USHER 1F COLLABORATIVE

NEWSLETTER
Fall 2022

DONOR SPOTLIGHT
David and Elizabeth Shapiro

We took the opportunity to hear from two of our dedicated donors, David and Elizabeth Shapiro, about why they have chosen to support Usher 1F Collaborative.

Q: We know that your sister Dorie lives with Usher 1F, and she is your main motivation for giving. Why do you think Usher 1F Collaborative is best poised to help Dorie and others? What do you think is most effective about the Collaborative?

A: There is no question that Usher 1F Collaborative is the organization best poised to find a cure for folks like my sister and others with Usher 1F. The Collaborative has an exclusive agenda to find a cure and treatment for this devastating disease. They have put together an executive team as well as the top researchers in the world to tackle Usher 1F. While there are other great organizations, Usher 1F Collaborative's organization, team and researchers are unmatched.

Q: In the last couple years, you increased your giving to Usher 1F Collaborative. Why?

A: Easy answer: time. We do not have time on our side. Folks like Dorie, my sister, and others don't have time for individuals to *not* step up their giving. Therefore, my wife Elizabeth and I have decided that we need to increase our donations in order to maximize the funding that the researchers need now to find the treatment and cure. It is a race against time, and we need everyone's maximum support.

Q: What would it mean to you, as Dorie's brother and sister-in-law, to see a treatment for her vision loss? How would that impact your family?

A: Everything: treating this horrific disease and restoring her vision and ability to see the world like everyone else would ensure that she can live the life that she was born to live. For Dorie's family, it would provide peace, knowing that Dorie will never have to suffer or worry another day about whether she will see less of the world with every breath.

Q: What do you enjoy doing in your spare time?

A: Elizabeth and I are raising our three year-old twin boys, Max and Hudson. When we're not chasing our little twins around, we love spending time with family and friends. Our passions include traveling, wine-tasting, golf, spa time and, of course, volunteering and supporting causes (such as Usher 1F) close to our heart.◆

Victor's Story,
Growing Up with Usher 1F in France

by Victor's parents, Alexandre and Melanie

Victor is a 3-year-old boy, born in September 2019 in Lille in the North of France. He is our first child.

We learned of his profound deafness very quickly. At the maternity ward, the now standard hearing screening was unsuccessful. We understood that there was a significant problem when we left the maternity ward to go home because the SAMU emergency helicopter was taking off near us and did not wake Victor, who was sleeping in his infant car seat while we were carrying him in the parking lot.

When he was one month old, an auditory brainstem response hearing test confirmed that Victor was profoundly deaf. We were very sad and lost because a medical team did not meet with us to explain the results. Fortunately, through extensive research on the internet and thanks to other doctors, we were able to bounce back and learned of the existence of cochlear implants and that our son could one day manage to hear us. We were determined that the operation be carried out as soon as possible. At three months, in December 2019, Victor had an MRI to find out if he was a candidate for the implant, along with a blood test for genetic testing.

Despite Covid, Victor was able to be implanted in two stages at eight and 15 months and activated at nine and 16 months.

During the lockdown, I often told his dad that he appeared quite dazzled by sunlight but had no idea what was about to happen to us.

Victor was late to sit and stand, and so there were clearly issues with his motor skills and balance.

After his two cochlear implant operations, we thought we had experienced the worst in our journey, but a month later, in February 2021, we received the genetic testing results and learned that Victor has Usher 1F.

I had already heard about this syndrome and was very afraid of it because the absence of hearing coupled with the loss of vision was something terrible for me. Unfortunately, our baby has this syndrome...and I understood that everything I had noticed in him as a young mother of my first child was related to the disease.

Victor is a happy, smiling child. He is a sweetheart who loves spending time with all his family. He likes to joke a lot and is very active - You never get bored with him! He brings us so much love and happiness despite a daily life that is not easy for him. He almost never complains and is very strong in the face of his day-to-day challenges from his stability/sight/hearing problems. He amazes us every day. He is our ray of sunshine.

Victor managed to walk on his own in January 2022 and has since made enormous progress: he jumps, runs, dances, in short amazing us every day!

Since the beginning of September, he has been going to school in our town. He attends a mainstream school with kids with normal hearing. Victor is delighted to go there and be with his friends and teachers. His special assistant teacher helps him progress further every day.

Victor also has a little secret. 🙂 Soon he will become the best big brother, we are sure!

There is no specific follow-up and support path for Usher syndrome in France. We struggled with the administration to set up appropriate monitoring. The only follow-up for which it was simple was speech therapy; Victor has been having speech therapy sessions since he was six-months old and so even before his implantation (before his implantation, he had hearing aids which sadly brought no benefit).

Today, Victor has two speech therapy sessions per week, one hand-eye physical coordination session per week and one physiotherapy session per month. At the same time, we were interested in Auditory-Verbal therapy, which is not well known in France (there are only a few trained speech therapists and no financial support through the government social security system), and so we practice this at home.

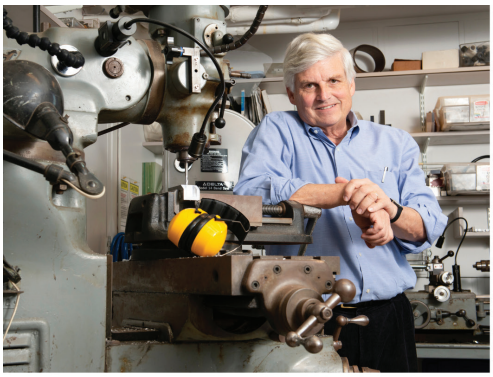
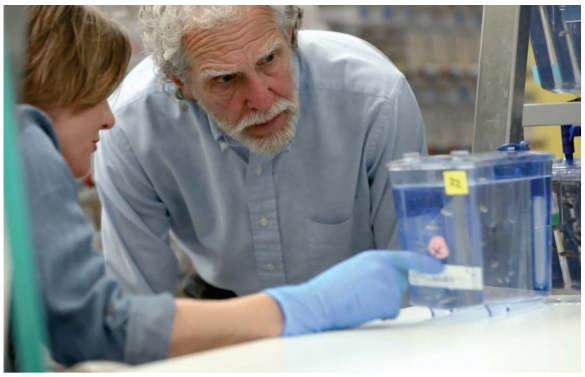
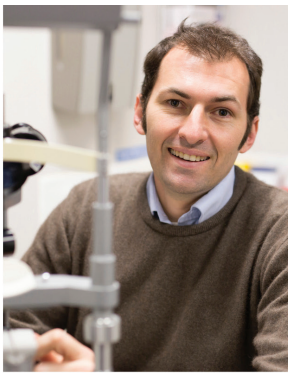
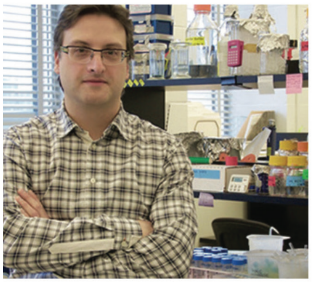
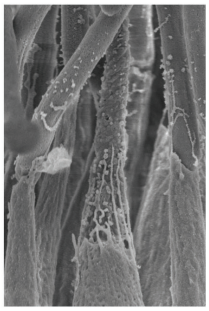
The placement and supply of cochlear implants is covered by the government. We pay for the accessory equipment (battery, cables, etc.), as well as the specific insurance for the implants.

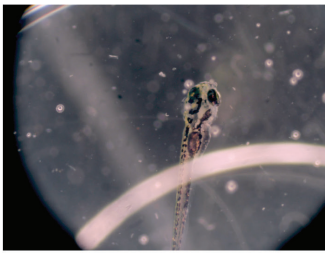
For the retina and following the news of the disease, I searched a lot. We are now seen once a year at the 15-20 Hôpital National de la Vision in Paris by Professor Audo in person, which is very positive indeed. We also have an ophthalmologist near our home.

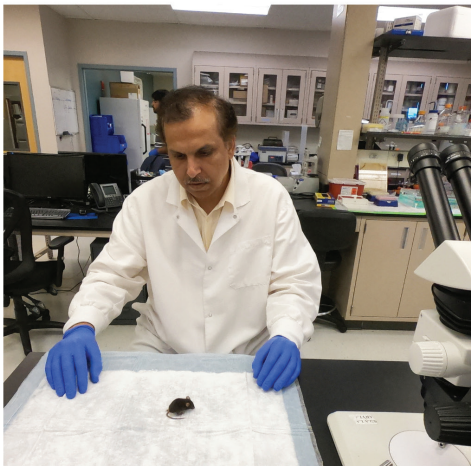
Victor's night vision is already quite affected. This causes him much anxiety at night, and his sleep routine is not easy, which is why he sleeps in our room (in his own bed, next to ours).

Our biggest dream is that a cure will be found so that our son will never be in the dark! We so hope that this treatment arrives before it is too late for him! ◆

Report from Our October Usher 1F Scientific Research Conference



USHER 1F COLLABORATIVE

On October 6th, our researchers gathered for a half-day virtual research conference to present updates on their work. Here are the highlights from the talks:

Livia Carvalho, PhD, University of Western Australia

Dr. Carvalho developed a dual vector gene therapy that Dr. Ahmed, University of Maryland, is testing in his lab. She is now working to develop additional and improved vector systems. She is testing her vectors in retinal organoids, which are retinas grown in a dish in the lab from stem cells derived from the skin cells of a patient with Usher 1F.

Alex Hewitt, MD, PhD, Centre for Eye Research Australia

Dr. Hewitt is developing a gene editing system to create precise changes in a single DNA base. Gene editing differs from gene replacement in that the mutation is corrected in the affected person.

David Corey, PhD, Harvard Medical School

Dr. Corey's mini-gene restores hearing in an Usher 1F mouse model. Because babies with Usher 1F are born deaf but with normal vision, researchers believe the hearing is more sensitive to the absence of the Usher 1F protein protocadherin 15 than the eye. Therefore,

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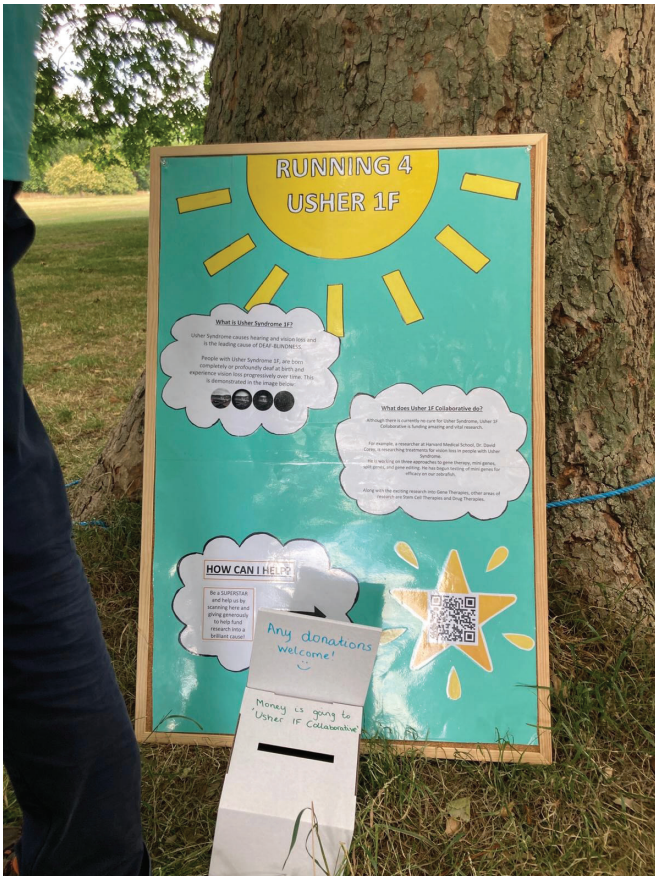
Usher 1F Fundraising in the U.K.

by Victoria Butler-Sloss

In July, my amazing niece Lucy Butler-Sloss organized a fun day in Regent's Park to raise money for Usher 1F. People gathered to walk, run, or just picnic in the rare London sun. My sons Arum and Roibhilin were able to join them. Lucy and family raised over $6500. They even also triggered a donation from the Linbury Trust, bringing the total for the event to over $11,000.

My son Arum has Usher 1F and has already begun to experience loss of his peripheral vision. Real help is on the way, and, with the research we are funding, we hope that human trials will be available in three to five years. Every little step helps! ◆



success in the ear suggests that success in the eye will follow. He has begun testing his mini-gene in our zebrafish, and preliminary results appear promising.

Zubair Ahmed, PhD, University of Maryland

Dr. Ahmed has developed an Usher 1F mouse model that displays visual deterioration on an electroretinogram (ERG). His team is collaborating with Dr. Carvalho. They have tested a gene therapy that she developed, a dual AAV approach, which delivers the large Usher 1F gene in two pieces that reassemble in the eye. This approach resulted in improved retinal function and, thus, improved vision in their mouse model.

Samuel Pfaff, PhD, The Salk Institute

Dr.Pfaff is the newest addition to our research network. He spoke about his new approach to gene therapy that is showing great promise at delivering the corrected Usher 1F gene to the retina. In testing in his lab of this approach for other types of inherited retinal diseases, they have been able to demonstrate delivery of more of the gene resulting in rescuing of more of the visual field.

Vincent Tropepe, PhD, University of Toronto

Dr. Tropepe has developed an Usher 1F zebrafish model to understand the role of the Usher 1F protein protocadherin 15 in retinal photoreceptor function. His goal is to investigate the possibility of genetic compensation in this model.

Monte Westerfield, PhD, University of Oregon Institute of Neuroscience

Dr. Westerfield reported on testing on our zebrafish of a new compound, a potent antioxidant made from the extract of the magnolia tree. He and Jennifer Phillips, PhD, have found that this compound holds potential for rescuing vision in Usher 1F. The compound was donated for testing by Jack Arbiser, PhD, Emory University.

Katarina Stingl, MD, University Hospital Tübingen

Dr. Stingl is the lead clinical investigator for RUSH1F, our four-year natural history study in collaboration with Foundation Fighting Blindness. This study will provide critical data for a future clinical trial to measure efficacy. Dr. Stingl reported that we are getting closer to full enrollment and that many patients have completed the first-year appointment. For those with Usher 1F who meet the qualifications, we need you! Please sign up.

We are so grateful to all of our researchers for their hard work and dedication toward finding a cure. We look forward to seeing the follow-up from our conference of new information learned and collaborations formed. ◆

Take Back the Light

The third Saturday in September is Usher Syndrome Awareness Day, this year falling on September 17th. This day marks the time of year when navigating becomes more difficult for those with Usher syndrome because the days start to contain more darkness than light. Several families participated in our Take Back the Light fundraising campaign, which helped us raise almost $11,000. We appreciate all those who set up fundraising pages, and we're excited to acknowledge our top three fundraising families: the Roots, the Doerrmanns, and the Derumieres.