2024

CURE CADASIL ANNUAL REPORT

HIGHLIGHTS – JANUARY 1, 2024 TO DECEMBER 31, 2024

CONTENTS

Hello and greetings,

We continue to grow and move steadily closer to finding effective treatments, and ultimately a cure for CADASIL. In 2024 we achieved a number of our goals, and made substantial progress on others:

> **We completed our 2024-2026 Strategic Plan**. This comprehensive plan outlines clear objectives and actionable strategies to drive our organization's growth and impact. The plan aligns our resources with our mission, positioning us to achieve our long-term goals.
>
> **We began onboarding the CADASIL Community Natural History Study**. We have been working with the National Organization of Rare Disorders (NORD), and a Registry Advisory Board made up of six volunteers with knowledge of CADASIL, to establish an ongoing repository of patients with, and at-risk for, CADASIL. This effort will position our community for therapeutic trials whenever they become available.
>
> **We secured $1 million funding from the Chan Zuckerberg Initiative (CZI)**. We received the second round of funding (for 2025 and 2026, this detail could be moved to the main text of the annual report) from CZI based on our successful patient-partnered research and patient engagement led by our co-investigator, Dr. Fanny Elahi. This funding will support our continued efforts to advance patient-centered research.
>
> **The CADASIL community had another successful Million Dollar Bike Ride (MDBR)!** Together we once again raised over $100,000 and accepted applications for investigator-initiated research projects. Like the CZI funding, every dollar raised for the MDBR goes to research.
>
> **We established a Scientific Advisory Board (SAB) charter and began recruiting new members.** This important milestone enhances our organization's ability to make informed decisions on potential therapeutic opportunities. By approving the SAB charter, we can better focus our efforts on promising initiatives with potentially impactful outcomes.

We hope that this brief summary of some highlights from 2024 will provide an overview of where we have been and where we hope to go. We are extremely grateful of all the help and financial support we have received from the CADASIL community!

With many thanks, we are your Board of Trustees:

WHO WE ARE

Cure CADASIL is a 501(C)3 nonprofit organization incorporated in the US state or New Jersey. Our Board of Trustees are all volunteers who have CADASIL, or relatives and/or close personal ties to CADASIL.

OUR VISION:

A world without CADASIL.

OUR MISSION:

Cure CADASIL is a patient-led organization committed to advancing CADASIL research through uniting patients, researchers, and clinicians to find a cure for CADASIL.

On March 6, 2024, the cureCADASIL Board of Trustees approved our Strategic Plan (Strategic-Plan-2024-2026). Initiatives and activities on 2024 reflected this plan.

CZI Patient Partnered Collaboration for Rare Neurodegenerative Disease

Patient Organization PI:
Jane Gunther, Science Officer, cureCADASIL

Coordinating PI:
Fanny Elahi, Icahn School of Medicine, Mount Sinai

CADASIL-centered Modeling of Immunovascular Neurodegenerative Disease

2024 was the 2nd year of the CZI grant awarded to cureCADASIL and Mt. Sinai. Highlights included:

January-December: Ongoing patient-partnered research—achieving a milestone of 200 patient enrollees.

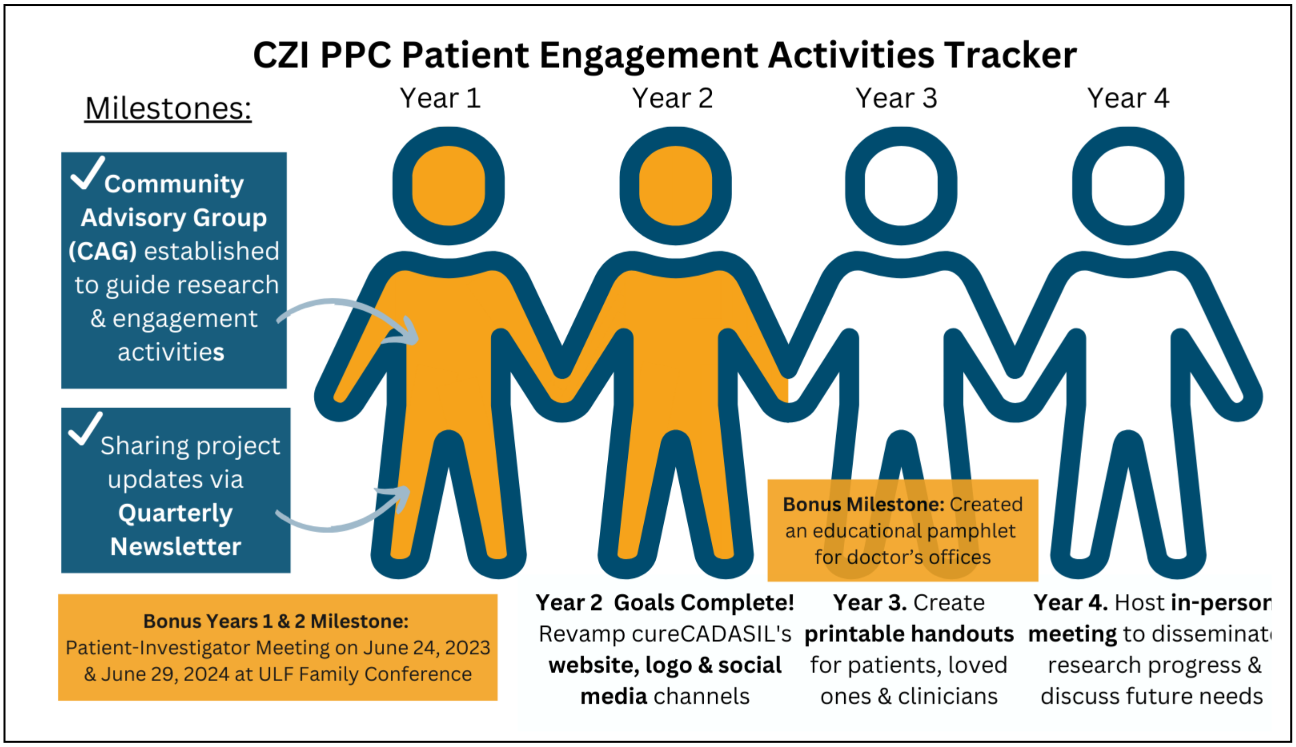
June: Patient-Investigator Meeting featuring the Community Advisory Group presentation and discussion of the results of a survey exploring what is most concerning to patients.

July: A patient perspective presentation at the CZI Neuroscience Meeting.

July: Initiating on-boarding of the “CADASIL Community Natural History Study” with the National Organization of Rare Disorders (NORD).

October: Participation in the 2024 Science in Society Meeting, and hosting a Spotlight Session on Tissue Biobanking.

November: Successful application and renewal of the CZI grant for two more years of funding (2025-2026).



CZI PPC Patient Engagement Activities Tracker

Milestones:

Year 1
Year 2
Year 3
Year 4

✓ **Community Advisory Group (CAG)** established to guide research & engagement activities

✓ Sharing project updates via **Quarterly Newsletter**

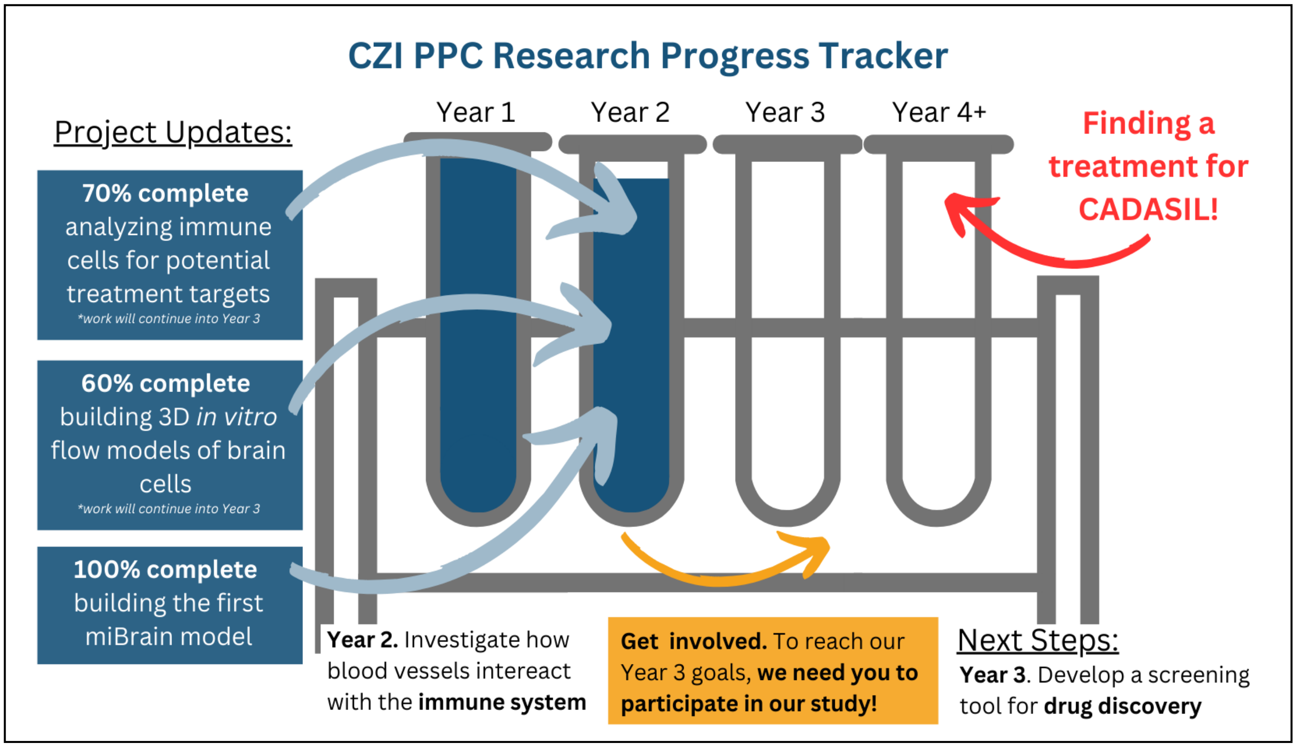
Bonus Milestone: Created an educational pamphlet for doctor's offices

Bonus Years 1 & 2 Milestone: Patient-Investigator Meeting on June 24, 2023 & June 29, 2024 at ULF Family Conference

Year 2 Goals Complete! Revamp cureCADASIL's **website, logo & social media** channels

Year 3. Create **printable handouts** for patients, loved ones & clinicians

Year 4. Host **in-perso** **meeting** to disseminat research progress & discuss future needs



CZI PPC Research Progress Tracker

Project Updates:

Year 1
Year 2
Year 3
Year 4+

Finding a treatment for CADASIL!

70% complete analyzing immune cells for potential treatment targets
**work will continue into Year 3*

60% complete building 3D *in vitro* flow models of brain cells
**work will continue into Year 3*

100% complete building the first miBrain model

Year 2. Investigate how blood vessels intereact with the **immune system**

Get involved. To reach our Year 3 goals, **we need you to participate in our study!**

Next Steps:

Year 3. Develop a screening tool for **drug discovery**

2024 Patient-Investigator Meeting

June 29, 2024 from 9:00am - 12:30pm CDT

held in conjunction with theUnited Leukodystrophy Foundation

ANNUAL FAMILY CONFERENCE

Eaglewood Resort and Spa, Itasca, IL

Dr. Jamie Elliott

Dr. Elisa Ferrante

Dr. Fanny Elahi

Dr. Julie Rutten

Dr. Helena Karlström

cureCADASIL Community Advisory Group

cure**CADASIL**

cureCADASIL Patient-Investigator Meeting

Saturday June 29, 2024; 9:00 am to 12:30 pm CDT

at the United Leukodystrophy Foundation Family Conference
in person at the Eaglewood Resort, Itasca, IL and online via Zoom

Agenda

09:00-09:10	**Welcome and Introduction** - *Bertram Kasiske, cureCADASIL President*
09:10-10:00	**The Power of Patient-Partnered Research in CADASIL** *Community Advisory Group Panel, moderated by Fanny Elahi*
10:00-10:15	**The CADASIL Consortium, an Update** *Jamie Elliot*
10:15-10:30	**National Heart Lung Blood Institute Study, an Update** *Elisa Ferrante*
10:30-10:45	Break
10:45-11:10	**Immunotherapy as treatment strategies for CADASIL** *Helena Karlström*
11:10-11:35	**Patient stratification and biomarker development for NOTCH3-targeting therapies** *Julie Rutten*
11:35-12:25	**Panel Discussion** *All in person and online participants*
12:25-12:30	Announcements: cureCADASIL fall Fundraising campaign! Informal social hour at 5:30 pm for in person attendees

Patient-Investigator Recording Is Live

Categories: CADASIL Awareness Events, CADASIL Conferences, CADASIL Webinars

2024 Patient-Investigator Meeting

Conference Recording Now Available!

View the cureCADASIL meeting on YouTube.

cureCADASIL Community Advisory Group

cureCADASIL

cureCADASIL Patient-Investigator Recording is LIVE!

cureCADASIL is excited to share the recording from the 2024 Patient-Investigator Meeting, which was held on June 29 at the ULF Annual Family Conference.

[Patient-Investigator Meeting Recording – cureCADASIL](https://curecadasil.org/patient-investigator-recording-is-live)
https://curecadasil.org/patient-investigator-recording-is-live

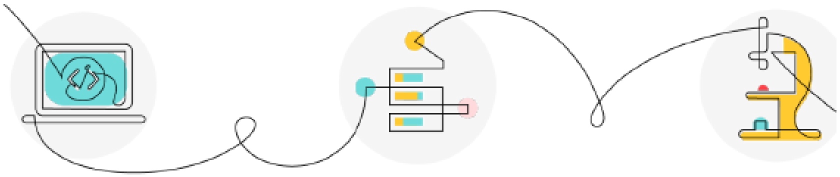
The 2024 Chan-Zuckerberg Initiative Neuroscience Meeting
July 9-12, Monterey, California

The 2024 Neuroscience Meeting brought together CZI Neuroscience program investigators and collaborators, CZI program staff, and Chan Zuckerberg Biohub Network staff. The meeting highlighted the diversity of projects and invited investigators to discuss fundamental neuroscience and neurodegenerative disease.

CureCADASIL, Fanny Elahi, and the Community Advisory Group (CAG) were invited to present patient perspectives on CADASIL. Ki Coale, a CAG member, and Dr. Elahi spoke on the importance of including the patient perspective in research and led an open discussion on the topic at the meeting.

Other sessions discussed new technologies and methods, Artificial Intelligence applications in neuroscience, and bridging the gap in neurotherapeutics from basic research to clinical trials.

Chan
Zuckerberg
Initiative



Science in Society 2024 Meeting

Tuesday, October 15th - Thursday, October 17th
Hayes Mansion, San Jose, CA

CZI grant recipients were invited to participate in a meeting that brought together patients, patient advocacy groups and investigators to forge connections, stimulate collaborations and identify ideas and opportunities for research and development.

CZI SiS Spotlight Session on Tissue Biobanking

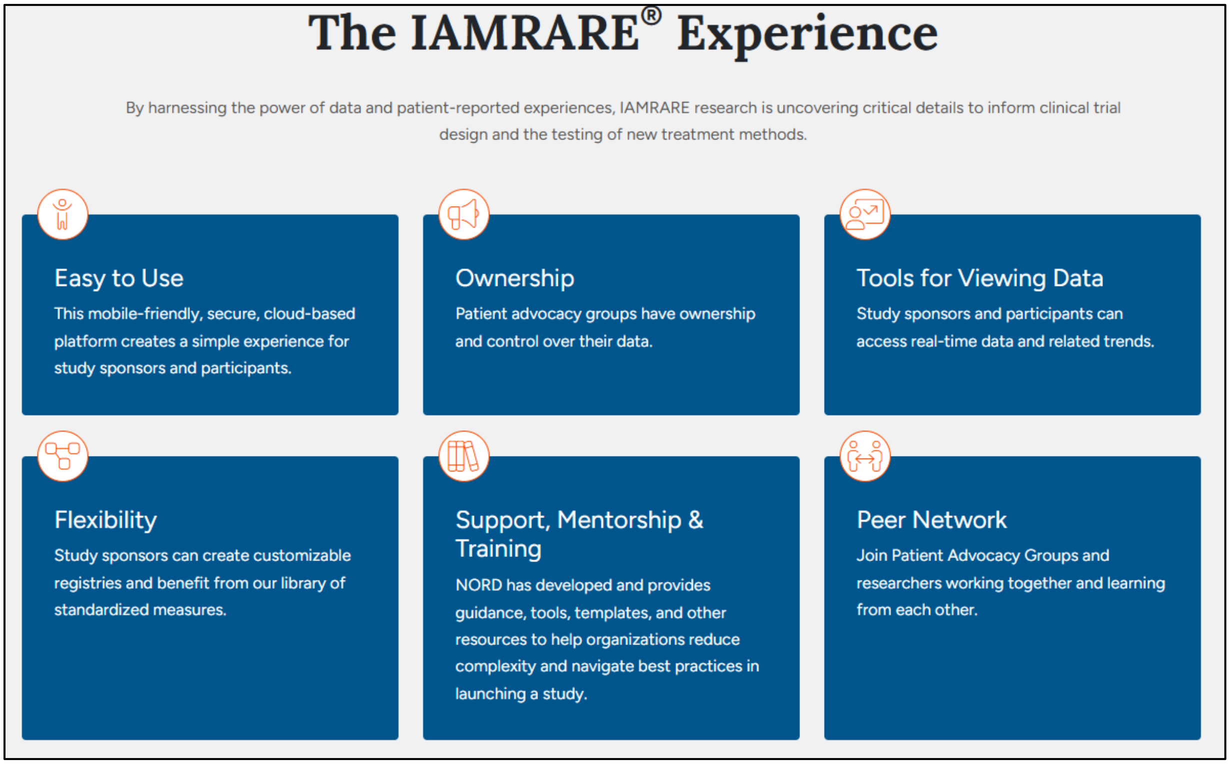
CureCADASIL and our partner investigative team at Mount Sinai held a CZI Science in Society Spotlight Session on Wednesday October 16 at the meeting. The session was chaired by Bertram Kasiske (cureCADASIL) and Fanny Elahi (Mt. Sinai) and brought together investigators that discussed the current challenges and opportunities of specimen biobanking in the US.

CADASIL Community Natural History Study

WE DON'T KNOW HOW STRONG WE ARE UNTIL
BEING STRONG IS THE ONLY CHOICE WE HAVE

In July 2024, cureCADASIL began a registry onboarding process with the National Organization for Rare Disorders (NORD). Our selection of NORD was the result of an extensive and prolonged search for the platform that would best suit the needs of cureCADASIL.

NORD has been in the registry business for over 40 years, and NORD'S IAMRARE® platform offers a number of advantages compared to other registries:



The IAMRARE® Experience

By harnessing the power of data and patient-reported experiences, IAMRARE research is uncovering critical details to inform clinical trial design and the testing of new treatment methods.

Easy to Use
This mobile-friendly, secure, cloud-based platform creates a simple experience for study sponsors and participants.

Ownership
Patient advocacy groups have ownership and control over their data.

Tools for Viewing Data
Study sponsors and participants can access real-time data and related trends.

Flexibility
Study sponsors can create customizable registries and benefit from our library of standardized measures.

Support, Mentorship & Training
NORD has developed and provides guidance, tools, templates, and other resources to help organizations reduce complexity and navigate best practices in launching a study.

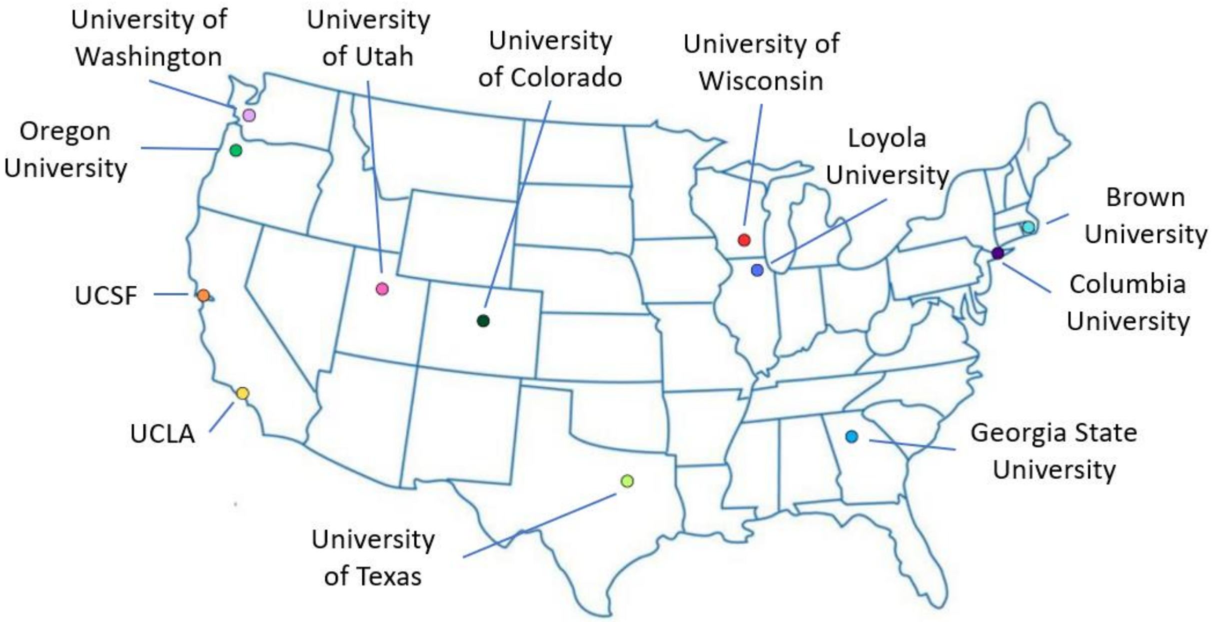
Peer Network
Join Patient Advocacy Groups and researchers working together and learning from each other.

NORD®
National Organization for Rare Disorders

The onboarding process is ongoing, but we anticipate that it will be complete some time in the summer of 2025, and we will start enrolling patients. In addition to enrolling and following our own patients, we also hope to be able to include consenting patients from other observational studies that have collected extensive, valuable data that should be preserved with follow-up updated periodically.

Cure CADASIL Supports the CADASIL Consortium Study!

The CADASIL Consortium is a group of 12 study sites across the United States striving to identify the biological and clinical markers that can inform basic science research and clinical care. The goal is to generate information that can be used to design treatment studies. The main coordinating center is the University of Wisconsin, Madison but individuals can be seen at any of our 12 sites.



Funded by the National Institutes of Health

Co-PI's: Jane Paulsen and Michael Geschwind.

Now approaching enrollment target of 500 participants!

833-795-3016
info@cadasil-consortium.org

CADASIL Consortium

CULTIVATING COMMUNITY

16 NOVEMBER 2024 • ST LOUIS, MO
DR. JANE PAULSEN

@CADASIL_CONSORTIUM

CADASIL Consortium Educational Webinars

UNRAVELING SLEEP IN AGING

Dr. Christine Walsh and
Dr. Liza Ashbrook
UCSF

THURSDAY
29 FEBRUARY 2024

THE GENETICS OF CADASIL

Suman Jayadev, MD
University of Washington

WEDNESDAY
29 MAY 2024

CONTROVERSIES IN CADASIL

Michael Geschwind, MD, PhD
Informed DNA

MONDAY
29 JULY 2024

UNDERSTANDING GENETIC COUNSELING, GENETIC TESTING, AND NEXT STEPS

Tricia See, ScM, CGC
Informed DNA

WEDNESDAY
28 AUGUST 2024

UNDERSTANDING THE CAREGIVER EXPERIENCE

Dr. Allison Lindauer
Oregon Health Sciences
University

WEDNESDAY
25 SEPTEMBER 2024

RETINAL IMAGING IN NEURODEGENERATIVE DISEASES

Dr. Jessica Alber
University of Rhode Island

WEDNESDAY
23 OCTOBER 2024

MRI IN CADASIL
WHAT ARE WE IMAGING AND WHY?

Dr. Laura Eisenmenger
Neuroradiologist, UW Madison

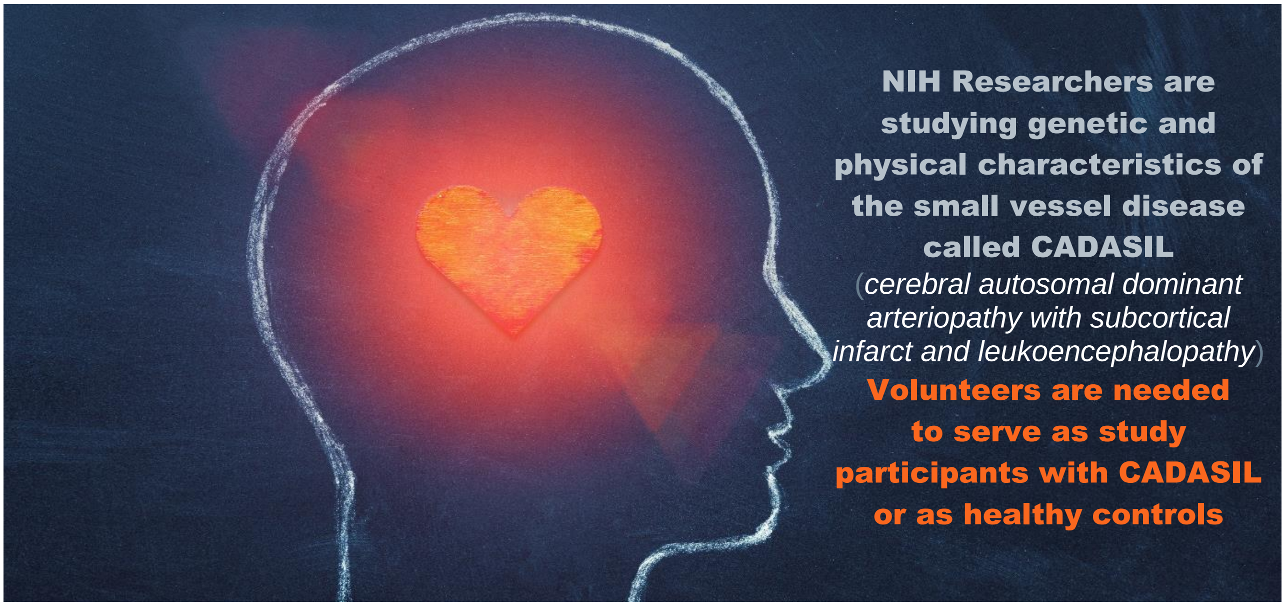
WEDNESDAY
20 NOVEMBER 2024

FAMILY PLANNING AND THE IVF PROCESS IN CADASIL

Dr. Melissa Russo
Women & Infants Hospital

MONDAY
09 DECEMBER 2024

NHLBI – Natural History Study of CADASIL



NIH Researchers are studying genetic and physical characteristics of the small vessel disease called CADASIL
(*cerebral autosomal dominant arteriopathy with subcortical infarct and leukoencephalopathy*)
Volunteers are needed to serve as study participants with CADASIL or as healthy controls

- A pilot natural history study enrolled 20 patients between 2016 – 2022.
- Yearly visits for 3 years were completed.

cDNA Position	Amino acid change	Exon
c.1279C>T	p.(Arg427Cys)	8
c.1364G>A	p.(Cys455Tyr)	8
c.278G>T	p.(Cys93Phe)	3
c.3026G>A	p.(Cys1009Tyr)	19
c.3664T>G	p.(Cys1222Gly)	22
c.397C>T	p.(Arg133Cys)	4
c.397C>T	p.(Arg133Cys)	4
c.397C>T	p.(Arg133Cys)	4
c.397C>T	p.(Arg133Cys)	4

cDNA Position	Amino acid change	Exon
c.421C>T	p.(Arg141Cys)	4
c.421C>T	p.(Arg141Cys)	4
c.505C>T	p.(Arg169Cys)	4
c.665G>A	p.(Cys222Tyr)	4
c.665G>A	p. (Cys222Tyr)	4
c.671G>A	p.(Cys224Tyr)	4
c.697T>G	p.(Cys233Gly)	6
c.778T>C	p.(Cys260Arg)	5
c.994C>T	p.(Arg332Cys)	6
c.994C>T	p.(Arg332Cys)	6

- Now enrolling up to 100 with CADASIL/NOTCH3 variants
- Up to 40 age- and sex-matched healthy volunteers
- 4 visits, 3 years apart over 9 years

For more information: https://go.usa.gov/xtB6E
Email: ccopr@nih.gov
Phone: 1-800-411-0027

National Heart, Lung, and Blood Institute

The 2024 Million Dollar Bike Ride

For several years, the major fundraising event for cureCADASIL has been the Million Dollar Bike Ride, sponsored by the University of Pennsylvania Orphan Disease Center (ODC). All of the donations raised for the MDBR go to fund 1-year, “seed” grants. These grants go directly to the investigators and do not pay indirect costs to institutions.

After the MDBR event has taken place, a request for applications is written by cureCADASIL and posted by the ODC. Applicants fill out online forms, and applications are reviewed by an independent grant review committee convened by the ODC. Typically, the funding period begins in in February in the year after the MDBR, which is usually held in early June.

In 2024, cureCADASIL raised $101,776 and an award was made to Michael Wang, MD, PhD, at the University of Michigan for “Small Molecule Inhibition of NOTCH3 Conformational Alterations”.

Since 2020, cureCADASIL has been proud to support groundbreaking CADASIL research studies through Million Dollar Bike Ride grants, which are only possible through donations and fund-raising efforts. See list of awardees below.

2025

Awardee: Michael Wang, M.D., Ph.D., University of Michigan

Title: "Small Molecule Inhibition of NOTCH3 Conformational Alterations"

Grant Amount: $101,776

Funding Period: February 1, 2025 – January 31, 2026

2024

Awardee: Helena Karlström, Karolinska Institutet

Title: "Immunotherapy and Improved Diagnosis and Prognosis of the Small Vessel Disease CADASIL"

Grant Amount: $109,856

Funding Period: February 1, 2024 – January 31, 2025

2023

Awardee: Fabrice Dabertrand, MD, University of Colorado

Title: "Advance in PIP2 Treatment to Restore Capillary Blood Flow"

Grant Amount: $117,734

Funding Period: February 1, 2023 – January 31, 2024

2022

Awardee: Israel Fernández Cadenas, Fundació Privada Institut de Recerca de l'Hospital de la Santa Creu i Sant Pau
Title: "Single-Nuclei RNA-Seq for CADASIL Understanding and Therapeutic Target Discovery"
Grant Amount: $60,228
Funding Period: February 1, 2022 – January 31, 2023

Awardee: Saskia Lesnik-Oberstein, Leiden University Medical Center
Title: "Modelling CADASIL with Patient iPSC Based 3D Vessel-on-Chip"
Grant Amount: $60,228
Funding Period: February 1, 2022 – January 31, 2023

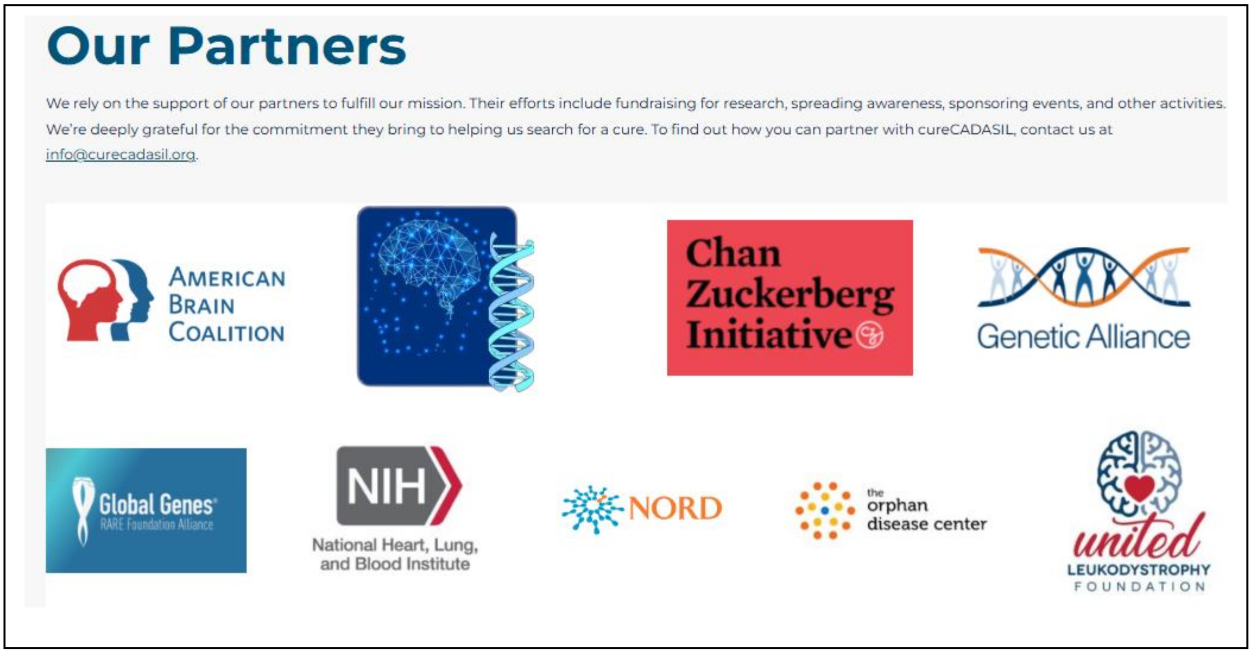
2021

Awardee: Masayo Koide, University of Vermont Larner College of Medicine
Title: "HB-EGF/EGFR Signaling in Capillary Dysfunction in CADASIL"
Grant Amount: $82,795
Funding Period: February 1, 2021 – January 31, 2022

2020

Awardee: Fabrice Dabertrand, MD, University of Colorado
Title: "Pericyte Contractility in CADASIL"
Grant Amount: $81,951
Funding Period: February 1, 2020 – January 31, 2021

Thank You!



Our Partners

We rely on the support of our partners to fulfill our mission. Their efforts include fundraising for research, spreading awareness, sponsoring events, and other activities. We're deeply grateful for the commitment they bring to helping us search for a cure. To find out how you can partner with cureCADASIL, contact us at info@curecadasil.org.

And thanks to all of you who have donated your time and financial support!