



Citrin Foundation

Citrin Foundation Introduction

Section 1: Citrin Foundation introduction

Who we are

Citrin Foundation is a research-driven, non-profit organization set up in 2016 to tackle citrin deficiency (CD), a monogenetic inborn error of metabolism, as well as a secondary urea cycle disorder. Our goal is to find effective treatments and ultimately a cure for the condition, and we also provide support to citrin deficiency patients and their families globally.

The Foundation has committed to invest USD30 million, which is entirely provided by our co-founders, in the next decade to achieve our aims. We fund research projects by offering generous grants to clinicians and researchers who wish to better understand the condition and develop new therapies.



Mission & Vision



There are two cornerstones to the foundation's mission, finding a cure for CD and providing life-long support to CD patients. We believe that a multi-disciplinary, innovative and long-term approach will deliver breakthrough treatments and address the well-being of CD patients holistically. We seek to work with top scientists, researchers, and clinicians who are in related fields globally to solve this medical problem together.

We have developed the following list of objectives to achieve this:

- Identify patients with citrin deficiency worldwide
- Study the natural course of disease in large patient cohorts
- Improve the diagnosis of citrin deficiency
- Understand the basic science and pathogenesis of the disease
- Explore the benefits of existing therapies
- Develop new therapies
- Support affected patients and their families

What is Citrin Deficiency?

Citrin deficiency (CD) is an underdiagnosed and understudied inborn metabolic condition that is also a secondary urea cycle disorder characterized by four distinct phenotypes: 1) NICCD, 2) the adaptation or silent period, 3) FTTDCD, and 4) CTLN2, with the latter representing the final and most severe form of the condition with recurrent hyperammonaemia. There is currently no cure for CD besides liver transplantation and patients manage their symptoms with lifelong dietary intervention and regular check-ups with their attending clinicians.

Section 2: Research funding and ongoing projects

We believe that having a global consortium of scientific researchers and clinicians collaborating in an open, non-competitive, and synergistic manner will allow us to achieve our goals.

Research grants

We are looking to expand the scope and number of research projects funded by our Foundation to accelerate the scientific development and understanding of this condition. Clinical, translational, and basic science proposals will be considered, while innovative and/or interdisciplinary grants are encouraged. Our Foundation will also work with biotech and pharmaceutical companies to develop potential therapeutics for this condition.

Our funding does not rely on any external factors or targets, so those who are successful in their grant applications have a real shot at producing ground-breaking research. Furthermore, we are the bridge between clinicians and basic scientists; rarely do these two entities meet but the best research tends to happen when they do.

For more detailed information on our research aims and objectives, please look through the Foundation's research strategy on our website.

Our Ongoing Research Projects

Citrin Foundation is currently funding numerous projects working with top scientists, researchers and physicians globally to improve/discover effective therapeutics. Please find more details about each project and the projects we have previously funded on our website.



Basic Science Projects

Mitochondrial function & cellular bioenergetics of CD

Prof. Edmund Kunji, University of Cambridge

Biogenesis & trafficking of Citrin in CD

Dr. Diana Stojanovski, University of Melbourne

Post-translational regulation of ASS1 in CTLN2

Prof. Ituro Inoue, National Institute of Genetics



Liver-specific Therapies

Clinical study of LOLA in CTLN2 patients

Prof. Masahide Yazaki, Shinshu University

CRISPR gene editing therapy

Prof. Gerald Schwank & Prof. Johannes Häberle, University of Zürich

Small molecule compounds

Prof. Joseph Baur, University of Pennsylvania

Nanotechnology on amino acids

Prof. Yukio Nagasaki, University of Tsukuba

Replace citrin with aralar isoform

Prof. Jorgina Satrústegui, Autonomous University of Madrid

mRNA therapy

Work with a leading biotech company

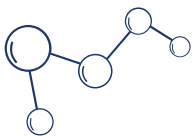


Pre-clinical research models available



Various preclinical cellular and animal models are available from Citrin Foundation to aid in your research on citrin deficiency on a case-by-case basis. For mouse models, the Foundation has citrin/mGPD double-KO strains available for order from the Jackson Laboratories mouse repository.

Section 3: Examples of clinical studies



Global multi-omics study in citrin deficiency for biomarker identification

A major hurdle in developing effective treatments for CD is the lack of effective biomarkers that track well with disease severity or measure the effectiveness of therapeutics. This Foundation-initiated study aims to identify robust circulating biomarkers of CD through targeted and untargeted metabolomics, proteomics, lipidomics, and transcriptomics analysis of blood samples collected from CD patients. The Foundation has gathered a global patient cohort of over 300 patients to participate in the study and will target over 100 CD patients of all ages. Study results are expected to come out in 2024/25. The co-PIs of this project are: Prof. Johannes Häberle at the University Children's Hospital in Zürich and Prof. Kimitoshi Nakamura at Kumamoto University in Japan.



Ureagenesis function test

The ureagenesis test, developed by Prof. Johannes Häberle at the University Children's Hospital in Zürich, accurately determines ureagenesis functions in patients by measuring the incorporation of orally ingested ammonium chloride tracer into urea. CD patients, particularly those with CTLN2, often have perturbations in their urea cycle which may lead to hyperammonemic episodes. The ureagenesis test can test whether their urea cycle functions are compromised and enables better prognosis. This test has already been conducted in some CD patients and has been proven to be very safe. If you have a patient with citrin deficiency and are interested in this test, please reach out to our Foundation at shaimalterkawi@citrixfoundation.org

Register with us

If you are a medical practitioner who is interested in citrin deficiency and would like to be kept informed of any updates or development, please register with us via our website to become a part of our global professional network.



Resources

Patient flyer

We have developed a comprehensive, downloadable resource which covers:

- Overview of the condition
- Current treatment and management
- Available support and resources
- Ways in which patients can get involved with the Foundation



**Your guide to
citrin deficiency**

SYMPTOMS TREATMENT SUPPORT

Patient website

We have created a dedicated citrin deficiency patient website which includes resources such as patient stories, diet management tips, and more.

Global digital community



Upcoming Global Citrin Deficiency Symposium

18th-20th September 2023
Magdalene College, Cambridge University



The Foundation is pleased to host the second in-person Global Citrin Deficiency Symposium this autumn. This conference seeks to provide a comprehensive update of the latest scientific and clinical research findings on citrin deficiency, with the hope to foster in-depth discussions, brainstorm new ideas, and spark further collaborations among those in our professional network. This will provide an effective avenue for us to move closer to our ultimate goal of solving this condition collectively.

We will be bringing together world-class scientists and clinicians who conduct research on citrin deficiency and/or related areas as well as those who have an interest in the condition. Some of the patients from our network will also be joining for the last half day of the conference.

This event will be held at Magdalene College, Cambridge University, a beautiful venue with a rich history in the academic city of Cambridge, UK this September. There is no registration fee. For more information please contact: andreatan@citrinfoundation.org



Citrin Foundation

Citrin Foundation Ltd.



6 Temasek Boulevard
#38-05 Suntec Tower Four
Singapore 038986



info@citrinfoundation.org



<https://citrinfoundation.org>



Citrin Foundation

Find a cure, Fund research, Support Patients and Families

