Rare Parents as Drug Development Catalysts

Rare Bootcamp 2024

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Pre-Rare Parent

Journey to a Diagnosis

Getting a PhD Overnight

> Dev Med Child Neurol. 2016 Jun;58(6):639–44. doi: 10.1111/dmcn.13033.
Epub 2016 Jan 27.

Eye movement disorders are an early manifestation of CACNA1A mutations in children

Esther M Tantsis [1], Deepak Gill [1], Lyn Griffiths [2], Sachin Gupta [1], John Lawson [3], Neven Maksemous [2], Robert Ouvrier [1], Florence Riant [4], Robert Smith [2], Christopher Troedson [1], Richard Webster [1], Manoj P Menezes [1]

Affiliations + expand

PMID: 26814174 DOI: 10.1111/dmcn.13033

Free article

Abstract

Aim: The alpha-1 isoform of the calcium channel gene is expressed abundantly in neuronal tissue, especially within the cerebellum. Mutations in this gene may manifest with hemiplegic migraine, spinocerebellar ataxia type 6 (SCA6) and episodic ataxia type 2 (EA2) in adults. There are reports of children with CACAN1A mutations presenting with paroxysmal tonic upgaze, abnormal saccades and congenital nystagmus as well as severe forms of hemiplegic migraine. The aim of this study was to review the clinical presentation and subsequent course of all children with a CACNA1A mutation who presented to a tertiary children's hospital.

Spectrum of *CACNA1A*-related Disorders

Developmental Delay/IDD/ Autism Spectrum Disorder

Congenital Ataxia/Hypotonia

Seizures/Developmental and Epileptic Encephalopathies

Eye Movement Disorders

Sleep Disorders

Opportunity for Human Impact Has Never Been Higher

Accelerating Pace of Breakthroughs in...

- Gene Discovery
- Diagnostic & Therapeutic Tools

...is leading to exponential increase in possible

- Targeted Therapies

But...

- 95% have no treatment

...leading to community-driven disruption.

CACNA1A FOUNDATION

CACNA1A Foundation

Vision: A world free of the debilitating effects of CACNA1A-related disorders

Our Advantage: As parents, our children are at the center of our work. We are goal-oriented, determined and working with a sense of urgency to find effective treatments.
Our Promise: We will not give up until we are successful. Our kids are depending on us.

Short-Term Goal (by 2027): Have at least one symptomatic treatment in the clinical trial pipeline

Long-Term Goal (by 2037): Have an FDA-approved gene therapy to address the root cause of disease

The Power of a Rare Community

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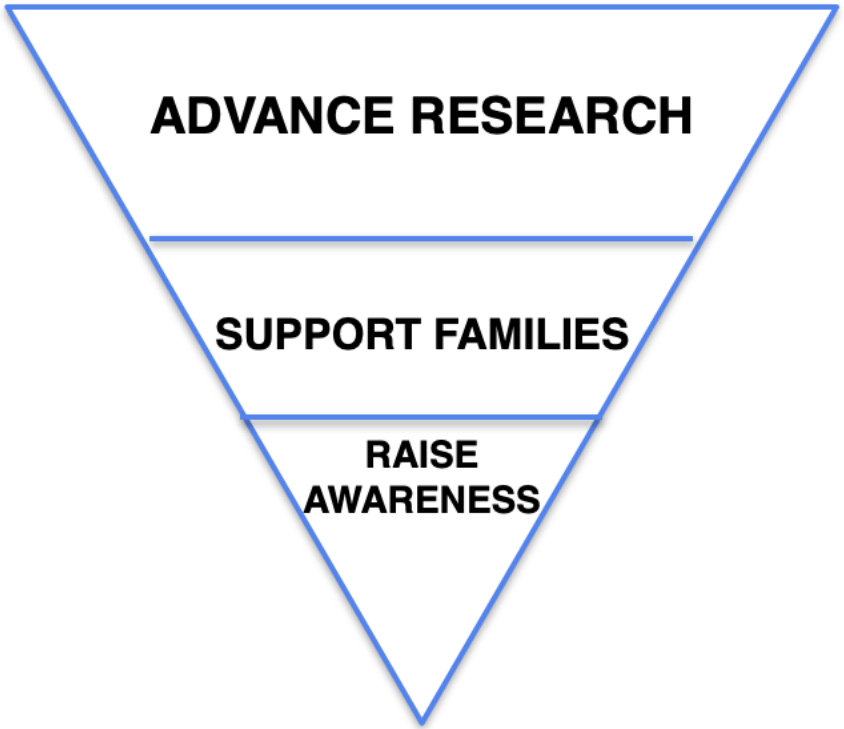
Speeding Progress Towards a Cure



Fund translational research that holds the promise to improve the lives of individuals with CACNA1A-related disorders and their families

Connect families around the world and provide resources to make their journeys easier

Increase recognition among the general public and health care professionals to facilitate earlier diagnosis through genetic testing, find more families to participate in research and improve health outcomes

Advance Research

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Understanding Disease Burden

- CACNA1A Natural History Study
- CACNA1A Clinical Assessments Research Study
- Rare-X Data Collection
- Citizen Medical Records Collection
- Quality of Life & Patient Priorities Survey
- Disease Concept Model Study

Building Preclinical Assets

- Patient-derived iPSCs
- Animal Models

Promoting Collaboration

- CACNA1A Data Portal
- CACNA1A Research Network

Funding Research

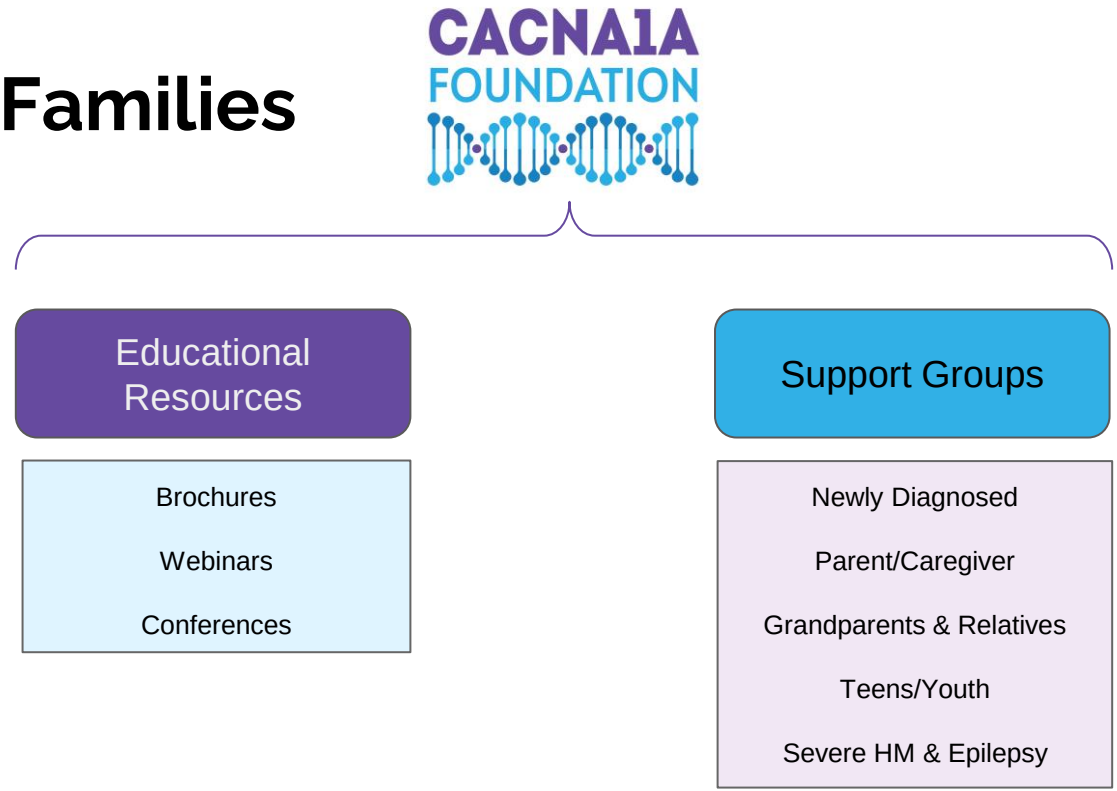
Seed Grants for

- Disease Mechanisms
- Identifying Novel Therapies
- Proof of Concept Studies

Working Groups

- **Natural History Study/Biomarkers**
- **Clinical Care Guidelines**
- **Variant Classification**
- **Preclinical to Clinical**

Support Families



Raise Awareness

CACNA1A FOUNDATION

Global Ambassador Program

- Australia
- Italy
- Netherlands
- Others (needed)

Attend Professional Conferences

- Clinician (AES, NAF, AAPOS)
- Advocacy (GG, NORD)
- Industry (WOD, BIO)
- Funders (CZI, Milken)

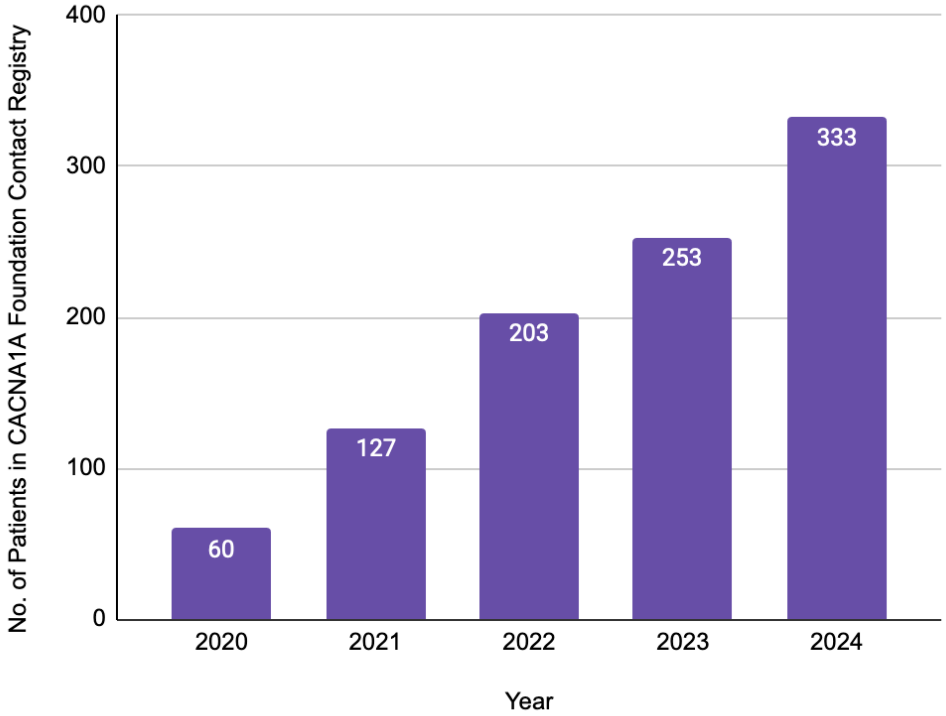
Partner w/Genetic Testing Labs

- Newly Diagnosed Materials
- Genetic Testing for Symptomatic Individuals
- Updating/Changing Variant Classifications

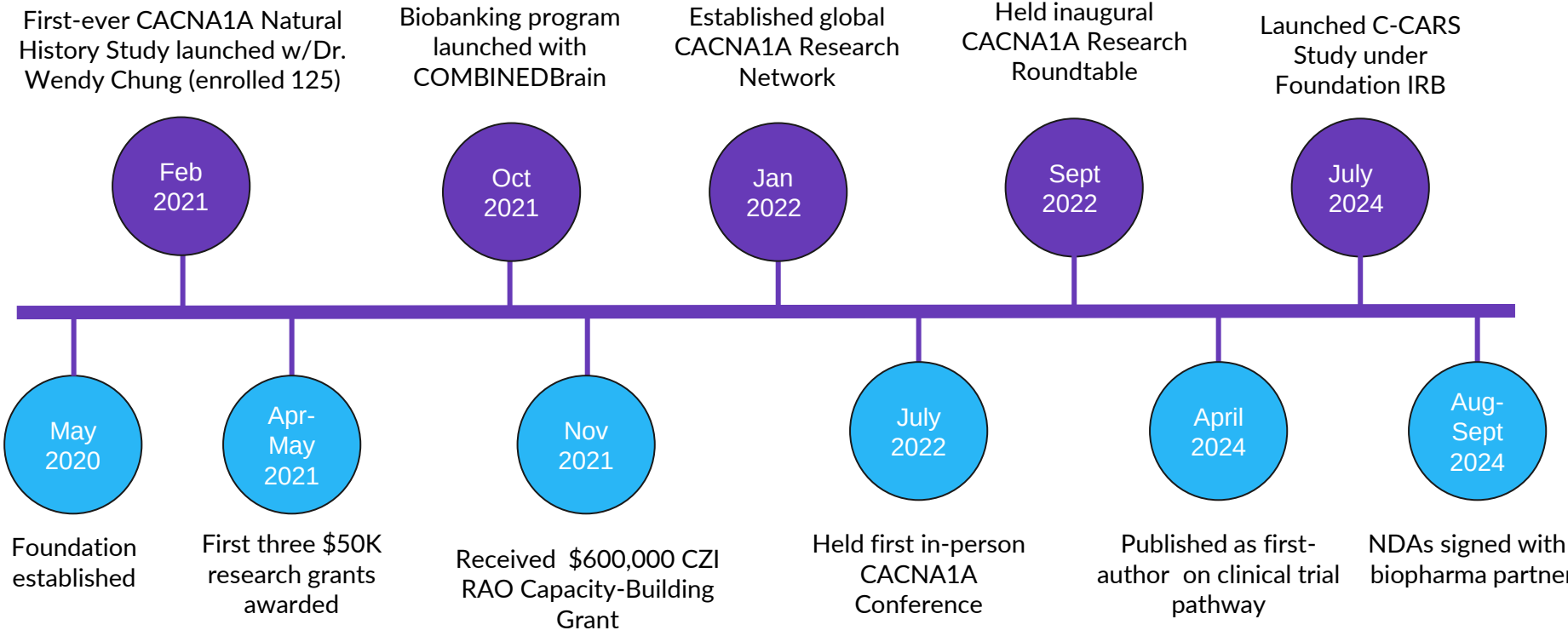
Communications

- Newsletter
- Social Media
- Op-eds/Media Placement

Finding CACNA1A Families



Key Milestones in First 4 Years



Hurdles to Advancing Community-Led Efforts

Research Translation to Human Impact Not Prioritized

Funding Gaps at the "Valley of Death"

Siloed Scientific Infrastructure Rooted in Academia

Lack of Cross-Disease Learnings

Who charges the storm?

1. Buffalo
2. Rare Parents

Buffalo: Charging Through the Valley of Death

Leveraging Proven Pathways to Success

Rare As One

- Innovators are proximate to the problem
- Long-standing philanthropic networks from other sectors
- Greater synergies and potential for success in a portfolio approach

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Hurdles in Current System	
Research Translation to Human Impact Not Prioritized	**Focus on Translation to Humans**
Funding Gaps at the "Valley of Death"	**Investment Networks**
Siloed Scientific Infrastructure Rooted in Academia	**Shared Infrastructure**
Lack of Cross-Disease Learnings	**Open Sourcing of Knowledge**

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It always seems impossible until it’s done.

N. Mandela

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