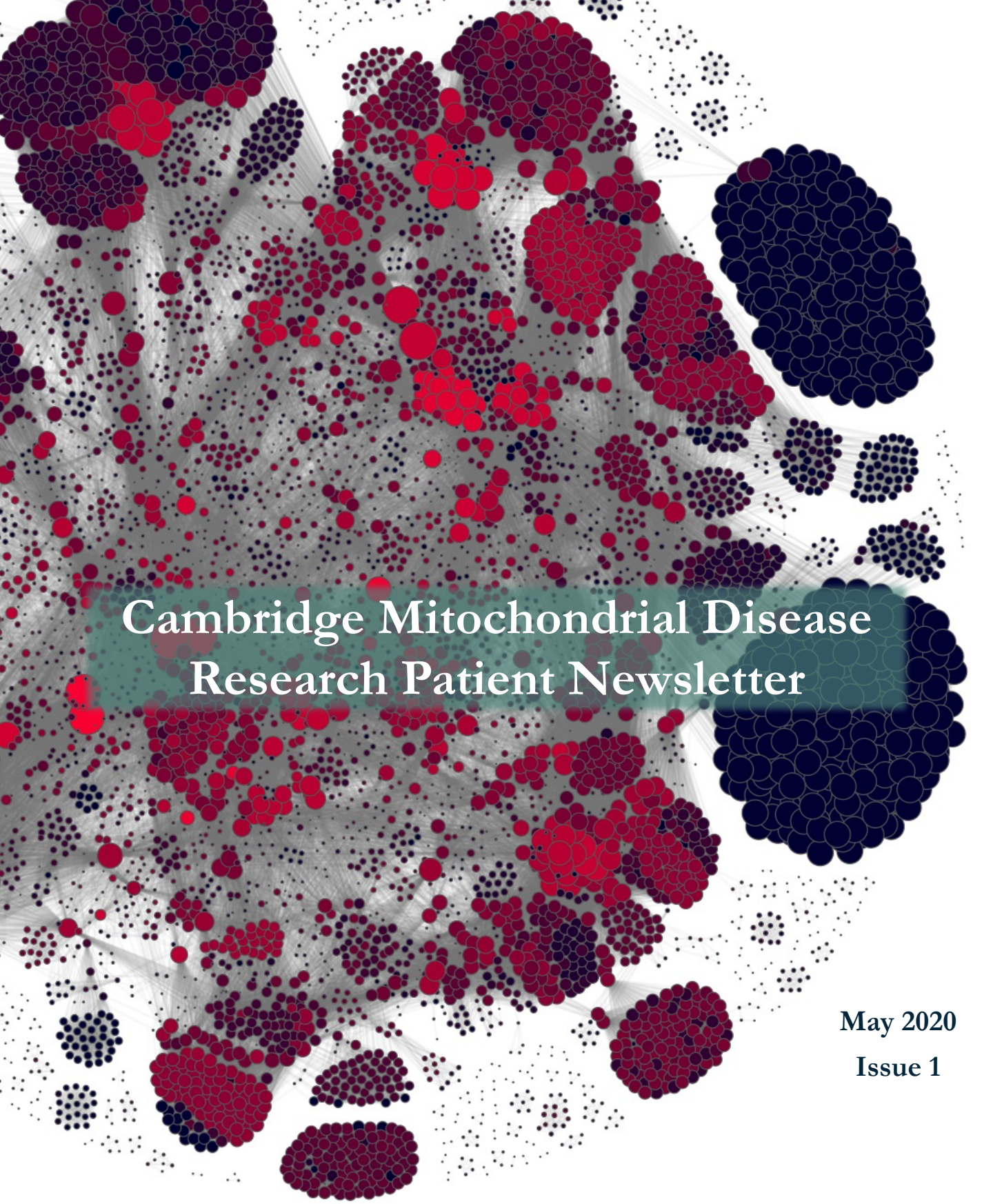


Cambridge Mitochondrial Disease Research Patient Newsletter

May 2020

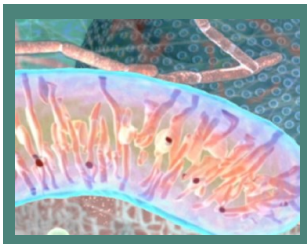
Issue 1

Image: Protein interaction network
Provided by Dr Florian Klimm

UNIVERSITY OF CAMBRIDGE

Cambridge University Hospitals NHS
NHS Foundation Trust

MRC Mitochondrial Biology Unit



CAMBRIDGE MITOCHONDRIAL DISEASE RESEARCH NEWSLETTER

Issue 1
May
2020

WELCOME!

Welcome to the first issue of the Cambridge Mitochondrial Disease Research patient newsletter! 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.

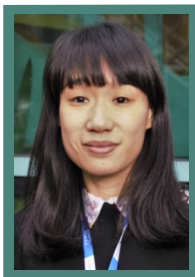
MEET THE CLINICAL TEAM

The Cambridge Mitochondrial Disease Research team aims to understand the genetic causes of mitochondrial diseases and other neurodegenerative conditions and how best to monitor and treat them. In this issue we would like to introduce to you the clinical team working hard to achieve this...

Patrick Chinnery is Professor of Neurology and head of the department of Clinical Neurosciences. He leads the research programme studying mitochondrial diseases, with the aim of developing new treatments. This is combined with his laboratory research into the genetic factors responsible for the variable presentation of mitochondrial diseases.

Rita Horvath is a clinical academic and Honorary Consultant in Neurology. The focus of her research group is to identify disease mechanisms for the treatment of patients with rare inherited neurological conditions such as Charcot-Marie-Tooth disease & mitochondrial disease.

Patrick Yu Wai Man is an academic neuro-ophthalmologist with a major research interest in mitochondrial eye diseases. His research programme is focused on uncovering the genetic basis and disease mechanisms leading to progressive retinal ganglion cell loss in mitochondrial optic neuropathies, with the aim of developing effective therapies.



May Yung Tiet recently joined the team as a Neurology registrar, after completing her MSc in Genomic Medicine. She is now an Honorary Clinical Research Associate studying the role of mitochondrial dysfunction in Ataxia -Telangiectasia.

Jelle van den Ameele is an Honorary Consultant Neurologist who moved to Cambridge in 2014 and joined the mitochondrial disease clinic. In the lab, he works with fruit flies to create models of mitochondrial disease and study how this affects the different types of cells in the brain in order to better understand why patients have such a range of symptoms.

Katherine Schon is doing a PhD in the clinical and genetic aspects of mitochondrial disease. She trained in Medicine, specialising in Clinical Genetics. She has clinical expertise in the diagnosis of genetic disorders and in genetic counselling. Katherine's research interest is in using genomics to improve the diagnosis of mitochondrial disorders.

Katrina Dedman is secretary to Professor Patrick Chinnery. Katrina is not only central to the department and the research team, she is also the main point of contact for patient enquiries regarding routine NHS (i.e. non research) clinic appointments.

Heather Biggs is Research Project Manager for the team. She is responsible for coordinating the design, set up and running of the team's studies, and can also be found in clinics on a regular basis, acting as a point of contact for researchers, patients and their families.

Emma Harrison recently joined the Department of Clinical Neurosciences as a data manager. She works with the clinical and laboratory teams to design streamlined methods for the collection of high quality clinical and sample data. She can often be found in clinic working directly with clinicians and patients.

OUR RESEARCH STUDIES - UPDATE

The role of oxygen in the context of mitochondrial dysfunction (MitOx)

What's it about?
When people with mitochondrial disease are unwell or have routine operations, they are given high oxygen (O2) to breathe. We want to know if this is safe and helpful. We will study the effects of inhaling high O2 in mitochondrial disease patients, compared to people who do not have mitochondrial disease.

Who can take part?
- People with MELAS, m.3243A>G
- Aged 16-70, male or female

The role of Nicotinamide Riboside in mitochondrial biogenesis

What's it about?
We want to find out if the modified B vitamin, Nicotinamide Riboside, can help energy production in people with mitochondrial disease.

Who can take part?
- 18-70 years, male or female
- Progressive external ophthalmoplegia (PEO) caused by a single deletion of mitochondrial DNA
    - Mitochondrial disease caused by the m.3243A>G mutation

Genotype & Phenotype in Inherited Neurodegenerative Diseases

What's it about?
Understanding the genetics of a range of conditions called 'neurodegenerative disorders' and how to treat them, using blood samples and clinical data.

Who can take part?
- Individuals with a suspected or confirmed genetic neurological disorder (any age).
- Unaffected relatives (parent/ sibling) of someone with a suspected or confirmed genetic neurological disorder (>16 years).

International Centre for Genomic research in NeuroMuscular Diseases (ICGNMD)

What's it about?
A new international study across 4 continents led by UCL to identify the genetic causes of neuromuscular & other neurogenetic conditions (conditions caused by genetic changes affecting people's nerves).

Who can take part?
- Affected participants;
- Related control participants (relatives);
- Unrelated control participants (who do not have a condition).

[^{11}C]PK11195 PET as a biomarker to diagnose and monitor natural history in mitochondrial disease

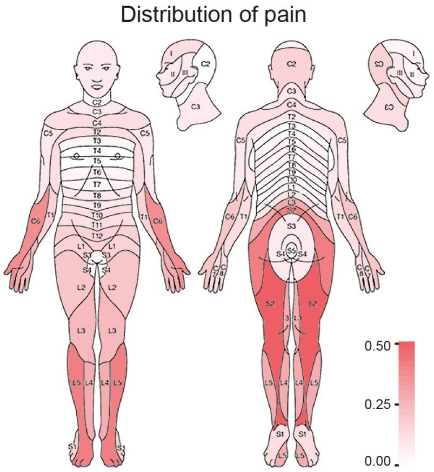
What's it about?
Using PET-CT to estimate the amount of mitochondria in different regions of the brain and compare it to the brains of people who don't have mitochondrial disease. Can this be used to monitor progression of mitochondrial disease?

Status:

14 patients scanned; interim analysis being performed; aim to publish the results.

In the coming months, the research team may be in contact with you to invite you to participate in one or more of these studies. However, if you would like further information on any of these studies in the interim, please contact the research team (contact details on the next page). New studies are being developed, and we will update you on these in future issues.

FOCUS ON...



The team recently published some of their research into **pain symptoms in patients with mitochondrial disease**. Dr Jelle van den Ameele tells us more....

Adults with mitochondrial disease often mention pain symptoms in the clinic. Headaches are very common, often caused by migraine. Nerve pain is frequently reported as well, and patients often complain of pain in their muscles. Other complications, such as movement disorders or problems with gut motility may all cause chronic or acute pain symptoms that are sometimes very disabling.

So far, pain symptoms have not attracted much attention in the medical and scientific literature about mitochondrial diseases. We therefore teamed up with **Dr Michael Lee** from the pain clinic in Addenbrooke's and with the mitochondrial genetics clinic of **Dr Pitceathly** and **Prof Hanna** at UCL, London, to set up a survey about how much and what type of pain adult patients with genetically confirmed mitochondrial disease experience.

2 out of 3 adults with mitochondrial disease who responded to our survey had experienced some form of **chronic pain** during the last 6 months. This is about twice as much as expected from the general UK population. Pain was often described as "tingling" or "burning" and was mostly located in the lower back and legs. This suggests that the majority of pain might be **neuropathic** i.e. caused by damage to the nerves. The likelihood of having neuropathic pain seems to increase if the patient has a particular mutation in the mitochondrial DNA (m.3243A>G). However, we would have to repeat the study with many more patients in order to find a possible relationship between pain and specific genetic mutations.

We were surprised to see that many patients who experienced chronic pain, did not feel this had a major impact on their daily activities and overall wellbeing. Although pain was clearly disabling for some, chronic pain did not affect **quality of life** for most patients. We don't yet know how to explain this and we welcome any comments or suggestions on this. The results were recently published in the journal **Neuromuscular Disorders (doi.org/10.1016/j.nmd.2020.02.017).**

We are currently conducting a similar survey into **sleep disturbances** in patients with mitochondrial disease (via our **Genotype and Phenotype study**—see previous page) and your help is very much appreciated with this. Please do not hesitate to get in touch if you have lost your copy of the questionnaire, or if you need any help completing the questions.

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**