CRITICAL PATH INSTITUTE

Ultra Rare: A Mission to Discover the Cause Behind a Young Boy's Developmental Delays

Kelly Carwile, mother to Reed and sister of C-Path Director Mike Minchik, has been on a mission to discover the cause behind her son's developmental delays. Initially diagnosed with autism, further research discovered a variant in the FOXP4 gene. She recently shared her journey with the C-Path team, detailed below.

Please share a bit about your rare disease journey. When and how was a diagnosis reached for you/your child? How did you get connected with genetics? Is there a family history of the condition, or are you/your child the only person in your family with the condition? Were you showing symptoms before his diagnosis?

Kelly Carwile with her family, including Reed (far left).

We first noticed our son, Reed, showing developmental delays around age two, particularly with speech. He wasn't hitting milestones like other kids his age, and we began to feel that something more was going on. Initially, we were told that Reed definitely didn't have autism, but as time went on, developmental pediatricians shifted their stance to "maybe" he did, and eventually, he was diagnosed with autism. However, there was always a suspicion that an underlying issue was contributing to his challenges. The genetic component didn't come into focus until later when we pursued whole-genome sequencing. That's when we discovered a variant in the FOXP4 gene, which has been linked to developmental delays, speech difficulties, and autism-like symptoms. At first, this variant was classified as a variant of unknown significance (VUS). However, after conducting RNA sequencing, it revealed abnormal RNA splicing, leading to the variant being reclassified as "likely pathogenic." Even with this finding, we're still uncertain about how much of Reed's symptoms stem from this variant versus autism—or possibly both. We continue to seek research that can help clarify the full picture.

We also recently discovered that I carry the same FOXP4 variant. While I experienced some developmental delays as a child, they were far less pronounced than Reed's who is now seven years old and currently nonverbal. We are awaiting further RNA sequencing to understand how this variant affects me, which could provide insights into its broader impact on both Reed and me. As of now, Reed is the only person in our family who has exhibited significant symptoms. We have another child who has no developmental delays and has tested negative for the variant.

What are the challenges that come with being ultra-rare? What does it mean to you to be considered "ultra-rare?"
The biggest challenge is the uncertainty — there's no roadmap. With more common conditions, there are established treatment plans, support systems, and communities that provide guidance. In our case, it often feels like we're constantly playing catch-up, waiting for answers that may take years to come. Additionally, research on ultra-rare conditions is extremely limited. It's frustrating because Reed's condition is unique to him, and we're still trying to understand the full picture of what's contributing to his developmental delays. There's very little existing knowledge to rely on, which makes advocacy and persistence essential.

Are there patient advocacy groups for your condition? Are you involved in the group? Are you involved in advocacy efforts?
FOXP4 variants are rare, with only a couple dozen known cases worldwide. I started a Facebook group and have tried reaching out to other families through genetic websites, but it's been challenging to connect. We're hopeful that as whole genome sequencing, whole exome sequencing, and RNA sequencing become more widely available, more cases will be identified, helping to drive further research.

What resources have you learned about along the way to help you understand the condition, research options, and treatment options?
One of our biggest resources has been connecting with specialists like Dr. Wendy Chung, who has guided us through testing and helped identify the next steps in our journey. Beyond that, we've had to be proactive — seeking out research opportunities, reaching out to experts, and staying up to date on the latest genetic studies.

Are you involved in research? How did you get involved? What does research look like for the condition? What avenues have you tried, and have you had success? Have you needed to advocate for research and/or expert care?
We are currently participating in a FOXP4-specific study based in the Netherlands.

Additionally, at Boston Children's Hospital, we are comparing Reed's RNA sequencing data with mine. Since I also carry the variant but present with very different symptoms, this comparison could provide valuable insights into how FOXP4 functions. Eventually, we hope to compare this data with other individuals who have FOXP4 variants and clinical symptoms. This is a crucial step in understanding how FOXP4 affects Reed and in determining whether there are potential treatment pathways.

What have been your sources of hope or motivation as you move forward on this rare journey? Who have you turned to for support?

Reed Carwile

Reed is my greatest motivation — he will always be the reason I keep pushing forward. Every bit of progress he makes, no matter how small, gives me hope and keeps me focused. I also find optimism in the work of dedicated doctors and researchers who continue to search for answers. Knowing that there are people out there willing to push the boundaries of what we know about rare diseases keeps me going.

What advice would you give to providers and researchers working with patients/families facing barriers to diagnosis, care, research, and/or treatment? What advice would you give to patients/families?

For providers and researchers, I would say: listen to the families. Parents notice subtle changes in their children that may not be immediately obvious in a clinical setting, and those insights can be crucial in finding the right diagnosis. Don't be afraid to think outside the box and be open to patient-driven ideas.

Additionally, if possible, please share your data and research. So much valuable information is collected but never shared, which can slow down research and, ultimately, treatment development.

For families, my advice is to keep pushing forward, even when it feels overwhelming. Don't hesitate to ask questions, seek second opinions, or connect with others who are on a similar journey. Most importantly, advocate for your child — after all, you are their best advocate.

Is there anything else you would like to share with the audience? Any other messages you would like to convey?

I want to acknowledge the doctors and researchers who are committed to finding answers for families like ours — families without a clear diagnosis or established treatments. It makes a significant difference when experts continue to ask questions instead of stopping at the first explanation that fits. There's still so much we don't know, and the only way forward is through collaboration and dedication to understanding these rare conditions.