my balance limitations and struggles, they refused to let that deter me from participating. They created a safe community for me to work out.*

Continued from cover page

Realistically though, I had to plan my future and career choices on living where I could live independently. It meant moving away from Arizona and my home and family because of this disease. I focused on San Francisco because I knew that it was close to home. I had many college friends that lived there already. Most importantly, it offered great public transportation! I moved out there six years ago…best decision I ever made. It took me some time to get used to those hills, but thanks to those, I have strong calves!

I became part of this amazing community at a gym earlier this year, Project 13. When I told them about my balance limitations and struggles, they refused to let that deter me from participating. They created a safe community for me to work out. Earlier this year, when I asked if they would consider letting me host a workout fundraiser there for Usher 1F research, they said "yes" without hesitation! They shared my story with all the members, and we had over 50 people join us raising over $6000! I was so grateful to have such a great support system in San Francisco. It boosted my optimism for a bright future.

Despite maintaining a positive outlook that a cure for Usher 1F will be found, I was hiding something earlier this year from myself, my family, and my friends. I knew that my eyes were getting worse but was too scared to face the truth. I did not know if I should visit my retinal specialist, Dr. Stone in Iowa, to confirm my fears or just suffer silently and hope for the best. For the past six months, I knew that I was feeling more uncomfortable in my workplace, my home, my daily walks, and evenings out with friends. I just didn't feel safe anymore. Now I dread going out at nighttime or being in dark settings. I struggle reading books even with glasses, reading the close captioning on television, or even reading emails and text messages on my phone.

Imagine trying to look through smog or haze…that is what I am experiencing right now. Last month, I received my annual eye exam and learned my cataract condition is really bad. My eye doctor confirmed that my central vision has deteriorated so badly…it's like looking through a snowstorm.

So another shoe drops…another setback. I understand that cataract surgery will restore my central vision to its former clarity. However, this early onset of cataracts was caused by having Usher 1F. Sometimes all these setbacks shake my confidence that I will be able to continue living a happy productive life. It also feels like a wake-up call to what my vision will become without a cure. It's frightening! This realization motivates me to continue to fight to find a cure not only for myself, but for all affected by Usher 1F and the future generations that will inherit this condition. No baby, child, or adult should have to be burdened with deafness and blindness. I invite you to help me find a cure for Usher Syndrome Type 1F. Please join our crusade to end this disease that robs us of both sight and hearing. ◆

2019 – A Year of Progress

This year has been a year of progress for all of us, a year of development of potential treatments reaching the phase of testing in both our zebrafish and mouse models. While we don't expect to hit the jackpot on round one with a treatment that is ready for human trials, we have made great strides in the right direction. Advancements this year include testing for efficacy of mini genes in our zebrafish and of gene therapy in our mouse model. Further exciting approaches to gene therapy are in development. In addition, we have begun development of a protocol to perform a comprehensive drug screen in our zebrafish. This screen will test a library of 2000 already FDA-approved drugs for efficacy for Usher 1F. We will begin the screen in 2020.

As we develop and test potential therapies with the goal of moving to a clinical trial in humans, we have identified a pressing need for a natural history study, which is a study documenting the natural progression of vision loss in those with Usher 1F. Such a study is essential for future clinical trials as a benchmark against which the effect of potential treatments can be measured to prove efficacy.

While Usher 1F Collaborative grew out of one family's quest to find a cure for their daughters, now six years later, our Usher 1F family has multiplied many times over. We are a patient-led research network, driven by the work and energy of our many affected families, the stakeholders in this journey. Patients and their families, more than anyone, fully appreciate and experience what it truly means to live with a rare disease like Usher 1F and how it impacts so many lives. Utilizing our combined knowledge, skills, connections, and energy, our network has engaged investigators, raised funds, and driven the direction of the research, focusing on translational research with a goal of moving from lab to the clinic.

With much attention focused on cancer, heart disease, Alzheimer's, and other diseases that affect large numbers of individuals, obtaining funding and attention for this rare disease remains a challenge. Patient-led research networks such as Usher 1F Collaborative can and are changing the status quo. Philip Reilly notes in his book, Orphan, that "…there are countless mothers who rise each day determined to move mountains." Please make an end of the year gift to help us move mountains so that all with Usher 1F can see the future, and help us fund these programs critical for Usher 1F research. With your help, we can ensure our progress continues to help us find a cure. ◆

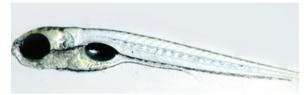
Usher 1F Research at the Corey Laboratory, Harvard Medical School

By David Corey, PhD

A challenge for research on Usher 1F is that the standard animal model for research, a mouse lacking the Usher 1F gene, has only mild impairment of vision. This may be because the structure of the photoreceptors in mice differs from that in humans, and PCDH15—the protein that is absent or dysfunctional in Usher 1F, just isn't as important for vision in mice.

David Corey and his colleagues at Harvard Medical School are trying to develop gene therapy methods to treat the deafness and blindness of Usher 1F. They have focused thus far on preventing the deafness. The mice lacking PCDH15—being profoundly deaf—are a good model for those studies. But they recognize that reversing the congenital deafness in Usher 1F patients will be challenging, and that progress may come sooner in preventing the progressive blindness. So which animal model to choose?

Corey and his group were excited to discover that the photoreceptors of a small tropical fish, the zebrafish, were more like those in humans. These fish are a favorite laboratory animal because they are small and easy to maintain, and because they can see and hear within about a week of fertilization. Corey was additionally excited to learn that Monte Westerfield and Jen Phillips at the University of Oregon had already made a zebrafish model of Usher 1F. At the Usher 1F meeting in Vancouver last May, the two laboratories met to collaborate on using zebrafish to test strategies for delivering a functional PCDH15 gene to the retina. The fish were sent to Harvard, and Jen Phillips soon visited to contribute her experience. Maryna Ivanchenko in the Corey Laboratory and Artur Indzhykulian of Massachusetts Eye and Ear are assessing the retinal pathology in the fish with scanning electron microscopy and electroretinogram recording, and are designing new versions of the PCDH15 protein that can function in the eye but still be small enough to put in a conventional AAV gene therapy vector for human therapy. It's just a start but they hope that the zebrafish will allow them to test strategies faster. ◆



A five-day-old zebrafish. The eye, at far left, takes up a lot of the head at that age. (Shuh-Yow Lin, Harvard Medical School)

Running Marathons for Usher 1F Research

By Jaime Recht

Jaime Recht, who has Usher 1F, ran both the Berlin and New York marathons and raised $2000 for Usher 1F research with both races.

I ran the Berlin Marathon with my guide on September 29th to help fund research for a cure for Usher 1F. It was a wonderful experience running through the beautiful city, especially through the Brandenburg Gate. It rained on and off during the race, but the temperature was good. I had been training hard for this race, which was my fifth marathon, so I was very excited to have improved my personal best by 32 seconds!

It was also an awesome experience running the New York City marathon (my 6th marathon) on November 3rd, especially since NYC is where I grew up. It also helped that we had great weather. The course was tougher than Berlin because of the bridges and hills, whereas Berlin was mostly flat. Thus, I was not aiming for a personal best, and I also ran without my guide and tether for the last several miles, so I was quite happy to have completed it well. ◆

« *Jaime Recht running the New York Marathon*

« *Jaime Recht with her guide running the Berlin Marathon*