JULY, 2025

CITRIN FOUNDATION NEWSLETTER

RECENT EVENTS

Citrin Foundation Global Symposium 2025

This June, the Foundation hosted its third in-person symposium on citrin deficiency at the Møller Institute, University of Cambridge. Spanning two and a half days, the scientific program featured a dynamic schedule of talks and a dedicated poster session. Topics ranged from exploring the biochemical mechanisms, new preclinical models, new diagnostic and bioprofiling tools to advancements in therapeutic approaches for citrin deficiency.

On the final day, the sessions explored topics ranging from clinical trial design and execution to the financial viability of novel therapies for rare diseases and AI-driven drug repurposing. Six posters from the poster walk had also been selected for flash talk presentations, offering researchers a platform to showcase their work. In addition to the formal program, the Foundation hosted an afternoon of social activities, giving attendees an opportunity to experience Cambridge while continuing to build relationships in a more informal setting.
This was our largest symposium to date, reflecting both the momentum of ongoing research and the continued growth of our community through expanded funding and an increasingly connected consortium network. More than 80 delegates (clinicians, scientists, dietitians, biotech representatives, patients and families) joined us from Australia, Bulgaria, Canada, Finland, Italy, Japan, Malaysia, Singapore, South Korea, Spain, Sweden, Switzerland, Taiwan, the United Kingdom, the United States, and Vietnam.

While citrin deficiency remained the central focus, the event also addressed broader rare disease challenges through cross-sector collaboration. We move forward with renewed conviction that this gathering has helped accelerate our shared mission—and we are excited for what lies ahead.
Thank you again to all who participated and contributed to this remarkable event. To relive some highlights, we invite you to visit our YouTube channel and view the *symposium highlights reel.*

Opening Ceremony:
Urea Cycle Disorders Translational Center Universität Zurich - Citrin Foundation

On 22 May 2025, the Citrin Foundation and the University of Zürich announced the launch of a ground-breaking initiative: the world's first center fully dedicated to translational research in urea cycle disorders (UCDs), to be hosted at the University Children's Hospital Zürich.

With a significant financial commitment from the Foundation for 10 years, the Center is uniquely positioned to accelerate progress in UCDs. By using citrin deficiency as a model disease, the Center aims to build a scalable model for translational research that addresses the broader family of urea cycle disorders. These rare conditions share overlapping metabolic pathways and clinical features—making them ideal for a unified, cross-disease approach that emphasizes clinical impact and scalability.

Led by Professor Johannes Häberle, a global expert in UCDs and inherited metabolic disorders, the Center will focus on high-priority translational research areas such as:

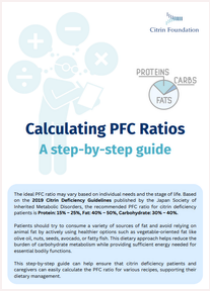
- Multi-omics biomarker discovery
- Liver metabolic function research
- Development of novel therapies, including gene therapy
- Clinical trial readiness

This milestone brings us ever closer to our ultimate goal: curing citrin deficiency, whilst also making a lasting impact on the wider rare disease landscape. You can learn more about the Center on our website.

PATIENT ENGAGEMENT UPDATES

PFC Resource Now Available

To support dietary management, the Foundation has created a step-by-step guide for calculating Protein-Fat-Carbohydrate (PFC) ratios using USDA Food Data. A downloadable Excel tool is also available to simplify the process. This resource is designed to help patients and caregivers better manage nutritional needs with confidence and accuracy.



Expanding Our Team to Vietnam

The Citrin Foundation has recently expanded its global outreach to Vietnam with the addition of a part-time Patient Engagement Assistant. This local role will help improve access to resources by translating and tailoring materials to meet cultural and linguistic needs, while also fostering stronger community ties through in-person events and ongoing engagement. This move reflects our continued commitment to supporting the global citrin deficiency community.

Recent Events

Hong Kong Webinar

The Foundation hosted a webinar for patients, families, and healthcare professionals in Hong Kong. The session offered updates on Foundation initiatives, dietary guidance, and peer insights, creating a valuable space for education and community connection.

Attendees gained a deeper understanding of the Foundation's work, including its research focus and patient support initiatives. The session also covered practical strategies for managing the condition, including dietary tips and lessons learned from other patient groups.

Rare Disease Day 2025

TThe Foundation was honoured to contribute to this year's Rare Disease Day symposium, hosted by the Pacific Northwest Research Institute. The event gathered over 30 rare disease organizations and emphasized collaboration in accelerating research and innovation across the rare disease space.

RESEARCH UPDATES

New Publications

Deciphering the Mutational Background in Citrin Deficiency Through a Nationwide Study in Japan and Literature Review

Published in Human Mutation, this paper combined nationwide data from Japan with a literature review to analyse genetic and clinical information from 345 patients to examine if there are any genotype-phenotype correlations in citrin deficiency. Among 68 identified variants, c.852_855del and c.1177+1G>A were the most common. The c.852_855del mutation—predicted to cause a severely truncated and nonfunctional citrin protein—was strongly associated with more severe disease features. This work enhances our understanding of citrin deficiency and lays important groundwork for future therapeutic strategies, such as gene-targeted interventions. Supported by the Citrin Foundation, led by Jun Kido (Kumamoto University) and Johannes Häberle (University Children's Hospital Zürich), the study exemplifies international collaboration, with contributions from Japan, the UK, and Switzerland. We congratulate all authors on this impactful contribution to the field.

Current Understanding of Pathogenic Mechanisms and Disease Models of Citrin Deficiency

Published in the Journal of Inherited Metabolic Disease, this review offers new perspectives on the underlying disease mechanisms by examining how specific mutations may lead to distinct dysfunctions, and presents an in-depth look at citrin's structure, transport mechanisms, as well as provides evidence suggesting it is unlikely regulated by calcium. The review also explores both cellular and animal models of citrin deficiency. Supported by the Citrin Foundation, this work marks a significant contribution to the field. The review was co–first-authored by Denis Lacabanne and Alice Sowton, with Edmund Kunji and Sotiria Tavoulari as senior authors—all from the University of Cambridge. We extend our congratulations to the authors for this publication.

New Funded Projects

Characterization of Cellular and Murine Models for Citrin Deficiency and Discovery of Therapeutic Compounds and Gene Editing Strategies

The Foundation has funded a new project with Gerald Schwank and Johannes Häberle (University of Zürich and University Children's Hospital Zürich), building on earlier funded research and now focused on therapeutic discovery for citrin deficiency. New mouse models with common SLC25A13 mutations will be used to test base editing, prime editing, and whole-gene insertion, while citrin-KO HepaRG cells previously developed by the team will be used to explore other therapeutic options including compound screening.

Elucidating Citrin Deficiency through iPSC-Derived Hepatocyte-like Organoid and AGC2/AGC1 Rescue Strategies

The Foundation has funded a new study led by Giuseppe Fiermonte (University of Bari Aldo Moro), that aims to develop a new 3D hepatocyte-like organoid model from patient-derived iPSCs. This cellular model may offer further insights into the pathogenesis of citrin deficiency and help identify new therapeutic approaches.

Citrin Deficiency Wikipedia Page

Citrin deficiency now has a dedicated Wikipedia page, a significant step toward increasing awareness of this rare metabolic disorder. As one of the most widely used online resources, Wikipedia ensures that patients, caregivers, and healthcare professionals can easily access reliable information on the condition, its symptoms, and management. Greater visibility can lead to earlier diagnoses, improved support, and broader recognition within the medical community. This is an ongoing project, which we will be continuously updating. If you have any suggestions, please get in touch.

Thank you for being a part of the Foundation's journey to finding a cure for citrin deficiency. We welcome suggestions on how we can improve our resources as well as ideas for new projects to explore and support you better. If you would like to get in touch, please email us at patients@citrinfoundation.org. We look forward to continuing to support you and your family.

You can look forward to the next edition of our newsletter in the Autumn.