CITRIN FOUNDATION NEWSLETTER

CONFERENCES & EVENTS

Highlights from ICIEM 2025 Kyoto

In September, over 2,800 attendees from across the globe came together in Kyoto, Japan, to exchange knowledge and inspire progress in the field of inherited metabolic diseases at the International Congress of Inborn Errors of Metabolism (ICIEM) 2025. We were very honoured and grateful to **Professor Kimitoshi Nakamura**, the President of the ICIEM 2025, and the organizing committees for letting us take part in this global meeting to share our ongoing efforts and to contribute to the progress in the rare disease field. Below are some highlights where these joint efforts were reflected in action.

Our Scientific Supervisory Board Chair and Nobel Laureate in Chemistry (1997), **Professor Sir John Walker** (University of Cambridge, UK), delivered an inspiring opening keynote lecture. In his talk, "My Life in the Mitochondria", he reflected on his lifelong dedication to scientific discovery and outlined his pioneering research on ATP synthase, the enzyme that powers our cells. This groundbreaking work, which earned him the Nobel Prize, continues to shape our understanding of metabolism and metabolic disorders.

We were particularly grateful that Professor Walker highlighted his identification of the citrin protein, a breakthrough that ultimately enabled the discovery of citrin deficiency in Japan. His remarks underscored the vital role of fundamental research in advancing medical progress and reaffirmed the alignment between his scientific contributions and the mission of the Citrin Foundation.

Citrin Deficiency Special Symposium

The Citrin Foundation proudly organised a symposium, **"From Pathogenesis to Therapy, From Japan to the World: Global Translation, Metabolic Flux, and Gene Editing for Citrin Deficiency"** exploring how citrin deficiency can serve as a model for global translational innovation. Co-chaired by **Kimitoshi Nakamura** (Kumamoto University, Japan) and **Barbara Yu** (Citrin Foundation, Singapore and UK), the session brought together leading experts from Japan, Switzerland, and the United States.

Speakers addressed diverse themes, including:

- *Understanding Citrin Deficiency Within the Spectrum of Liver Metabolic Diseases and Urea Cycle Disorders* - **Johannes Häberle** (University Children's Hospital Zürich, University of Zürich, Switzerland)
- *Metabolic Flux Analysis and New Biochemical Insights in Citrin Deficiency* - **Marc Hellerstein** (University of California, Berkeley, USA)
- *Correcting Genetic Liver Diseases by Prime Editing* - **Gerald Schwank** (University of Zürich, Switzerland)
- *The Status of Adult Patients with Citrin Deficiency in Japan* - **Jun Kido** (Kumamoto University, Japan)
- *Proteomic Approaches to Newborn Screening for Citrin Deficiency* - **Yoichi Wada** (Tohoku University, Japan)
- *Financial Realities and the Way Forward for Novel Therapies in Rare Diseases* - **Barbara Yu** (Citrin Foundation, Singapore and UK)

This multidisciplinary dialogue underscored citrin deficiency's potential to bridge basic science, emerging therapies, and real-world patient care.

Artificial Intelligence (AI) Plenary Lecture and Roundtable Discussion

At a conference plenary session, **Barbara Yu** co-chaired with **Marshall Summar** (Uncommon Cures, USA), to welcome **Marinka Žitnik** (Harvard University, USA), a global leader in applying AI to biomedical science, who delivered her lecture, **"Empowering Biomedical Research with AI Scientists"**.

It emphasised how AI can accelerate scientific research, drug discovery and clinical translation, ultimately improving outcomes for individuals affected by IEMs.

The Citrin Foundation also convened a closed-door roundtable with Marinka Žitnik and an international group of leading clinicians and researchers. The discussion explored the transformative potential of AI in advancing the study of citrin deficiency and possible collaborative pathways to effectively harness this cutting-edge technology. We are deeply grateful to Marinka Žitnik and all participants for contributing to this forward-looking exchange.

6th International Symposium on Urea Cycle Disorders

As part of the satellite meetings to ICIEM, the 6th International Symposium on Urea Cycle Disorders (UCDs) brought together the global UCD research community to share discoveries, strengthen collaborations, and inspire the next generation of investigators.

The meeting was co-hosted by the National Urea Cycle Disorders Foundation (NUCDF) and the Urea Cycle Disorders Consortium (UCDC). The Citrin Foundation was proud to serve on the organising committee and scientific program committee.

In a joint session, **Barbara Yu** and **Tresa Warner** (NUCDF, USA) presented "Innovative Therapies: Patients' Expectations". This session highlighted the need to integrate scientific progress with patients' lived experiences, as well as the roles that can be played by patient organisations in driving innovative therapies.

Reflecting on ICIEM Kyoto

ICIEM Kyoto was a truly inspiring gathering that showcased remarkable progress across the field of inborn errors of metabolism. Our heartfelt appreciation and congratulations to the organisers for hosting such a successful and impactful event.

RESEARCH UPDATES

New Publications

The status of adult patients with citrin deficiency in Japan: A report from the nationwide study

We are excited to share that a new study has been published in Molecular Genetics and Metabolism.

Long-term outcomes in adult citrin deficiency patients are poorly understood and underrepresented in cohort studies. This research provides a large-scale analysis of 128 adult citrin deficiency patients in Japan. This is the largest cohort and first study of its kind, providing important insights into the clinical course of citrin deficiency in adulthood.

Key findings include:

- Adults with early diagnosis of citrin deficiency generally showed favourable long-term outcomes.
- Those diagnosed later, with adolescent and adult CD (AACD), were at higher risk of persistent or worsening symptoms, including hepatic encephalopathy, intellectual disability, and reduced quality of life.

- Late-onset cases may develop liver conditions resembling end-stage metabolic dysfunction-associated steatotic liver disease (MASLD), suggesting that patients may experience irreversible liver damage.

These findings highlight the importance of early diagnosis and ongoing proper management and care.

Partly supported by the Citrin Foundation, this work was first authored by **Jun Kido**, with **Kimitoshi Nakamura** (Kumamoto University) as senior author, and included contributions from their long-standing collaborator, **Johannes Häberle** (University Children's Hospital Zürich).

New Research Projects

We are pleased to announce the following recently funded research projects.

Molecular mechanisms underscoring citrin biogenesis and dissecting compensatory pathways in CD using CRISPR screens
Diana Stojanovski - University of Melbourne, Australia

Metabolic changes and disease progression in citrin deficiency
Laura Contreras and Araceli del Arco - Autonomous University of Madrid, Spain

Elucidating citrin deficiency through iPSC-derived hepatocyte-like organoids and AGC2/AGC1 rescue strategies
Giuseppe Fiermonte - University of Bari, Italy

WELCOME TO OUR NEW TEAM MEMBER

It is with great pleasure that we announce that Su Kit Chew has joined us as Senior Director of Translational Research and Partnerships. In this role, he will oversee the Foundation's translational research programs, while also fostering strong collaborations across the diverse stakeholders we work with. Coming from an experienced background in biotech and academic research, Su Kit holds a BA in Biological Sciences from the University of Oxford and a PhD from UT Southwestern Medical Center.

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.

If you would like to get in touch, please email us at info@citrinfoundation.org for general inquiries or grants@citrinfoundation.org for research grant inquiries. If you are a patient, please email us at patients@citrinfoundation.org. We look forward to continuing to support you and your family.