KCNT1 EPILEPSY FOUNDATION

Honoring Our Founders Five Years Later

Justin West, MD

As a plastic surgeon Justin West spends his days fixing human bodies. Yet, when his son Andrew began experiencing seizures as a newborn and was diagnosed with KCNT1 epilepsy in 2017, he and his wife Lisa felt helpless. Both surgeons, their initial thought was to launch their own research foundation, however, conversations with experts in rare disease changed their minds.

“I want to hear my son's voice before I die.”

“It's not helpful to have multiple foundations in a very small disease space,” Justin says. “In breast cancer, where one in eight people are affected, you can have 50 different organizations and they don't really overlap because there's so much money in breast cancer and so many people working on it. But in a very niche space, it's much better to have one. So that's what we did.”

The Wests joined forces with Seth and Susan Greenblott, and were soon joined by Samantha MacMechan and Sarah Drislane. “The idea was to make sure we get a seat at the table with pharma and researchers, and be taken seriously in our goal of advocating for Andrew,” Justin explains.

Like other founders, the West's priority was developing a treatment quickly.

"Parents in this community face a 50% mortality rate by age 10; there is a massive sense of urgency. So the driving force was to save our child's life," he says.

"But number two, recognizing that every year means less potential to rescue the things stolen from us, namely Andrew's voice and his ability to communicate and walk, was to slow the disease."

As the sole physician among the founders, Justin was able to speak to scientists and other physicians in their language and terms. "Scientists take doctors seriously, doctors take doctors seriously, but scientists and doctors don't tend to listen to anybody else," he says. "So that gave me a big in. I know how to speak doctor."

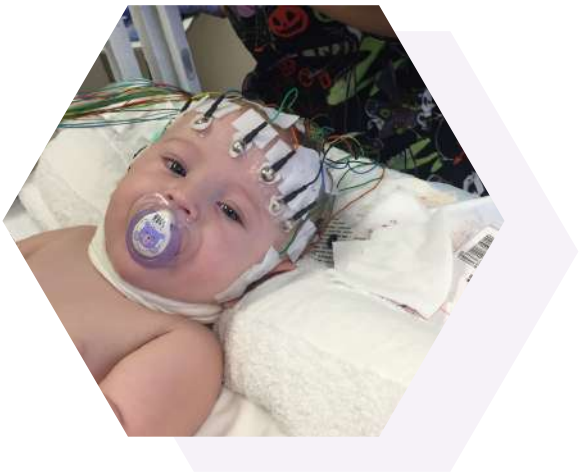
Justin's ability to speak 'doctor' has opened doors for the Foundation, including an invitation to meet with the executive team of UCB, a pharmaceutical company that has long worked in common epilepsy. "I approached UCB leadership at a conference and said 'I want you to work faster because we lose a kid every month. Every month that goes by that you don't move forward, you owe me a child'," Justin relays.

“You can take 10 years, even 20 years, developing a drug for common epilepsy because most people with epilepsy have drug choices that are at least helpful. The difference with KCNT1 is we're drug resistant. Ninety percent of our kids are on five or more anti-epileptic drugs, which is insane. And we have that very high mortality rate.”

His dual role as father and physician has helped executives and researchers better understand KCNT1’s impact: “I've had four high level pharmaceutical executives visit Andrew in our home because I tell them, look, you can't ever understand my child's disease unless you meet my child. You can read all the papers you want and I can tell you all about them, but you need to meet him. They come and they try picking up a 50-pound baby and see what it's like, and they see the equipment and all the modifications to our house so they can really understand. And they take that back to their teams.”

Like other founders, Justin is both proud of the Foundation's successes and frustrated by the pace of progress. Among his proudest accomplishments is a potential treatment identified through a drug repurposing screen the Foundation initiated at Vanderbilt University. The screen validated more than 20 drugs with an impact on the channel mutated in KCNT1 patients. A panel of clinicians and pharmacologists eliminated those not tested in children or otherwise not suited to KCNT1 epilepsy, and identified one used extensively in the pediatric population, meaning it had decades of safety data. Justin and a team of investigators designed an observational study and there are currently several children, including Andrew, taking the drug. If it works, the Foundation and its partners will share results with the international community.

“Personally, we've already seen a difference on this drug, things Andrew is doing that he never did before,”



Justin reports. “Eye contact is one. He used to scan his eyes and never lock, which as a parent is awful because you have no sense if your child even sees you or distinguishes between you and a stranger. On this drug, he will look at us for like two minutes straight. And when somebody comes in the room, he'll turn and look, and he'll watch them cross the room. And, he's making vocalizations that he's never made before. It's not solving his disease and it will never be his long-term answer, but it's something while we wait.“

In my view, drug discovery for our disease is a 10-year process. By the time a drug goes from an idea into a child's mouth, $100 million-$1 billion has been spent. And, 90-something percent of those efforts fail either because of the science or funding runs out. My goal for our children in the short term is to keep them as healthy as possible. And this drug may help do that while we're waiting for our real targeted therapies.”

Despite that long horizon, Justin is encouraged by the generosity of strangers and hopeful for Andrew and others with KCNT1: “You realize that despite best intentions, science is hard, funding is unpredictable, and the human body is supremely complicated. I've honestly been surprised at how remarkably successful we are. We've convinced a lot of people to start working on KCNT1 without exchanging any money,” he says. “We're having impact in pretty impressive ways, we've had a lot of firsts, and we've done this on a shoestring budget. I have friends who raise $2-3 million a year for their foundations. We're lucky to raise a couple of hundred thousand and yet we're further ahead. We're doing something right.”

Of his work with the Foundation, Justin says, “There's no worse feeling for a human than not having something to contribute and feeling powerless. As a surgeon it's a particularly tough place to be because people come to me every day to solve their problems and I do that. Being involved with and running the Foundation has given me a sense of purpose. I can look at Andrew knowing I'm doing everything I can to save his life, to hear his voice, to see him move, to get him the hell out of his chair. And to my other two children, they need to see that we are doing every single thing that we can. Because I don't want to, you know, go to my deathbed looking at these kids saying, ‘I could have done more’.“

What is Justin’s wish for the Foundation’s future? “A cure and retirement. I want to close the foundation,” he says. “I want to find a cure and then never discuss this again. I'd like to see our mortality go away.”

And for Andrew? “Personally, I want to hear my son's voice before I die. If I can see him walk, that would be a bonus.”

KCNT1 Epilepsy Foundation: Beyond KCNT1

Although the KCNT1 Epilepsy Foundation was founded to find and fund effective treatments for KCNT1-related epilepsy, the research and findings are likely to have implications for other diseases.

Foundation Founder and President Justin West explains, “The result of having thousands of seizures over a lifetime is similar to a traumatic brain injury (TBI) and causes neurodevelopment issues. There are similarities between more well known neurological conditions like traumatic brain injury (TBI) and Parkinson's, and KCNT1.

”An exciting thing is that helping our 500 kids around the world potentially could help thousands, if not millions, of people suffering from other neurological conditions.”

Recognizing those similarities, Justin and other Foundation leaders have prioritized connecting with experts working on other diseases to share information and research findings. One of those collaborations helped identify biomarkers shared between KCNT1-related epilepsy and Parkinson’s. Another will build on research out of China that identified dysregulation in the KCNT1 channels as the cause of drug-resistant seizures—similar to those experienced by KCNT1 patients—in a subset of TBI patients.

“We are unique in that we've got really good leadership that focuses on outside-of-the-box thinking,” Justin says.

He adds: “It's hard to talk to somebody about contributing to something, to a disease they just feel bad for, when there's no hope. We have unequivocal evidence, both in our labs and in humans, that you can change this disease. KCNT1 is a single gene, we understand the mechanism of action, and we've proven in labs in humans that you can reverse the phenotype, which means get rid of the seizures and show the beginning of improved cognitive function.”

Justin also notes the return on investment for Foundation supporters is significant both because the organization is primarily volunteer-run and because of the numbers impacted by KCNT1-related epilepsy.

“So if I'm a donor and I wanna give, I've got choices,” Justin says. “I can give to breast cancer. Breast cancer raises hundreds of millions a year. You can give 20 billion more dollars to breast cancer to change the survival by 0.5%. Or, you could give one million dollars to KCNT1 to change the survival by 100%, right?

“I mean, the impact, no single supporter is ever gonna have the impact on breast cancer or diabetes they could have on KCNT1 Epilepsy.”