PROJECT CASK

IMPACT REPORT 2024

FEBRUARY 2025

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EXECUTIVE SUMMARY

HITOMI KUBO

Co-Founder

In August 2023, Project CASK was founded with a single, urgent mission: to develop effective treatments and a cure for CASK gene disorders. As parents of children affected by this ultra-rare condition, we knew we could not wait for others to prioritize our community. We knew that advancing treatments required focused effort, collaboration, and an unwavering commitment to science and advocacy.

Since our launch 18 months ago, we have expanded the ecosystem of CASK research, planted critical seeds for therapeutic development, funded groundbreaking studies aimed at developing treatments, launched clinical studies to understand more about key symptoms of CASK gene disorders, and fostered community engagement and education.

In this journey, we have been guided and supported by an extensive network of rare disease organizations, our Scientific Advisory Board and a host of other experts and advocates across different phases of rare disease drug development. They have helped us learn, exchange and stay on the leading edge of scientific and medical developments of relevance.

Today, we stand at the forefront of a new era of possibility for therapeutic development for CASK gene disorders. By strategically funding research, collaborating with experts, and amplifying the voices of our community, Project CASK is paving the way for real hope and meaningful change.

Amidst this incredible progress, our community grieves deeply the heartbreaking loss this year of four beautiful individuals living with CASK. Their lives and legacy are at the heart of every decision we make and remind us of the urgency of our mission. We are eternally grateful to our CASK families whose resilience inspire our work and to our generous supporters and donors who help drive forward progress. None of this would be possible without all of you.

A NOTE FROM THE PROJECT CASK LEADERSHIP TEAM

DEAR FRIENDS AND PARTNERS,

For those of you who know us personally, you know we are mothers who refuse to accept “impossible” as an answer. For every roadblock in understanding and treating CASK gene disorders, we see a question to explore, a breakthrough to make happen, and a life to heal.

That is why Project CASK is moving forward with urgency. This past year, we have pushed forward with groundbreaking research, expanded our scientific collaborations, and strengthened the foundation for transformative therapies not as distant possibilities, but as real, tangible solutions in development today. Gene replacement therapy and small molecule treatments are underway, and new strategies are under development.

But this journey is not just about science. It is deeply personal for every one of us in the CASK community. It is about our children: their joy, their struggles, and their boundless potential. It is about honoring their lives and the lives of those who left us far too soon. It is about possibility, which grows stronger with every step we take together.

This report highlights key achievements from 2024, but it is also our commitment to continue to move forward with purpose and scientific rigor, guided by love, compassion and hope.

To the CASK community, our donors, supporters, partners and advisors – thank you for standing with us, believing in this mission, and contributing to our efforts. You have helped turn hope into action and promise into solutions.

With heartfelt gratitude,
Hitomi Kubo, Renée Roquet, Alexandra Dowell, Emily Stiglitz, Alexis Taylor & Megan Weber
Project CASK Leadership Team

2024 IN A NUTSHELL

As we reflect on 2024, we are incredibly proud of the progress we've made together as a community. Through a laser-focus on advancing research, we are creating the pieces of the drug development puzzle, and fostering collaboration to develop life-changing treatments for CASK gene disorders. Below are some of the milestones that define our journey this past year.

Jan 2024 - Launched first Project CASK Grants Program Request for Applications, **eliciting 15 proposals for studies on CASK**

Feb 2024 - Joined **CombinedBrain** - a consortium of rare neurodevelopment disorder organizations who come together to accelerate therapeutic development through collaboration

May 2024 – Kick CASK bracelet partnership with **Little Words Project**

June 2024 – The Magical CASKival a **family-led fundraiser** held in beautiful Lake George, New York - **$24,637**

June 2024 - Joined the **Rare Epilepsy Network** to collaborate to improve outcomes for rare epilepsy patients and families

Jul 2024 - **Awarded $375,000** two-year grant to Dr. Xue, Baylor College of Medicine, for early stages of **gene replacement therapy**

Aug 2024 – Launched Make A Splash for CASK! **community-wide peer-to-peer fundraiser** - **$44,878.66**

Aug 2024 - **Awarded $250,000** two-year grant to Drs. Kreienkamp (Hamburg) and Pak (Amherst) for **small molecule treatment**

Aug 2024 - Launched **first epilepsy study** with Dr. Shahid, NY Presbyterian Hospital, Weill Cornell Medical School

Sept 2024 - Tip Em Back for Tenley a **family-led fundraiser** in Rhode Island - **$45,537.00**

Nov 2024 - Partnered with **Citizen Health** for digital medical record collection and a **digital natural history study**

Nov 2024 - **Funded CASK prevalence study** with GeneScape and Dr. Xue, a crucial foundation for therapeutic development

Nov 2024 - **End Of Year Campaign** - **$48,535**

Dec 2024 – Partnered with **Bishop's Events** - Reindeer Rumble 5k/10k in Washington, DC

CASK STUDIES

Launching Groundbreaking Studies
and Building a CASK Research Network

* GENE REPLACEMENT THERAPY RESEARCH FOR CASK-RELATED DISORDERS

$375,000
Two-year grant

Dr. Mingshan Xue
Baylor College of Medicine

Awarded a $375,000 grant to Dr. Mingshan Xue at Baylor College of Medicine to optimize gene replacement therapy and develop advanced neurobehavioral mouse models for testing. This study represents a major step forward in creating a treatment applicable to all CASK mutations.

* THE ROLE OF THE CASK/LIPRIN-A INTERACTION IN PONTOCEREBELLAR HYPOPLASIA: A TRANSLATIONAL APPROACH

$250,000
Two-year grant

Dr. Hans-Jürgen Kreienkamp
University of Hamburg

Dr. ChangHui Pak
Umass Amherst

Awarded grant for collaboration between two CASK experts to deepen understanding of the interaction between CASK and Liprin-α, which appears to affect the survival of cerebellar granule cells. The PIs will test a compound that may replicate CASK's regulatory functions, potentially halting cell death and improving neurological outcomes.

CASK STUDIES

Launching Groundbreaking Studies
and Building a CASK Research Network

* IDENTIFYING BIOMARKERS FOR EPILEPSY IN PATIENTS WITH CASK-ASSOCIATED PATHOGENIC VARIANTS

Dr. Asim Shahid, MD
Rawan Elhag, MD
Oksana Nulman
Weill Cornell Medicine and New York-Presbyterian Brooklyn Methodist Hospital

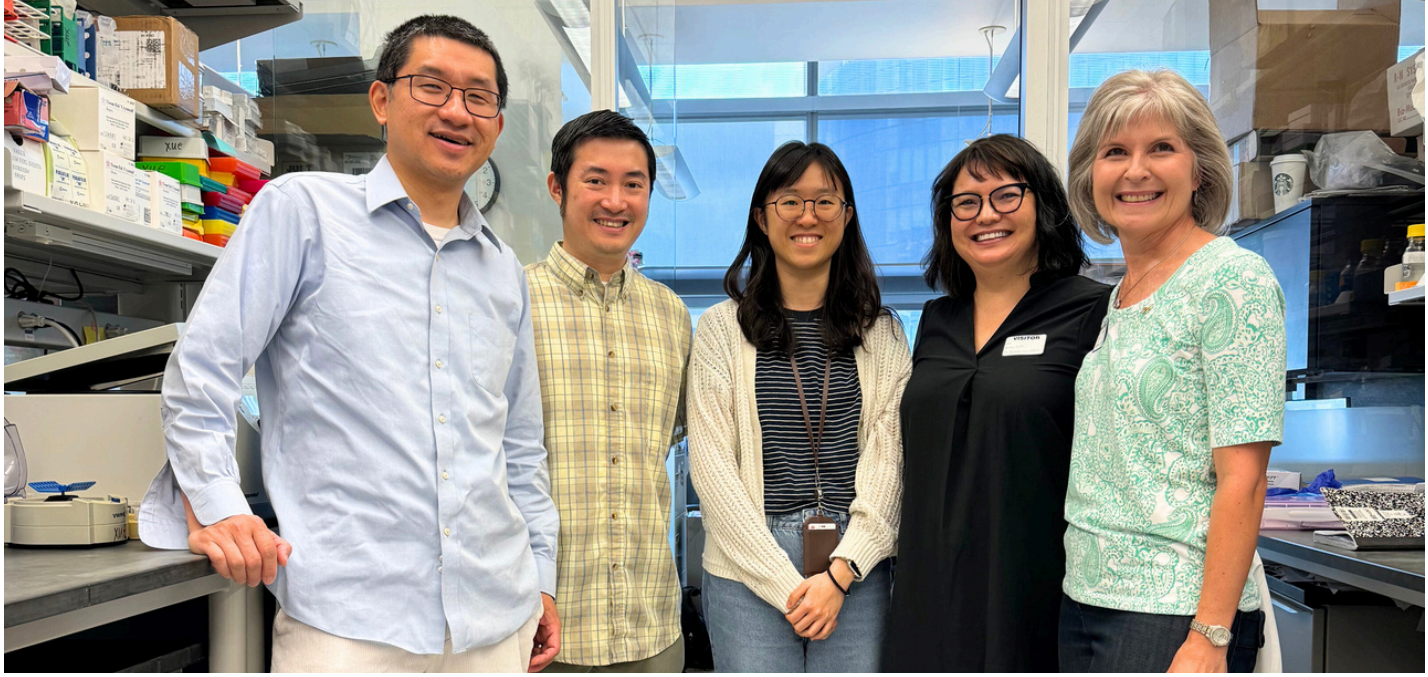
The first comprehensive, caregiver-informed study on CASK-related epilepsy, this study aims to develop an understanding of seizures in people with CASK gene disorders and to identify biomarkers to inform better identification, treatment and possible clinical trial endpoints.

* CASK GENE PREVALENCE STUDY

Dr. Karen Malone, PhD
GeneScape

Dr. Mingshan Xue, PhD
Baylor College of Medicine

The study seeks to quantify the prevalence of CASK-related conditions and understand the broader genetic landscape. Prevalence studies are crucial for rare disease drug development, providing essential data to guide clinical trial design, secure orphan drug status, and attract funding and partnerships.



CREATING THE BUILDING BLOCKS TO DEVELOP TREATMENTS

In 2024, Project CASK partnered with key platforms to ensure that treatments are developed with state-of-the-art models and real-world insights.

DEVELOPING MODELS FOR RESEARCH

Scientists need models, like cells and mice, to develop and test new treatments, helping them understand what works and to what extent. Project CASK is helping develop important models and working to ensure they are publicly available to accelerate research, foster collaboration and attract the biopharma industry.

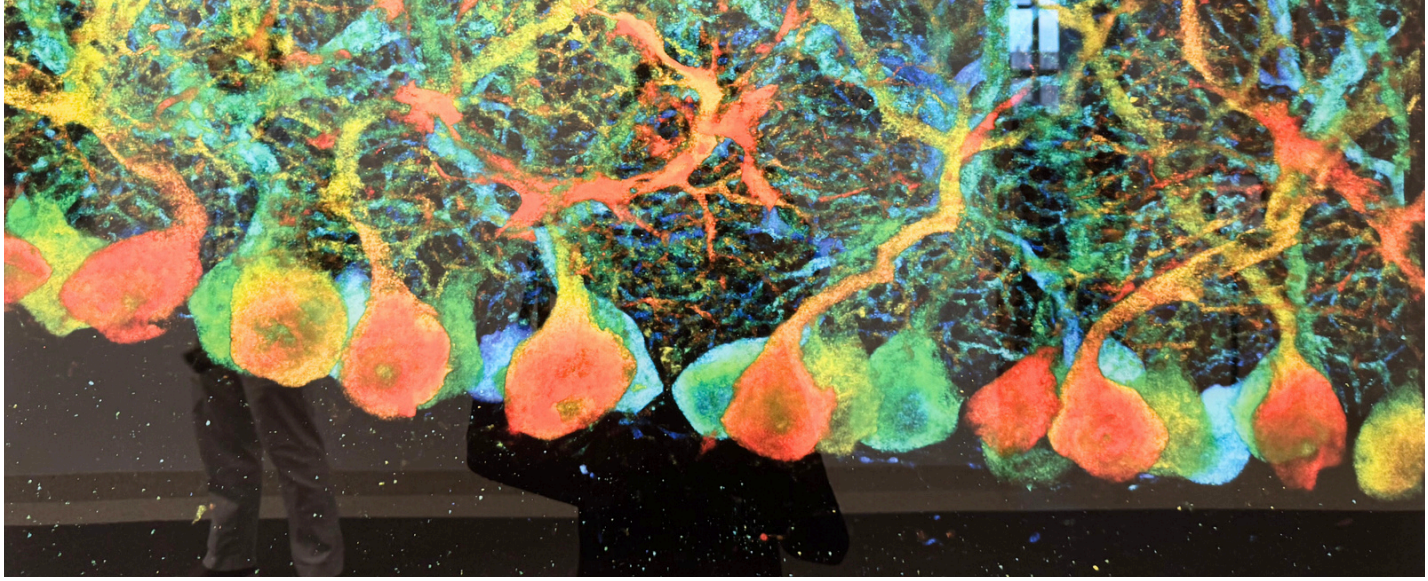
* MICE

Rare Disease Translational Center at Jackson Laboratory: Project CASK has partnered with the RDTC to develop a conditional knock-in mouse model. This model enables testing treatments across the lifespan.

Xue lab at Baylor College of Medicine: Part of the Project CASK funding is supporting the development of male and female mice to test neurobehaviors. These will be made publicly available after the research is published.

* BIOLOGICAL SAMPLESS - iPSC

Combined Brain Biorepository: Project CASK joined the Combined Brain Biorepository to collect biological samples, including human induced pluripotent stem cells (iPSCs). iPSCs are important because they let us create cells with specific CASK variants to learn more about cellular processes and test new treatments.



CREATING THE BUILDING BLOCKS TO DEVELOP TREATMENTS

ADVANCING PATIENT-INFORMED DRUG DEVELOPMENT

Patients are at the heart of every breakthrough in rare disease drug development, shaping research that truly meets their needs. We are grateful for the active engagement of the CASK community, driving a collaborative approach to accelerate our path forward.

CITIZEN HEALTH

Project CASK partnered with Citizen Health, a powerful platform for collecting electronic medical records that can be used, with caregiver consent, to create a digital natural history study (NHS). The insights from this NHS are essential for the drug development process.

RARE-X

The CASK Data Collection Program, powered by Rare-X, is a platform for collecting parent-report survey data to help us better understand CASK gene disorders.

RAISING AWARENESS AND ACCELERATING PROGRESS THROUGH PARTNERSHIP

In 2024, we also focused on expanding our network of partners. These collaborations keep us informed about the latest developments in rare disease research, learning from those who have paved the way, and connecting us with scientists, advisors and industry leaders. We are so grateful for the invaluable knowledge, support and guidance from each of these partners.

AGENDA
Combined Brain
Citizen Health
Global Genes
Jackson Laboratory
Orphan Disease Center
Probably Genetic
Rare-X
Rare Epilepsy Network
Seizure Action Plan Coalition

FOSTERING COMMUNITY CONNECTION AND ENGAGEMENT

* PROJECT CASK PODCAST

The Project CASK Podcast is a place for the CASK community to gather to share our stories, deepen our connections, learn from each other and from others, and hopefully find laughter and joy as we travel this rare disease journey together.

* SOCIAL AND WEBSITE

Grew our engagement through fun, informative and dynamic communications.

* [THE ROAR]

Part of the podcast series, the ROAR are short episodes to keep the CASK community up-to-date on research related information and other happenings in the community.

* PC OPEN HOUSE AND WEBINARS

Project CASK held research webinars and an “Open House” in 2024 to share information with the community and provide opportunities for them to ask questions about the status of therapeutic development for CASK gene disorders.

* ROAR & MORE

Led by CASK mother, Rachel Alves, these social hours bring CASK parents together to share, listen, laugh and sometimes cry. They are an important part of providing support to families on this journey.

FUNDRAISERS AND PARTNERSHIPS TO DRIVE FORWARD TREATMENTS

We are profoundly grateful to the families and businesses who have helped us raise awareness and critical research funds throughout this year. Thank you for being part of this journey. Your generosity fuels us, and we are honored to partner with you in creating a brighter future for all those affected by CASK gene disorders.

* FUNDRAISERS

CASKival
Make a Splash for CASK
TIp 'Em Back for Tenley
Bishop's Events - 5k/10k Reindeer Rumble

* CORPORATE PARTNERSHIPS

Little Words Project
Minted
Billy's Shoes

* CASK MAMA SHOPS

Blithe Little Things
The Girl and The Cookie
Hodgepodge Adaptive

FINANCIAL OVERVIEW

AS OF 31 DECEMBER 2024

FINANCIAL POSITION

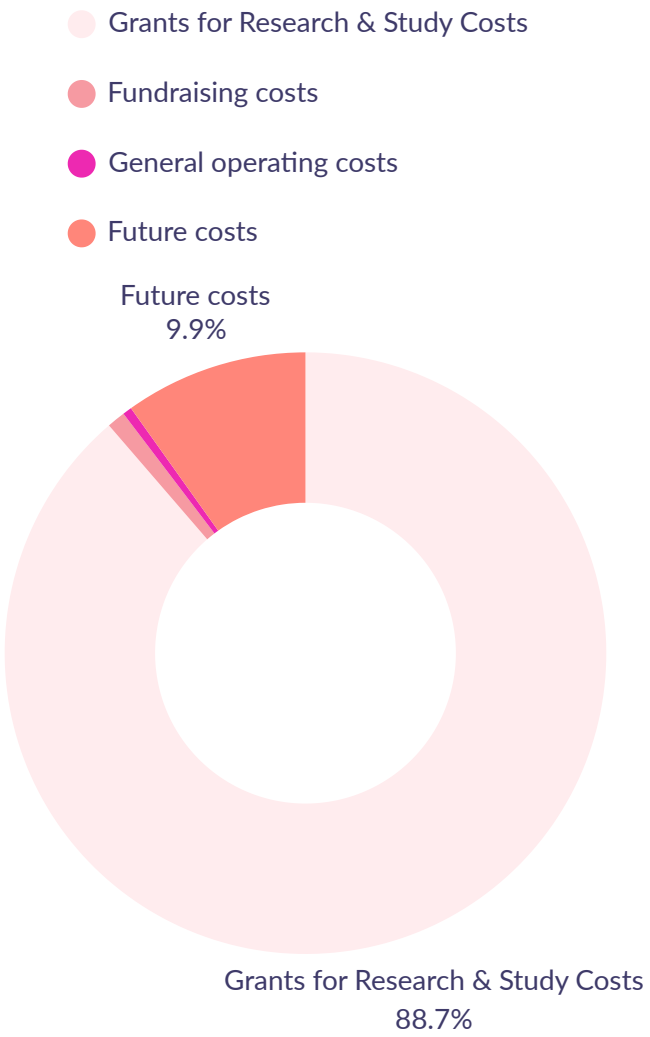
Net Revenue - 2023	**$80,812**
Net Revenue - 2024	**$694,135**
Contributions	$194,135
Grants*	$500,000
Total Assets (cash)	**$774,947**
Total Liabilities	**$631,408**
Baylor Grant	
Amherst Grant	
Hamburg Grant	
Prevalence Study	
Epilepsy Study	

EXPENDITURES

Project CASK invests 89% of its current resources into grants for research and other critical studies to drive therapeutic development for CASK gene disorders.

Less than 2% of net revenue went toward fundraising costs and general operating costs in 2024.

The remaining resources are saved for new therapeutic strategies and other essential studies.



* Grant agreement signed in 2024 with Sophie's Smile Fund

OVERVIEW OF PROJECT CASK

VISION

Project CASK believes in a world free of the life limitations and debilitating effects of CASK gene disorders.

MISSION

To accelerate breakthroughs in research to develop treatments and a cure for CASK gene disorders.

VALUES

Collaboration. Transparency. Urgency.

STATEMENT OF TRANSPARENCY AND COMMITMENT TO DONORS

At Project CASK, our donors are vital partners in our mission to transform the lives of individuals affected by CASK gene disorders. We are deeply grateful for your trust and generosity, and we are committed to upholding the highest standards of transparency, accountability, and impact in everything we do.

"A small body of determined spirits fired by an unquenchable faith in their mission can alter the course of history."
– Mahatma Gandhi

LOOKING AHEAD TO 2025

As we look ahead to 2025, **we remain committed to accelerating research, expanding collaborations, and deepening our impact within the CASK community**. Our focus will be on exploring **new genetic medicine strategies**, **strengthening data collection**, and ensuring that **families have access to useful resources** on therapeutic development. With the dedication of our community, scientists, and diverse partners, **we move forward with hope, urgency, determination, and a shared vision** for a future in which treatments are possible.

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