



2021 Annual Report

A cure is out there.
Help us find it.



Our Impact this year

2021 Year In Review

People with PCDH19 Epilepsy & their families depend on us to fulfill our mission, and they are at the heart of every decision we make.

Throughout 2021, the Alliance proved to be as strong and resilient as the families we serve. Perhaps it is *because* of our experience with PCDH19 that we were in some ways prepared for the uncertain. Though it may have looked different than a typical year, we were able to think creatively to ultimately continue our work toward our mission, finding ways to provide support to affected families, promote awareness, and fund three promising research projects. Our progress is possible only because of our generous donors & fundraising families, our world class Scientific Advisory Board, and the hard work of our dedicated staff & volunteers. Look at what we've accomplished together during an exceedingly challenging year in our world.

Our Mission

Our mission is to improve the lives of people with PCDH19 Epilepsy and their families. The Alliance focuses on raising and directing funds to scientific research with the goal of finding better, more effective treatments and, ultimately, a cure; providing information and support to affected families; and assisting the efforts of the medical community, so that no family suffers without a diagnosis and the most appropriate medical treatment.

PCDH19 Epilepsy

PCDH19 Epilepsy is a condition with a wide spectrum of severity in seizures, cognitive delays, psychiatric disorders and conditions such as Autism and OCD, which are all caused by a mutation of the PCDH19 gene on the X chromosome. We are still working to understand why some are impacted differently than others. PCDH19 affects females and mosaic males (i.e., males that have the mutations in some of their cells, but not all of their cells). Affected and unaffected males with the mutation will pass the mutation on to 100% of their daughters and none of their sons. Females will pass the mutation to 50% of their daughters and 50% of their sons.

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Research Grants

We believe research brings us hope, and it is by far our largest program here at the Alliance. With the guidance of our esteemed International Scientific Advisory Board, we are funding cutting edge PCDH19 research every year. In 2021 we were able to fund 3 grants: one was co-funded with The American Epilepsy Society and two were through our own research grant program. We received several scientifically strong proposals, and wish we could have funded them all. You can read about the projects we funded below. We are looking forward to hearing the researchers present at our 2022 Conference.

Our goal is to fund research directly targeted toward understanding the expression of the PCDH19 gene and the function of the PCDH19 protein, finding therapeutic treatments, and a cure for PCDH19 Epilepsy.

We also hope that projects we fund will lead to additional research support from government or other funding agencies. We are pleased to be able to support many different types of projects, each critical for advancing all phases of PCDH19 research, from basic, to clinical, to treatment.



PCDH19 Alliance/AES Research Training Fellowship for Clinicians, Funded at 40% by PCDH19 Alliance

Mechanisms of PCDH19 Clustering Epilepsy

- Julie Ziobro, MD, PhD

“Protocadherin 19 (PCDH19)-clustering epilepsy (PCE) is a developmental and epileptic encephalopathy characterized by intractable seizure clusters, often provoked by fevers, and neuropsychiatric co-morbidities. The X-linked PCDH19 gene encodes a transmembrane cell adhesion molecule critical for cellular interactions during brain development. PCE affects females and rare mosaic males, while male carriers are asymptomatic. This unique inheritance pattern is thought to result from cellular interference associated with random X-inactivation, such that neurons expressing wild-type and those expressing mutant PCDH19 fail to interact properly during development. Our exciting data using female PCDH19 knockout mice crossed with male X-GFP mice to model PCE support this idea. Female offspring display a segregation pattern of separately clustered PCDH19+/GFP+ and PCDH19-/GFP- cells, most strikingly in the cortex and hippocampal CA1 region. How this unique histologic pattern relates to PCE phenotypes remains an unanswered question. We hypothesize that PCE mice develop altered inhibitory synaptogenesis in the CA1 region of the hippocampus (Aim 1) and that the degree of cell segregation correlates with neuronal hyperexcitability and a lowered seizure threshold (Aim 2). This hypothesis will be tested using our novel mouse PCE model with advanced histologic and electrophysiology techniques. Our findings should provide key insights into mechanisms of PCE and potential therapeutic strategies”

Research Grants (cont'd)

Two Grants Awarded through the PCDH19 Alliance Grant Program, Funded at 100% by PCDH19 Alliance



PCDH19–N-cadherin Mismatch in PCDH19-Related Disorder

- Hisashi Umemori, MD, PhD

"A mouse model of PCDH19-related disorder shows female-specific defects in hippocampal synapse development, which causes cognitive impairment, and abnormal cortical neuron sorting, which may contribute to epilepsy. We found that the hippocampal synaptic defects are caused by a mismatch between two cell adhesion molecules, PCDH19 and N-cadherin. PCDH19 interacts with N-cadherin and activates downstream signaling. In normal mice, PCDH19 is expressed by all neurons so that it binds across the synapse and induces downstream N-cadherin signaling. In male mutant mice with no PCDH19, unmasked N-cadherin can bind with each other across the synapse to induce the same downstream signaling. However, in female mutant mice, some cells express PCDH19 and some do not, due to random X-inactivation. Therefore, there is a mismatch between synapses that express PCDH19 on one side and only N-cadherin on the other, and hence, no downstream signaling happens. Indeed, restoring N-cadherin signaling in female mutant mice rescued the synaptic phenotype. In this project, we will test whether the PCDH19–N-cadherin mismatch also underlies abnormal cortical neuron sorting and contributes to epilepsy. We will then design appropriate strategies to treat PCDH19-related disorder based on the PCDH19–N-cadherin interaction we identified."



Investigating the role of steroid hormone receptors and neurosteroids to improve outcomes for PCDH19 Clustering Epilepsy

- Jozef Gecz, PhD, Raman Kumar, PhD, and Paul Thomas, PhD

"Our research shows that one of the major forces behind the clinical complications of PCDH19 clustering epilepsy (CE) is hormonal imbalance in the affected individuals, boys and girls. This imbalance likely arises early in the development and through a fault or a loss of PCDH19 protein function. PCDH19 impacts not only estrogen receptor, but likely also androgen and progesterone receptors and vice versa. While we aim to work out which of the hormone receptors play the crucial role, we shall also be taking advantage of our PCDH19 CE in a dish model to test various hormone derivatives to suppress the 'seizures'. These experiments will provide proof of principle evidence for hormones and/or their neuroactive derivatives to be considered for treatment of PCDH19 associated clinical presentation(s)."



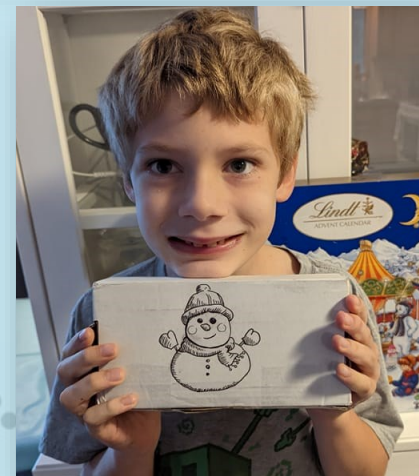
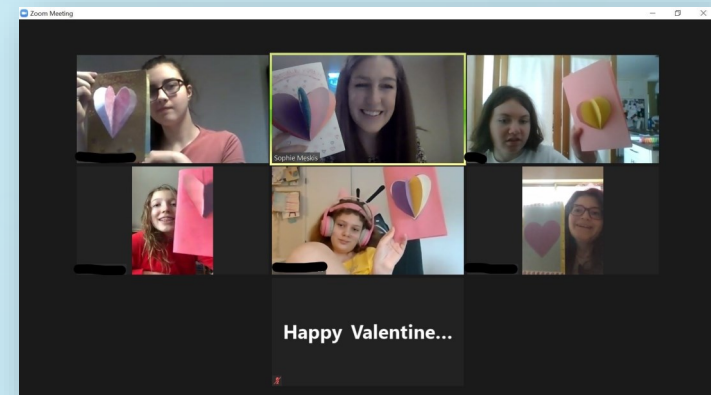
Patient & Family Support

Virtual Parent & Caregiver Support

Typically we would be able to share about the families for whom we provided financial support to attend our biennial Research and Family Conference. However, due to the pandemic, we were unable to have an in-person conference in 2020 or 2021. We knew that our families were still craving connection with others, especially as we stayed inside. In order to provide an alternative, we decided to launch and run virtual get-togethers via zoom. These online hangouts provided an opportunity for parents and caregivers from the UK and the US to come together to chat about their struggles and successes, do some “comparing of notes” and share what was going on in their lives. We also hosted an “Ask the Alliance” series for families to come with nonmedical questions for our veteran caregivers and board members. These online get-togethers provided much needed connection for our families unable to access their local support systems during the pandemic.

Virtual Parties & Events

Our support did not end with caregivers as we knew that individuals with PCDH19 were of course also craving those same types of connection. We were fortunate to have Sophie Ferreira, a former Special Education teacher and staff member at the Alliance, implement a variety of virtual hangouts for kids, teens, and adults living with PCDH19. Some of these events included activities such as a craft or games, and others were just an opportunity for the participants to connect with others living with PCDH19. The year ended with an Epic Holiday craft party complete with the cutest boxes of craft supplies (with hot cocoa included of course) which were all pre-shipped and packaged with love!



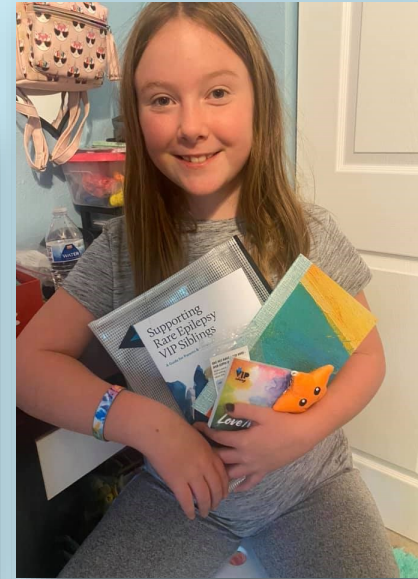
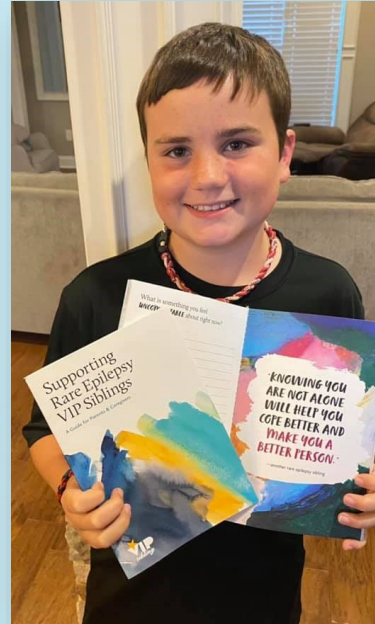
Patient & Family Support (cont'd)

Sibling Support

As our community knows, a diagnosis of PCDH19 can have an impact on the entire family, including the brothers & sisters of those with this rare form of epilepsy.

Living with a brother or sister who has a chronic disease can be challenging at times. The seizures themselves can cause fear & anxiety for siblings, but we also know that our loved ones with PCDH19 often have needs beyond just seizure management that can impact the daily lives of siblings as well. Just as seizure clusters & other related needs can cause disruptions to the lives of people with PCDH19 & their caregivers, it does for siblings too.

This year, in collaboration with Zogenix and several other rare epilepsy patient organizations, we introduced our VIP Sibling Program to help provide support to these amazing sibs! So far we have shipped 87 sibling kits, and the feedback from our families has been wonderful!



Facebook Support Group



Our Facebook support group continues to grow. Our group continues to grow while remaining a safe, non-judgmental home where families can go to celebrate, commiserate, vent, ask questions, find all kinds of support, and find the latest information about PCDH19 Epilepsy and the PCDH19 Alliance. PCDH19 can be isolating, and this group is a lifeline and a home. Alliance volunteers administer the group, checking in several times daily and also screening new member requests.

Patient & Family Support (cont'd)

Patient Assistant & Support—Bear Program

A much loved part of our Patient Assistance and Support program has been our bear program, in which we send PCDH19 Alliance Bears to affected children and families. Thanks to the amazing PCDH19 Alliance volunteer mom and daughter duo, Cindy and Emily Beers, we were able to continue this program throughout 2021. This program provides each newly diagnosed child with PCDH19 the opportunity to receive, at no cost to them, our sweet, cuddly and comforting symbol of hope - HOPE the bear. Thank you so much to Cindy and Emily for your continued support of this program and newly diagnosed families! Emily lives with PCDH19 herself and is finding meaning in spreading Hope to children.



Education, Awareness, and Advocacy

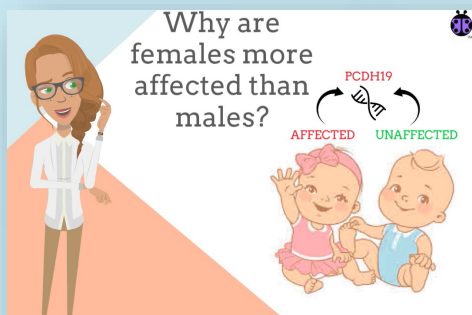
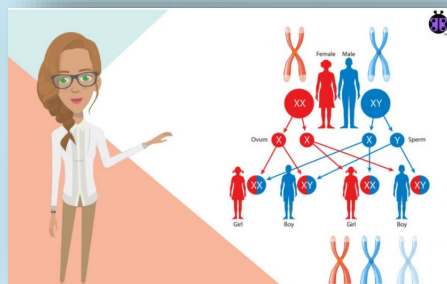


Town Hall

Typically we are traveling to conferences each year to educate medical professionals about PCDH19 and advocate for research, timely diagnosis and appropriate treatments. Every other year, we host a much loved and respected PCDH19 Research and Family Conference. We sure did miss all of the in-person opportunities in 2021. However, in April we were able to organize a free Virtual Town Hall featuring Researchers discussing PCDH19. Families and caregivers were invited to attend, ask their questions and engage directly with the research community.

Educational Video Series

In 2021, we launched our multi-part Educational Video Series in partnership with Dr. Kristy Donnelly at the University of Adelaide. This video series was designed to help families & other non-medical professionals understand more about the basic genetics related to PCDH19. These easily digestible videos are incredibly informative and have been well-received by our community. We released three videos throughout 2021 & are proud to continue this project into 2022.

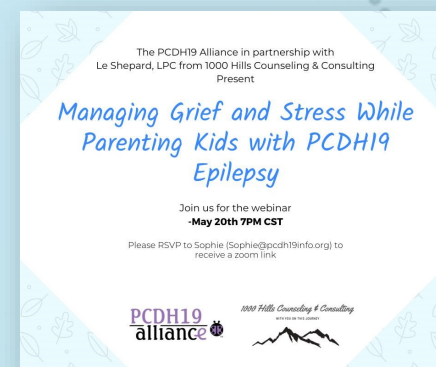


Family Education & Support

In partnership with Le Shepard, LPC of 1000 Hills Counseling and PCDH19 parent, the Alliance was able to provide two valuable live & recorded resources for our community. These videos addressed important topics and included two sessions:

- "Love in the Age of Epilepsy: Relationship Help for Parents of Children with PCDH19."

- "Managing Grief and Stress while Parenting Kids with PCDH19 Epilepsy"



We are so grateful to Le who volunteered both her time & expertise to benefit parents within our community.

Education, Awareness, and Advocacy (cont'd)

Fundraising & Awareness Events

Our families and their friends in Canada, Poland, the U.S. and the U.K. continued to support the Alliance with creative fundraisers, even through a challenging year where in-person fundraising was limited. Nearly all of our fundraisers are fueled by a personal connection— a desire to save the life of, ease the suffering of, and create a better future for their loved ones living with PCDH19. In 2021, our supporters organized online fundraising campaigns more than ever before, including a record-breaking fundraiser organized by the Martins family in honor of their brave warrior, Zoey.

Despite the challenges surrounding COVID, some of our families even managed to pull off some amazing in-person fundraisers, including an Annual Speedway fundraiser in honor of Maegan Haganey and the First Annual Louie's Kick-Off event, a now famous soccer tournament/live music/mini-fair event put on by the Rollins family.

These fundraisers give families a voice, a way to raise awareness, and a way to contribute to science, patient support and the fight for an effective treatment for their children and everyone affected by PCDH19. They are vital to making the research, the conferences and the support we offer possible. The time, effort and love that goes into these events is remarkable, and the courage shown by those willing to take action on behalf of the Alliance is inspiring and truly life changing.



The Numbers

Raising and Investing Funds

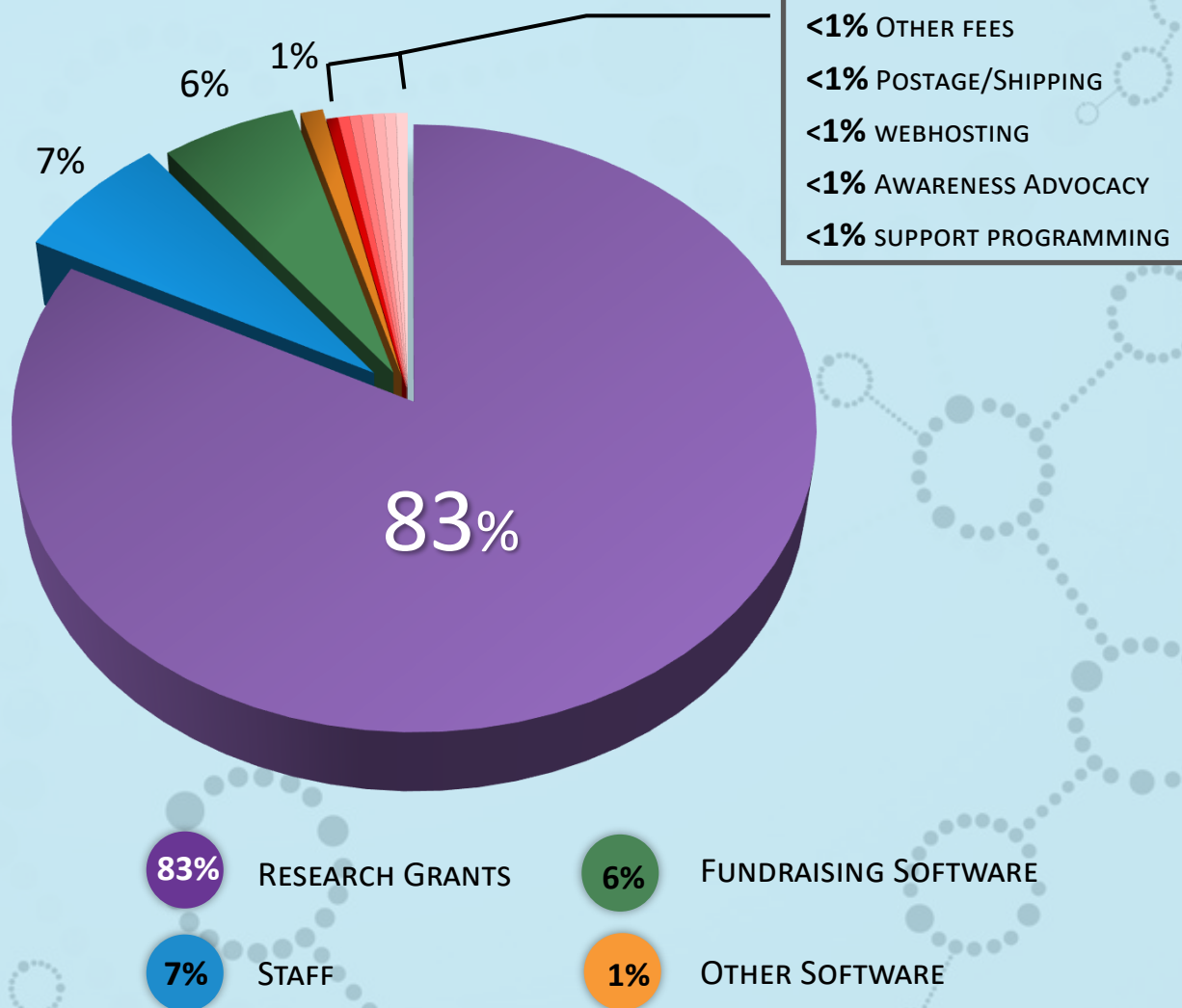
People living with PCDH19 are at the forefront of every decision we make, including where our funds are spent. Most of our donations continue to come from PCDH19 Families making personal contributions and reaching out to family & friends to join our cause through various fundraisers.

With the guidance of our Scientific Advisory Board, we continued to fund the most promising PCDH19 research in 2021 and are excited to have the researchers update us all at our Professional and Family Conference in July 2022.

With the hiring of a part-time staff member in 2020, we were able to grow many of our initiatives while still strategically leveraging our funds by relying heavily on volunteers for support as well.

We are inspired and grateful that you have joined us to make a real impact for individuals and families living with PCDH19 Epilepsy. We take stewardship of your hard earned funds very seriously. Here are the numbers.

EXPENDITURES



Thank you



Because of your support, we were
able to achieve so much even
throughout this challenging year.

THANK YOU!

A Note from the Alliance Board & Staff

The unique challenges that came with this year cannot be understated. While the world was filled with so much uncertainty, much of our community faced personal struggles too. Yet, in spite of it all, our supporters have continued to show up and push forward for the benefit of everyone living with PCDH19. Everything that was outlined in this report was only possible because of our generous donors & families, industry partners, Scientific Advisory Board, as well as our volunteers & staff.

Our biggest lesson of 2021 is that our community is undeniably strong & determined, and when we band together we are capable of accomplishing so much more than we can alone. Thank you for being a part of this story and for carving the way toward a better future for every person affected by PCDH19.

With grateful hearts, thank you for your support.

-PCDH19 Alliance Staff & Board: Sophie Ferreira, Julie Walters, Karin Wells-Kilpatrick, Jennifer Holland, Heather Fryman, and Christy Rollins