Adam Clatworthy & The CRELD1 Warriors Foundation

The CRELD1 gene is complex, producing several protein isoforms with varied levels of expression between tissues as well as during development. These proteins, which are part of an epidermal growth factor-related subfamily, have known roles in cardiac development and the immune system. Most recently, CRELD1 variants have been identified that, when present on both gene alleles, affect neurodevelopment. In these autosomal recessive cases, the condition is known as Jeffries-Lakhani Neurodevelopmental Syndrome, or JELANS.

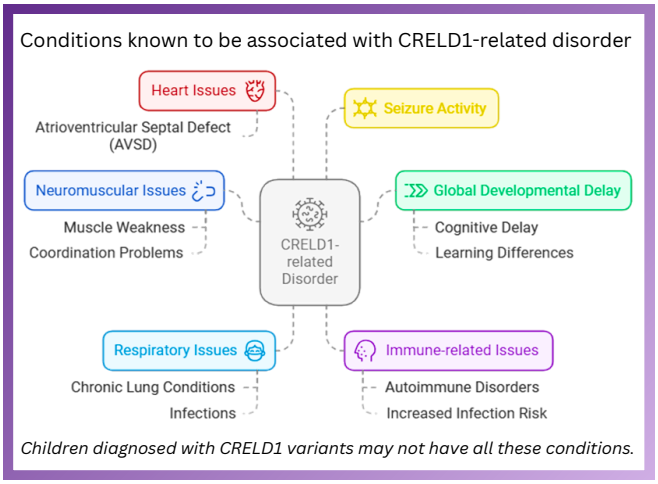
Creld1 Warriors
ALONE WE ARE RARE. TOGETHER WE ARE STRONG

From the early days of Lola's life, Jess and Adam Clatworthy noticed concerning signs — Lola struggled to feed, had low muscle tone, and was not hitting typical developmental milestones. As the weeks turned into months, Lola's condition only worsened, with the infant experiencing mysterious seizures and episodes where she would stop breathing for several seconds.

"It was really at three months where Lola started to do things that really scared us," Adam recounts. "She was having these blinking episodes, almost like she was trying to take a breath, and then her lips would go blue and she would stop breathing for a few seconds."

The family was thrust into a frustrating medical odyssey, as doctors prescribed a series of anti-epilepsy medications, none of which provided lasting relief for Lola's condition. Despite numerous tests, including an epilepsy panel and whole genome sequencing from the 100,000 Genomes Project, the underlying cause of Lola's struggles remained elusive. “Lola could have hundreds of seizures a day," Adam recalls. "We were doing our own research, speaking to loads of medical experts, and then suddenly it hit us like a ton of bricks ... she's now gone. What do we do?"

The devastating loss of their daughter Lola at the age of two, a victim of Sudden Unexpected Death in Epilepsy (SUDEP), just 4 days after their son Alfie was born, was a crushing blow for the Clatworthy family. But in the midst of their grief,



Adam and Jess knew they had to do something to honor Lola's memory and support other families facing a similar battle.

It was a chance Facebook connection that would ultimately lead the Clatworthys to the answer they had been searching for. A mother in Canada, whose daughter Hayden and son Levi had both been diagnosed with the rare genetic disorder CRELD1, reached out after seeing a video of one of Lola's seizures. Hayden had also sadly passed away. The similarities were striking.

"We took all this information to our geneticists, and they kind of brushed it off," Adam recalls. "They said, 'We've never heard of this condition, let alone it being linked to epilepsy.'"

"It was only after we lost Lola and then Alfie also started having the same intractable seizures at 3 months that the geneticists seemed to take us seriously. We persisted with them and they finally agreed to look further into Lola's gene sample. Within a few days they found irregularities in the CRELD1 gene, and then subsequently found it in Alfie's sample too."

This rare and little-understood condition had taken their daughter's life, but it would also become the catalyst for their next chapter. In the wake of their devastating loss, Adam and Jess founded CRELD1 Warriors, a charity dedicated to raising awareness, funding research, and building a community for those affected by this rare genetic disorder.

"We knew that we may never see the fruits of this in terms of will it impact Alfie's life," Adam says. "But you've got to start somewhere, even if it is baby steps to putting the foundation and the platform in place."

The Power of Community

Through the CRELD1 Warriors website and social media, the Clatworthys have connected with over 20 other families around the world who have also been diagnosed with CRELD1 variants.

Enabling diagnosis of patients with CRELD1 variants is a key effort. The Foundation was instrumental in getting CRELD1 added to the UK's epilepsy panel testing, so any child undergoing an epilepsy genetic test would be screened for the condition. Currently, the Clatworthys are advocating for the inclusion of CRELD1 in the Generation Study being run by Genomics England and the NHS. This

groundbreaking study aims to recruit 100,000 newborn babies and screen them for over 200 genetic conditions.

To help those diagnosed with CRELD1 variants, the foundation assembled a Scientific Advisory Board and are working with scientists at the University of Birmingham to advance the understanding and potential treatments for this rare condition. There are ongoing collaborations with researchers at Yale School of Medicine who provided additional insights from Lola and Alfie's cases and confirmed variants in CRELD1 as a pathogenetic cause of neurodevelopmental phenotypes in addition to cardiac dysrhythmias and compromised immune function. [Jeffries L, et al. 2024]

"We're just learning as we go along. But we know that if there are other children or people out there that have CRELD1, we have to find them. And sadly, we are. Since we set up the website in 2022, we've found over 14 new families who have received a diagnosis."

Though much has been accomplished, much remains to be done—continued research will require funds, an area of focus for the Foundation. The Clatworthys' first fundraising event, a karaoke evening with friends and family, was a small but meaningful step in this direction. Jess has completed the challenge of running the Great South Run, a 10-mile race, to raise money for the cause. Looking ahead, Adam is taking part in the annual London to Brighton cycling event, engaging a group of 35 people who have signed up to participate.

These grassroots fundraising initiatives are vital to sustaining the CRELD1 Warriors foundation and ensuring it can continue its vital work: to provide a supportive community, raise awareness, and ultimately, to pave the way for a brighter future for those affected by this rare genetic condition.

To support CRELD1 Warriors, please visit www.creld1.com/donate.

Resources

- CRELD1 Warriors Website - www.creld1.com
- 100,000 Genomes Project and Genomics England - www.genomicsengland.co.uk/initiatives/100000-genomes-project
- Jeffries L, Mis EK, McWalter K, et al. Biallelic CRELD1 variants cause a multisystem syndrome, including neurodevelopmental phenotypes, cardiac dysrhythmias, and frequent infections. Genet Med. 2024 Feb;26(2):101023. doi: 10.1016/j.gim.2023.101023. Epub 2023 Nov 7.

Rare Awareness Radio is made possible by support from Meeting You Podcast, OMSLife Foundation, and Principled Research Resources L3C.