



CITRIN FOUNDATION QUARTERLY NEWSLETTER

RESEARCH UPDATES

We are pleased to announce the recent publication of new review articles on citrin deficiency (CD), published in the Journal of Inherited Metabolic Disease (JIMD).

The first publication, titled *“The therapeutic landscape of citrin deficiency”*, (DOI: [link](#)) offers a comprehensive review of current treatment strategies for Citrin Deficiency (CD), evaluating their effectiveness, limitations, and explore potential new therapeutic options. It also provides an in-depth analysis of medium-chain triglycerides (MCT), the most widely utilized supplement for CD, assessing its impact on different CD phenotypes across multiple studies. This work is the result of a collaboration between Prof. Johannes Häberle’s team and the Citrin Foundation. We would like to express our deep gratitude to Prof. Häberle for his pivotal role in this publication.

This paper complements the previously announced publication titled *“Clinical landscape of citrin deficiency: A global perspective on a multifaceted condition”*, (DOI: [link](#)), with both articles set to be published back-to-back in an upcoming special issue of JIMD.

The next paper, authored by Prof. Johannes Häberle titled *“Citrin deficiency – The East-side story”* (DOI: [link](#)), provides a succinct overview of the history and phenotypes of CD, the importance of considering CD in differential diagnoses, and the current global prevalence of the condition.

Together, these publications represent a significant step forward in CD research. We extend our congratulations to all authors for their contributions and for achieving this important milestone.

CONFERENCES AND EVENTS

Society for the Study of Inborn Errors of Metabolism (SSIEM) Annual Symposium, September 2024, Porto, Portugal

[Citrin Foundation Sponsored Roundtable](#)

At this year’s SSIEM meeting in Porto, Citrin Foundation hosted a unique roundtable discussion titled *“Multi-Stakeholder Perspectives on the Development of Novel Therapies for Monogenetic Metabolic Diseases.”* Moderated by **Barbara Yu**, co-founder of the Foundation, and **Prof. Cary O. Harding**, from Oregon Health & Science University, the session brought together a highly relevant and diverse group of panellists, including the top global regulators, **Dr. Peter Marks**, Director of the Center for Biologics Evaluation and Research at the FDA, and **Kristina Larsson**, Head of the Office for Orphan Medicines at the EMA, alongside **Prof. Simon Jones** from St. Mary’s Hospital at the University of Manchester, **Prof. Dwight Koeberl** from Duke University School of Medicine, **Raquel Marques**, Founder and Head of the Sanfilippo Portugal Association, and **Tresa Warner**, President of the National Urea Cycle Disorders Foundation.



The panel explored the challenges of translating preclinical findings into clinical trials for monogenic metabolic diseases, with a focus on identifying appropriate biomarkers and clinical endpoints. They also discussed how to optimize clinical trial designs for different therapies, including the need for control groups, particularly in pediatric patients, and the advantages of involving patients and regulators early in the process. The session concluded on a positive note, highlighting the progress being made by the leading regulatory bodies to streamline the approval process for orphan drugs, and the potential for global collaboration in this effort.

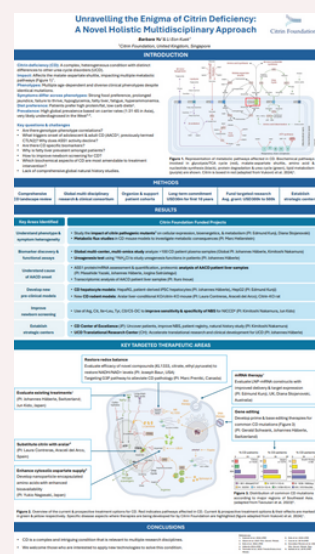


The event underscored the collaborative efforts needed to overcome barriers and advance novel therapies for patients. We are grateful to all of those who took part, particularly our panellists who contributed their valuable expertise and insight.



[SSIEM Poster Presentation by Citrin Foundation](#)

The Foundation also presented a poster titled *"Unravelling the Enigma of Citrin Deficiency: A Novel Holistic Multidisciplinary Approach"*. The poster outlined the complexity of CD and provided an overview of the Foundation’s multidisciplinary approach to address these challenges. By highlighting the intricate and complex nature of CD, the poster called for collaborative efforts and invited those interested to join us in advancing research and treatment for this condition.



[65th Annual Meeting of the Japanese Society for Inherited Metabolic Diseases \(JSIMD\), November 2024, Tokyo, Japan](#)

The Foundation will host a Citrin Deficiency Symposium during the 65th Annual Meeting of the JSIMD on the *"Advancements in Novel Therapies and New Cellular Models for Citrin Deficiency"*. The symposium will take place on 8th November from 15:00 to 16:30 (JST). **Barbara Yu** from the Foundation will be giving an overview presentation. The session will feature **Prof. Joseph Baur** from the University of Pennsylvania who will present on the use of novel redox-modulating compounds as potential therapies for CD. **Dr. Julien Baruteau** from Great Ormond Street Hospital for Children, University College London, will talk about the recent developments in mRNA therapies and potential applications for CD. Finally, **Prof. Jun Kido** from Kumamoto University will present on the evaluation of therapies in new cellular models of CD.

[British Inherited Metabolic Disease Group \(BIMDG\) Annual Meeting, June 2024, Newport, United Kingdom](#)

In June, our Patient Engagement Team attended the British Inherited Metabolic Disease Group Meeting in Newport, South Wales. This event is the largest meeting of its kind in the United Kingdom and Ireland. Our team was able to catch up with members of our professional network and foster new collaborations.

UPCOMING EXPERT TALKS

The Foundation has curated a programme of Expert Talks for our consortium and wider network. We have invited speakers who are leading experts in their respective fields to give presentations covering a range of topics relevant to our network and our mission. Please contact us if you are interested to attend.

Speaker: Prof. Donald E. Ingber

Founding Director, Wyss Institute for Biologically Inspired Engineering, Harvard University

Topic: Organ-on-a-chip technology & AI drug discovery approach

Date: Wednesday, 18th September

Time: 9am EST / 2pm GMT / 10pm JST

Theme: Organ-on-a-chip technologies as well as the use of artificial intelligence (AI) in high-throughput whole organism genetic screening and how this technology can accelerate the discovery and development of novel therapies for rare diseases.

Speaker: Dr. Andrew Anzalone

Co-Founder and Head of Prime Editing Platform, Prime Medicine

Topic: Prime Editing Technology

Date: Tuesday, 8th October

Time: 9am EST / 2pm GMT / 10pm JST

Theme: The latest developments in prime editing technology and its applications for clinical use.

Speaker: Hisaharu Shinohara

General Manager, GW Pharmaceuticals Japan

Topic: Rare diseases law and orphan drug approval in Japan

Date: Thursday, 21st November

Time: 7am EST / 12pm GMT / 9pm JST

Theme: The current regulatory landscape for rare diseases in Japan, including recent approvals for novel therapies, new measures and future outlooks.

PATIENT ENGAGEMENT

Vietnamese Resources

The Foundation is aware of a large patient cohort in Vietnam. We have had a variety of our [resources](#) professionally translated into Vietnamese so that we can reach those who may not speak English. These can be found on our [patient website](#).

Research Summaries

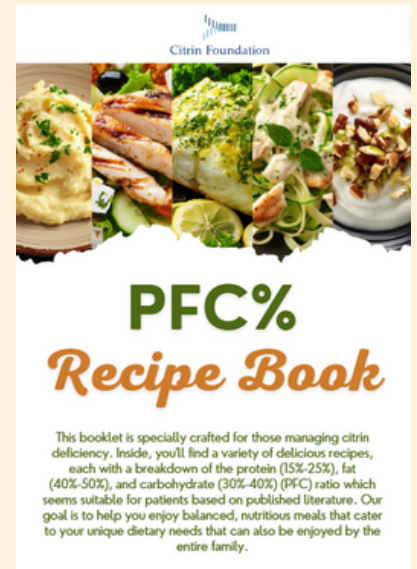
We understand that finding the time to read full-length research papers can be challenging, and the technical language may sometimes be difficult for some of our members to fully comprehend. Therefore, we have prepared concise summaries of key research papers on citrin deficiency. These summaries are available under the [Publications](#) tab on the patient website.



FOOD PREFERENCES OF PATIENTS WITH CITRIN DEFICIENCY	Summary of findings
<p>Other references: A balanced selection of amino deficiencies (SD) is a strong dietary preference towards high glycine and low methionine foods, high in carbohydrates and sugars. This study by Khanna and colleagues (Khanna et al 2022) investigated the food preferences and nutrient aspects of CD patients. The study aimed to understand their preferences for various foods and their nutrient composition (fibre, protein, fat, and carbohydrates) relative to healthy subjects, providing insights into dietary management for the condition.</p> <p>Study Design and Subjects: The study involved recruiting 10 patients with CD from various medical institutions and the National Institute of Child Health and Human Development (NICHD) in the United States. The study was conducted from October 2019 to February 2020. Participants were categorized by age and diagnosis stage.</p> <p>Diets: The diets included diets of food preferences using a scale ranging from ' dislike very much' to ' like very much,' including a 'neutral' option for specific food items across various categories. Nutrient and food intake information was also collected. Food data helped find preferences for young children.</p> <p>Findings: The food preferences (FP) ranged from 1 (least preferred) to 9 (most preferred). The FP of food items were calculated, and the FP of nutrients was determined using the Standard Tables of Food Composition (USDA 2019). Cooking data and recipes were utilized to adjust nutrient content of nutrients.</p>	<ul style="list-style-type: none"> The results showed that the foods marked as "liked" accounted for 88.3% in the patients versus significantly higher than the 69.3% in the controls. The results also showed that patients clearly disliked foods with 20-24% fat content in these categories, 95.8% fat average or less fat, and 24.5% fat average or more carbohydrates. For patients with CD, a strong preference for high protein, high-fat foods like meat, eggs, and fish, along with a selection to sugar is evident. In comparison to healthy subjects, patients marked significantly lower in their preference for foods containing 20-24% or less protein, 45-54% or less fat, and 85% or more carbohydrates. The study preference lists patients manage their symptoms and maintain a higher quality of life (QoL). The scores revealed that these patients liked a significantly higher percentage of foods compared to controls, especially those high in carbohydrates. The foods that patients liked also had higher protein, fat, and iron concentrations. Female patients generally used more foods as disliked compared to male participants with dietary intake differences. <p>Take home message</p> <p>For managing CD, it is important to focus on a diet high in protein and fat and low in carbohydrates. However, when foods like meat, eggs, and dairy, while avoiding sugar, foods and those high in carbohydrates. This dietary approach can help you manage your symptoms and maintain a better quality of life. However, with CD, other dietary issues, such as food intolerance, nutrient deficiencies, and other health issues, may exist. Therefore, these preferences and your body's way of thinking you open with your condition. Stick to this diet to help your symptoms and live healthy.</p>

PFC Recipe Cookbook

Our new [PFC recipe booklet](#) for citrin deficiency patients is now available to download on our patient website. We hope this resource helps make the day-to-day planning of meals easier for patients and parents.



Peer Support Community Overview

Launched in January 2023, our global peer support group now includes over 30 members from around the world. This group provides a space for patients and families to share experiences, support one another, and collaborate with the Foundation's Patient Engagement team, fostering new resources and initiatives. Some of the key topics discussed have been breastfeeding, MCT oil supplementation, food recommendations, and symptom management.

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.

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