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# MitoCAMB Patient Newsletter

Issue 9
February
2024

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# WELCOME

…to our 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.

## RARE DISEASE DAY 29 FEBRUARY 2024

The global annual event is due to take place this year on one of the rarest days of the year – 29th February! The aim is to raise awareness and generate change for the 300 million people worldwide living with a rare disease, their families and carers. The movement's goal is to work towards 'equity in social opportunity, healthcare, and access to diagnosis and therapies for people living with a rare disease.'

In support of this day, you are invited to SHARE YOUR COLOURS via social media, take part in events, and share your experiences online or with friends. In doing so you will be joining other patients, families, caregivers, clinicians, researchers, policy makers and more around the world to raise awareness of rare diseases.

Check out their website https://www.rarediseaseday.org/#share-your-colours to read stories of some heroes affected by rare diseases, join the community, find an event near you or download resources to help you share your colours.

300M
PEOPLE WITH RARE DISEASES

600+
EVENTS WORLDWIDE

106
COUNTRIES INVOLVED

## LifeArc ART-TRAnslation Project

The MitoCAMB team are taking part in an exciting collaboration between artists and researchers to develop a collection of artwork inspired by insights into rare diseases research. The artist that we are paired up with is particularly interested in the process to reach a diagnosis for rare disease. If you would like to share anything with the artist from your own experience, we would love to hear from you (email add-tr.mitoteam@nhs.net).

The artwork will be displayed at two exhibitions this year:

LifeArc's Translational Sciences Summit - 23rd April 2024 (Business Design Centre, London)

CamRARE's RAREfest24 launch evening - 29th November 2024 (Guildhall, Cambridge)

camRARE
Cambridge Rare Disease Network

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# STUDY UPDATES NEWSFLASH

Here's a quick overview of what's been going on in the world of MitoCAMB in the last few months…

## Studies closed to recruitment – where we are now…

### MITOX

After 2½ years we have now finished recruitment to this study. Thank you to the patients and healthy volunteers who took part. The samples and data are now being analysed to help answer the important question around the effects of giving **high flow oxygen** to patients with mito disease. What we learn from this study may help researchers develop more effective therapies for mitochondrial diseases in the future. We will be in contact with news on our findings later in the year.

### Nicotinamide Riboside (NR)

We would like to extend a huge thanks again to those who took part in the NR study. The last of the data is currently under analysis and the team aim to publish the results this year. We will share news of the publication as soon as this is released.

### PROSPAX Natural History study

Thank you to everyone who completed their final visits in 2023. More information, news and updates about the study can be found at the PROSPAX consortium's website https://www.prospax.net/

## Studies open for recruitment – what you could be involved in…

### Outcomes Research in Inherited Optic Neuropathies (ORION)

Baseline visits have started for the ORION study. By increasing our understanding of how inherited optic neuropathies progress over time, we hope to inform future clinical trials for potential therapies. ORION involves 4-6 visits over 3 years and includes a range of visual tests. We are open to recruitment and particularly looking for patients who are within 0-5 years of onset of vision loss.

### ION-PROM

Our new quality of life tool is still available to test online at: https://www.redcap-ide-cam.org.uk/surveys/?s=PAJWHNL9JPX3FYYH. We're looking for individuals 16 and over affected by **LHON** or **ADOA.** The questionnaire is anonymous and takes about 15 minutes to complete. There is also the opportunity to provide feedback. Thank you to everyone who has completed it already, online or in clinic.

### Trial REadiness in AT (TREAT-AT)

This study aims to assess the neurological progression of **Ataxia Telangiectasia** in patients with a variant that could be targeted with Anti-Sense Oligonucleotide therapy. This is to select the **best outcome measure** for use in future clinical trials. The study involves up to 4 visits over 2 years.

### DefiNe

The trial to investigate whether **deferiprone** (a drug that removes excess iron in the body) is an effective & safe treatment for those with **neuroferritinopathy** (a disorder in which iron builds up in the brain) is due to open in the next few months. Look out for updates & press releases.

If you are interested in any of the above studies, please get in touch with the research team or register via the website.

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NIHR | BioResource


The NIHR BioResource is a group of over **100,000 volunteers** who have agreed to take part in **medical research**, with the aim of improving healthcare and the long-term **prevention and treatment of disease**. These volunteers have agreed that they can be invited to participate in further research studies.

**NIHR 'RARE DISEASE' BIORESOURCE** recruits **affected participants** and their **relatives** in more than 50 disease areas, including in immunity, **neuroscience**, haematology and rheumatology. Modern technologies (whole genome sequencing) are used to study the DNA of participants. This genetic information is linked to the clinical characteristics of the participants, which researchers call the 'phenotype'. It is hoped that this will help researchers to understand more about the **genetic causes of rare disease**.

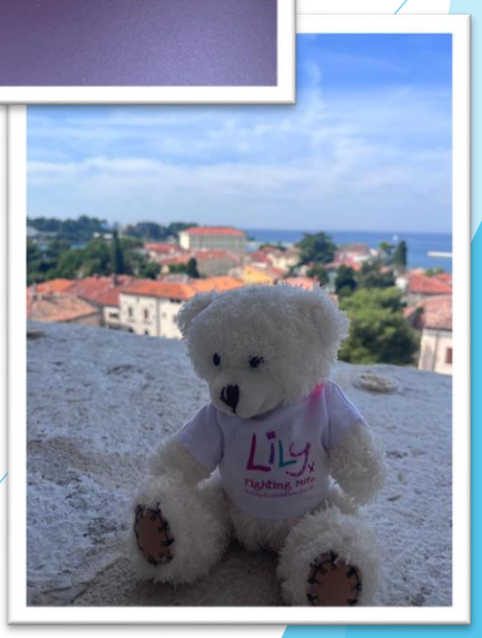
**RARE DISEASE RNA PHENOTYPING PROJECT** is a study to look at the **expression of genes in cells** of rare disease patients. The aims of this study are to **improve the diagnosis** of patients with rare diseases and to gain an insight into what **causes** rare disease and the potential development of **new treatments.** Patients **donate a sample of blood**, and then **'RNA sequencing'** is performed on each of the cell types isolated from the blood, which can tell us **which genes are turned on or off in a cell**. The data will be available to research teams such as ours to carry out further analysis in patients with rare disease. This may help us to diagnose or understand the mechanism or cause for a rare disease as a group.

If **you would like to be considered** for the RNA phenotyping project, **you need to be signed up to the NIHR 'Rare Disease' BioResource** first. This involves signing a consent form, completing a short questionnaire about your health, and attending for a blood sample. Once you are signed up, you can then take part in the RNA recall study. **Your travel costs will be covered** for attending this appointment.

You can contact us at **add-tr.mitoteam@nhs.net** if you would like more information or would like to register as a member of the NIHR BioResource.

## MITOCHONDRIAL DISEASE AWARENESS WEEK 2023 HIGHLIGHTS

In our last issue, we were celebrating World Mitochondrial Disease Week (18th – 24th September 2023). If you follow our Twitter/X page (@cam_mito) you may have kept up with the MitoCAMB Lily bear adventures. Spotty continued to raise awareness for mitochondrial disease through his travels around Cambridge and beyond! He even spent some time at the MRC Mitochondrial Biology Unit learning all about mitochondria!

WORLD MITOCHONDRIAL DISEASE WEEK

Lily

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# VIEW FROM THE LAB

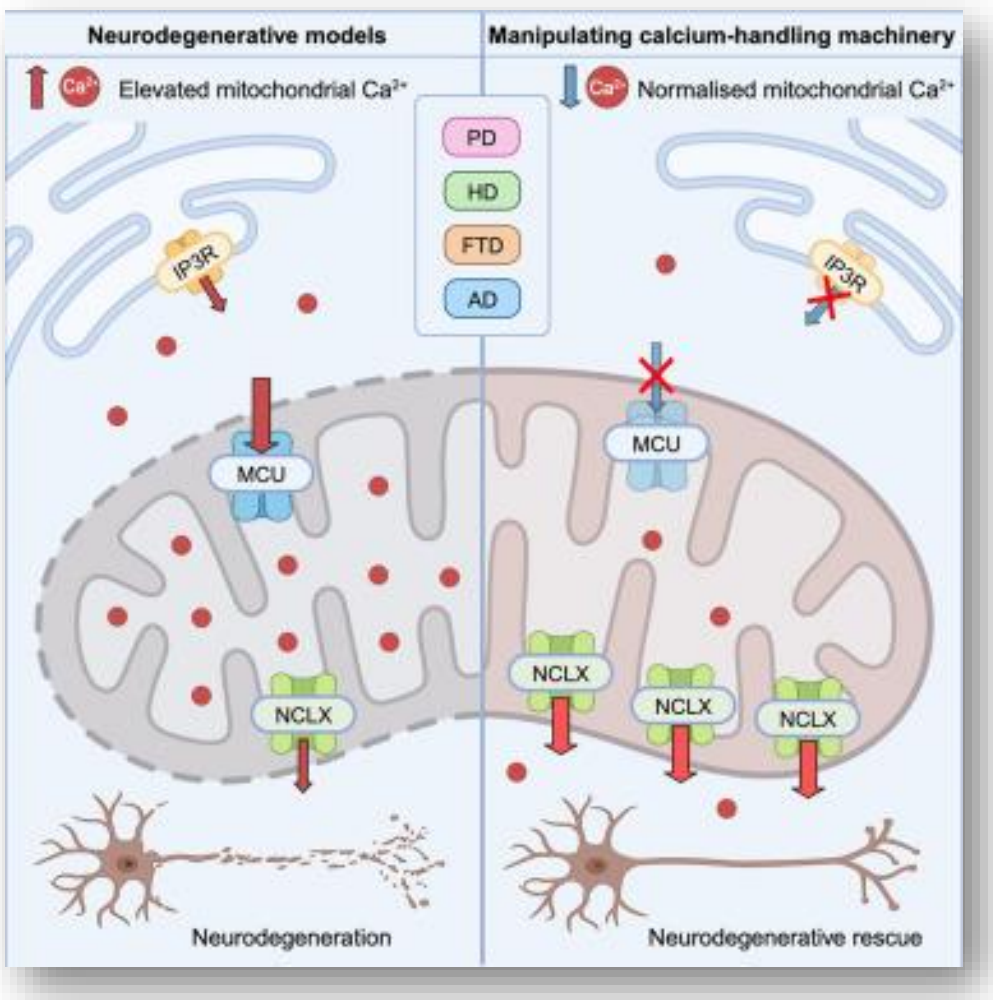
In this issue, we wanted to share some more of the exciting work from the laboratory programs at the **MRC Mitochondrial Biology Unit (MRC MBU).** The basic science research is fundamental to underpinning any clinical research. Read on for an interesting insight into how problems regulating calcium in the mitochondria contribute to neurodegenerative diseases.

The underlying cellular events that ultimately cause neurodegenerative diseases are poorly understood, hampering therapeutic drug design. It has been known for a long time that two crucial aspects of cell function go awry during the process of neurodegeneration. These are **disruption to mitochondria**, the metabolic hubs of the cell, and **dysregulation of calcium ions**, crucial messenger molecules. However, distinguishing whether these disruptions are a cause or a consequence of disease is notoriously difficult.

In a study led by **Dr Alex Whitworth** (MRC MBU) and recently published in Cell Reports, Twyning et al investigate the intricate dynamics of calcium ions that flow in and out of mitochondria and its significance to neurodegeneration in animal models of Parkinson's disease, Alzheimer's disease, Frontotemporal Dementia and Huntington's disease.

The concentration of calcium needs to be regulated within cells for normal functioning of the neurons (nerve cells). Twyning et al reveal that in multiple models of neurodegeneration, the mitochondria in nerve cells have **high calcium levels** and **reduced capacity for calcium buffering** (the process which helps to stabilise the concentration of calcium within cells). Stable levels of mitochondrial calcium are maintained through the tightly regulated balance of calcium uptake (via the mitochondrial calcium uniporter (MCU) complex) and calcium efflux via the sodium/calcium transporter NCLX. The researchers went on to show that reducing MCU or increasing NCLX was enough to normalise the abnormally high calcium levels. Strikingly, by **controlling mitochondrial calcium flow** in this way, they were able to reverse the neurodegeneration across a range of neurodegenerative models.

These findings reinforce the idea that mitochondrial dysfunction is a key contributor to neurodegenerative diseases of diverse origins. Twyning et al identify the careful balance of mitochondrial calcium levels as a common target for intervention. Importantly, the machinery responsible for mitochondrial calcium flow are druggable proteins making this mechanism attractive as a therapeutic target.




**If you wish to read further, please see the following reference:**


Twyning MJ, Tufi R, Gleeson TP, Kolodziej KM, Campesan S, Terriente-Felix A, Collins L, De Lazzari F, Giorgini F, Whitworth AJ.

Partial loss of MCU mitigates pathology in vivo across a diverse range of neurodegenerative disease models.

Cell Rep. 2024 Jan 17;43(2):113681. doi: 10.1016/j.celrep.2024.113681. Online ahead of print.PMID: 38236772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# BRAND NEW MITOCAMB WEBSITE

Our website has been revamped for the new year! Follow this link: https://mitocamb.medschl.cam.ac.uk/ to check out the new site. Here you can find more information about the team, the studies we are running and see the latest news. You can also find all the previous issues of this newsletter on the patient resources page along with some useful links to patient organisations.



# THE "LHON AND SHORT OF IT" PODCAST

A new podcast about Leber Hereditary Optic Neuropathy (**LHON**), hosted by Dr Benson Chen, has just gone live on the Buzzsprout website: https://www.buzzsprout.com/2315393

The podcast will also be available on Apple Podcasts, Spotify, and Google Podcasts. Supported by the University of Cambridge Public Engagement Starter Fund and the UK LHON Society.

# 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/would like to participate in, please contact the team on:

add-tr.mitoteam@nhs.net 01223 335106 @cam_mito

https://mitocamb.medschl.cam.ac.uk/

For queries regarding **routine NHS clinic appointments**, please contact Katrina Dedman: cuh.mitocambclinic@nhs.net or 01223 216751

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