Welcome to the second 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.

COVID-19 has presented us all with many challenges over the past year. We are aware that a number of our patients have been shielding, and we have all been apart from loved ones, working and communicating remotely. We would like to thank you for your on-going support and commitment to our research during this difficult time. We hope that the situation continues to improve and we look forward to seeing you in person over the coming months.

Despite these challenges, we have continued to be busy and in this issue we will update you on some of the work we have been doing, in the midst of national lockdowns and a global pandemic...

“BRAND REFRESH”

With a growing team of clinical researchers in Cambridge, focused on mitochondrial and neurodegenerative disease translational research, we wanted to encompass this group better with a more unified web presence.

Our researchers now come under the umbrella of The Cambridge Clinical Mitochondrial Research Group (mitoCAMB). The group is interested in the genetic basis of neurological disorders, particularly mitochondrial diseases (including mitochondrial eye diseases), and other rare inherited neurological conditions, such as Charcot Marie Tooth Disease and spastic ataxias.

We have a new logo to reflect this group, which you might see popping up on documents, and on our newly refreshed Twitter page (photograph of King’s and Clare colleges taken by our very own Dr Patrick Yu Wai Man). We are currently also working on the construction of a group website, which we hope will provide useful information for patients, research participants and other investigators, regarding our research, vacancies and opportunities.
The team recently published some of their research looking at the use of radioactive PET tracers as novel biomarkers for patients with mitochondrial disease. Dr Jelle van den Ameele tells us more...

Mitochondria are important parts of the cell, responsible for producing energy. The cells of people with mitochondrial disease can either have too few mitochondria (because problems with energy production cause the mitochondria to be removed), or too many mitochondria (when cells try to compensate for a lack of energy by constantly building new, but less functional mitochondria).

The clinical picture of mitochondrial disease is very variable. The brain is often affected, but symptoms can overlap with more common disorders and problems like fatigue, muscle weakness, headaches, diabetes or hearing difficulties. This makes it difficult to diagnose mitochondrial disease, and patients often remain undiagnosed or undergo an invasive muscle biopsy. Although genetic testing has improved the situation, we still need to develop new and non-invasive techniques. In addition, when developing new treatments, it would be helpful to have a way of measuring how someone’s mitochondria react to a specific drug or intervention.

We reasoned that by measuring the number of mitochondria in cells and organs with a scanner, we could have a new way to help diagnose mitochondrial disease, or to follow the impact of a particular treatment. [11C]PK11195 is a radioactive compound that binds to certain proteins in the mitochondria. This interaction releases a signal that can be detected using a specialised positron emission tomography (PET) scanner. Together with researchers from the Wolfson Brain Imaging Centre (WBIC) in Cambridge, we set up a small pilot study to see whether we can use this type of scanner to estimate the number of mitochondria in different regions of the brain.

We injected a small amount of radiotracer into the bloodstream of 14 participants, and then carried out a PET scan lasting roughly 90 minutes. At the same time, these scanners allowed us to perform a more standard MRI scan of the brain, to detect any structural abnormalities and correlate these with changes in the PET signal. We then compared these results with the brain scans from 33 control participants who do not have mitochondrial disease.

Our results showed that almost half of the mitochondrial disease participants did indeed have abnormal radiotracer binding in some regions of the brain. Importantly, patients with more severe symptoms had a larger increase or decrease in the signal detected by the PET scanner. This suggests that PET imaging has the potential to be used as a non-invasive biomarker of disease progression in the brain of patients with mitochondrial disease.

Future studies will have to look at larger groups of patients. We are also interested to find out whether the changes in one person may increase over time as the disease progresses, and whether this is caused by greater or fewer numbers of mitochondria in the cells. Eventually, we hope that we can use this type of scanner to test the effectiveness of novel treatments to help patients with mitochondrial disease.

The results were recently published in the journal Neurology, and can be found at: https://n.neurology.org/content/early/2021/04/21/WNL.00000000000012033.abstract

THANK YOU to all our patients who took part in the pilot study!
We would like to introduce you to two new members of the team:

Chloe Seikus joins us as a Research Assistant. She graduated with an MSci in Psychology and Language Sciences from University College London, where she worked on research projects within the Institute of Cognitive Neuroscience, the Anna Freud National Centre for Children and Families and the Cognition and Grammar Lab. Chloe is responsible for recruiting patients to our research studies and collecting clinical data and samples. She may contact you by telephone, or see you in person after your clinic appointment, to provide you with information about our research studies.

Benson Chen is a Clinical Research Fellow in the Cambridge Eye Unit, Addenbrooke's Hospital, and a PhD student in the Department of Clinical Neurosciences. Benson completed his medical degree at the University of Auckland and then undertook clinical training in neurology in Auckland, New Zealand. This was supplemented by subspecialty training in neuro-ophthalmology at Emory Eye Center in Atlanta, USA. His research focuses on inherited optic neuropathies and the experience of individuals living with LHON and DOA, and he is currently in the process of developing a patient reported outcome measure for patients with inherited optic neuropathy.

STUDIES (RE)OPENING

After the disruption caused by the COVID-19 pandemic, we are looking forward to opening new clinical studies, and re-opening studies that were ‘paused’ to recruitment. We will be contacting patients over the coming weeks and months about the following clinical studies, so do keep an eye out:

- The role of Nicotinamide Riboside in Mitochondrial Biogenesis
- The effects of oxygen in the context of mitochondrial dysfunction
- PROSPAX: Understanding the progression over time of Hereditary Spastic Paraplegia (HSP), ataxia and related conditions

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
@cam_mito

For queries regarding routine NHS clinic appointments, please contact Katrina Dedman: katrina.dedman@addenbrookes.nhs.uk or 01223 216751