

WELCOME!

Welcome to the latest issue of the **Cambridge Clinical Mitochondrial Research Group** patient newsletter. You are receiving this because you have previously signed up to help with research into **mitochondrial disease or neurodegenerative disorders**. Our aim is to provide you with the latest news from the research group, giving you more information on who we are, what we do, the science behind our work, and how we can support you, our patients.

In this issue, we will update you on some exciting new **clinical trials**/studies and put a spotlight on some of our laboratory work.

WORLD MITOCHONDRIAL DISEASE WEEK



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This year, **18th-24th September 2022** is **World Mitochondrial Disease Week**. This global campaign aims to raise awareness of the importance of mito health & the impact of mitochondrial disease.

Keep an eye on our Twitter page as we will be **'baking it green'** along with our colleagues in the MRC Mitochondrial Biology Unit (MRC-MBU)!

Also that week, we are running a small **focus group** of patients with mitochondrial disease - our "experts by experience" - in order to get their insights and input to ensure the quality and relevance of our research.

BAKE IT GREEN

FOR



WORLD
MITOCHONDRIAL
DISEASE WEEK

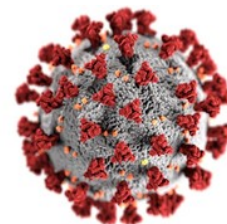
COVID-19 booster and immune responses - study update

In our previous issue, we wrote about the launch of a small study to look at whether the **immune systems** of patients with mitochondrial disease respond to the **COVID-19 vaccine** in the same way as the rest of the population. This study involves collecting **blood samples** (up to 30ml of blood (6 tsps)) on **two** occasions: around the time of the **booster** vaccine, and then again 28 days later. These samples will allow us to study immune cells in great detail.

THANK YOU to those of you who have already signed up and provided samples. If you have signed up but have not had your COVID-19 booster yet, we note that this should be happening in the autumn. **Don't forget** to get in touch with us to let us know the date of your vaccine, and we can organise the blood samples around you.

If you:

- **have not signed up to the study yet**
- **are a mitochondrial disease patient**
- **have not had your most recent COVID-19 booster vaccine**
- **would be willing to come to Addenbrooke's Hospital on two occasions for a blood sample**



then please contact the research team on: mitoteam@addenbrookes.nhs.uk or ring **01223 331506**. All travel expenses will be reimbursed.



FOCUS ON...

In this issue of our newsletter, we would like to share with you information on some new **commercial clinical trials and studies** that are about to open to recruitment in Cambridge, and which you might be contacted about...

The NuPower Study (SPIMD-301)

WHAT IS IT ABOUT?

SPIMD-301 is a 48-week, randomized, double-blind, parallel-group, placebo-controlled **trial** to assess the efficacy and safety of single daily subcutaneous administration of **elamipretide** as a treatment for subjects with primary mitochondrial myopathy associated with **nuclear DNA mutations** (nPMD). Subjects will be randomized 1:1 to 60mg Elamipretide or matching placebo groups.

WHAT IS INVOLVED?

The trial involves 7 visits to Cambridge over a 1 year period. Study visits will include physical & neurological exams, blood tests, questionnaires and some physical activities: the 6-minute walk test, the triple timed up and go test, and the five times sit to stand test. Participants will need to self-administer an injection of the study drug daily for 48 weeks, keeping a diary to log this.

WHO IS RUNNING THIS STUDY?

The sponsor for this trial is **Stealth BioTherapeutics Inc.** There are 3 sites within the UK taking part, with Cambridge being one of them! If you are interested in taking part, and would like to know which nuclear DNA mutations are eligible for this trial, please get in touch with us using the details on the last page of this newsletter.



FALCON study (ADOA)

WHAT IS IT ABOUT?

A prospective natural history study of patients with autosomal dominant optic atrophy (ADOA). The aim is to collect as much information about as many ADOA patients as possible, to increase our knowledge of the disease and investigate potential treatments.

WHAT IS INVOLVED?

This study will involve 5 visits to Cambridge over a 2 year period. Study visits will include collecting information about medical & family history, physical exams, blood tests, questionnaires and a number of different eye assessments.

WHO IS RUNNING THIS STUDY?



The sponsor for this trial is **Stoke Therapeutics.** There are 2 sites within the UK taking part, with Cambridge being one of them! If you have ADOA and are interested in taking part, please get in touch with us using the details on the last page of this newsletter.

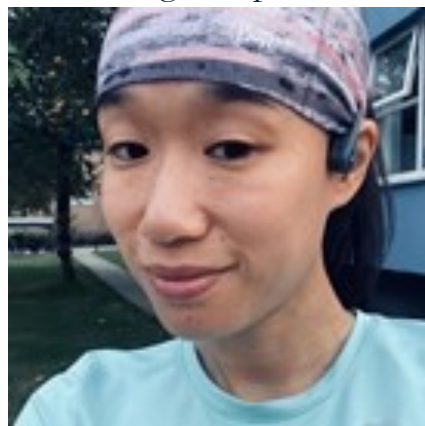


View from the lab...

As well as our clinical work, we also have a strong **laboratory programme**, based in the MRC Mitochondrial Biology Unit (MBU), and the John van Geest Centre for Brain Repair. We thought we would share with you some of the basic science that underpins our clinical research. In this issue, we are revealing more about two research projects.

Dr May Yung Tiet: Exploring the mechanisms of neurodegeneration in Ataxia-Telangiectasia:

Dr May Yung Tiet has been studying the mechanisms of neurodegeneration in Ataxia Telangiectasia (AT) as part of her PhD. She is currently assessing memory in AT patients compared to healthy volunteers, and she will explore affected brain pathways using MRI imaging. She has recently reported that micro-bleeds in the brain are more common in ‘classic AT’ patients, compared to more mildly affected ‘variant AT’ patients. Dr Tiet has been using AT patient skin samples to explore why the mitochondria do not work properly,



and she has found blood biomarkers that are increased in AT patients. The study is ongoing whilst she builds a biobank of AT patient samples. The aims are to find suitable pathways to target drug treatments, and biomarkers to assess the effectiveness of any future drugs in clinical trials.

In her spare time, May also found the energy to run the **Thames Path ultra marathon** on 10th September, raising money for the **AT Society!** WELL DONE May!

Citrin deficiency

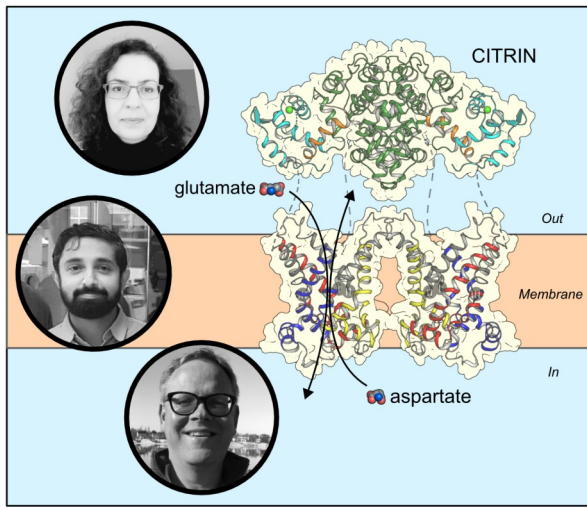
Metabolism is the processes in the cells of the human body that convert food into **energy**. **Citrin Deficiency** is an **inherited metabolic condition**, with a variety of symptoms, which vary between patients and in different stages of life. Children usually present with jaundice, weight stagnation and liver problems. As they grow older, these patients cannot easily process foods rich in carbohydrates, such as rice, bread, or pasta, because of their faulty metabolism. To get the energy they need, they eat food containing fat and protein, such as meat, milk, dairy products, and nuts. Patients can generally lead a normal life with diet management, but when the condition is not properly diagnosed or monitored, it can lead to a severe form of the disease in adult life, causing neuropsychiatric symptoms and liver failure. The disease is very common in East-Asia with approximately one patient in 7,000 people, but also occurs in other parts of the world.

Citrin is a **transport protein** that sits in the membrane of **mitochondria** and is used for the transport of key amino acids that are important for human metabolism. In Citrin Deficiency, citrin is missing or impaired because of genetic changes (“**mutations**”), and this leads to a reduced energy production and dysfunction of the liver.

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View from the lab continued...



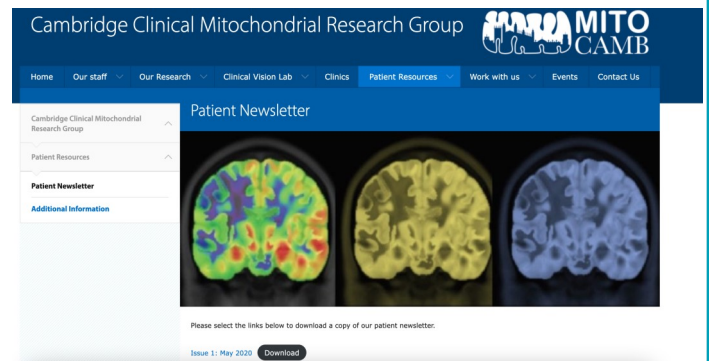
Funded by the **Citrin Foundation** (<https://patient.citrinfoundation.org/en/>), Drs Sotiria Tavoulari, Bosco Jose and Edmund Kunji (pictured top to bottom) study how these mutations affect citrin and how they in turn impact metabolism, energy production and the overall function of mitochondria and human cells, with the aim to explore new treatment options for the future.

A structural model of the **citrin protein** is illustrated here, showing the transport of the amino acids glutamate and aspartate.

Never miss an issue

Inbox heaving under the weight of so many emails? Remember reading something interesting in a previous issue of the newsletter, but you cannot remember where you saved it? Never fear! All of our patient newsletters get added to our **website**, so you can always go back to them. Just head to the following page to download them:

<https://www-neurosciences.medschl.cam.ac.uk/mitocamb/information-for-our-patients/patient-newsletter/>



CONTACT US

Thank you for your continuing participation in our research programme. If you have any queries relating to **research studies** that you have taken part in, or if you would like further information on any of our studies, please contact the team on:



mitoteam@addenbrookes.nhs.uk



01223 335106



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<https://www-neurosciences.medschl.cam.ac.uk/mitocamb/>

For queries regarding **routine NHS clinic appointments**, please contact Katrina Dedman:

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or 01223 216751

