NEWSLETTER

Issue 12, March 2022

Oxford Parkinson's Disease Centre

NIHR | Oxford Biomedical Research Centre

Funded by PARKINSON'S UK CHANGE ATTITUDES. FIND A CURE. JOIN US.

The only way is UPP!

Last year, we proudly announced that Parkinson's UK agreed to fund the OPDC Discovery Cohort follow-up for a further four and a half years from August 2021.

The project entitled 'Understanding Parkinson's Progression (UPP)' is led by Professor Michele Hu and funded by the Parkinson's UK Cohort Studies Council. The Covid pandemic brought round a whole new way of working, and this was no different for the OPDC research team. Follow-up of the cohort will primarily be using remote methods (such as video and telephone assessments) to help facilitate and ease burden on participants, whilst still allowing vital data and information to be collected, whilst also allowing participants to stay involved in the research. Follow-ups will allow us to capture the true course of Parkinson's Disease (PD), and better predict disease trajectory and outcomes on an individual basis.

The ongoing project will not only enhance our power and ability to test for prognostic biomarkers, but we will also be using telemedicine technologies which can be done in clinic and from the comfort of participants own home. This is hoping to both stratify and predict Parkinson's in a subgroup.

The aims:

1. Establish Discovery as one of the best long-term studied Parkinson's cohort worldwide
    - Capturing a natural history from prodromal through to complex phase
    - Improving outcome predictions for people with Parkinson's

2. Develop a prognostic index detailing the longer-term trajectory of Parkinson's
    - Individual basis following diagnosis

'I am absolutely delighted that Parkinson's UK have agreed to this funding. Since 2010, the cohort has already made significant contributions to our understanding of how Parkinson's begins and subsequently progresses, being independently cited as one of the world's top-ten leading Parkinson's biomarker cohorts. I would like to thank all our research participants and study staff for their time and energy which has helped to make the Discovery cohort a world-leading success' **-Professor Michele Hu**

CONTENTS

Website**:** www.opdc.ox.ac.uk
Twitter: @OxfordPDcentre
Facebook: www.facebook.com/OxfordPDCentre

OPDC Cohort Team:
Phone: +44 (0) 1865 223166
Email: parkinsons.discovery@nhs.net

OPDC Research Administrator:
Phone: +44 (0) 1865 282358
Email: opdc.administrator@dpag.ox.ac.uk

Introducing your Central Oxford Cohort Team

Professor Michele Hu,
Cohort Lead

Jessica Welch,
Clinical Project Manager

Jamil Razzaque,
Research Practitioner

Lorraine Johns,
Senior Research Administrator

Tyciane Benetton,
Research Administrative Assistant

For participants

Massive thank you to everyone for your ongoing work and commitment. The research we do would not be possible without you! As many of our clinics are done remotely, and we are increasing the use of technology, we have been in contact with a charity called **AbilityNet** who are helping us set up a small IT Volunteer Group. We have received some interest from a handful of PD and relatives who are interested in helping our PD participants who are not confident in using a computer, iPad or tablet. We now offer our PD participants a video appointment, as this enables us to capture their motor skills etc., but we have come across about 20% of participants who do not feel confident in using IT, or do not have access to a computer or tablet at home, our volunteers will be trained up to visit them in their homes and assist them with their video appointment.

We are currently sorting out full DBS checks for our volunteers, after which we will arrange training sessions and our volunteers will then be ready to help our participants in their own homes.

Update on the OPDC team

New to the team!

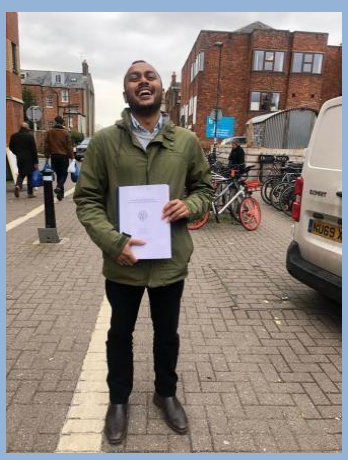
We would like to welcome Tyciane (Tyci) to the OPDC team as our new research administrative assistant!

'I have been with the University of Oxford since 2019, working within The Nuffield Department of Clinical Neurosciences. Started as a receptionist and then moving to Facilities Administrative Assistant, where I have obtained different capacities. The role has helped me to gain understanding of administration within the University. My background is Communication with an MBA in Marketing, and I am passionate about languages. Joining OPDC, I look forward to gaining research experience and improve my administrative capabilities. I will assist Lorraine, Jess and Jamil, all under Prof Michele Hu knowledge and management.'

With a sad goodbye…

It is with a heavy heart that we say goodbye to Tharuka, Navin and Cristina. They have been great assets to the OPDC team over the last year and they will be greatly missed. The time and knowledge they have contributed to OPDC has enabled us to really move forward in all areas of our work. From various clinical duties to wearable technology analysis, and everything in between, the work they have done has not gone unnoticed. We wish them the best of luck in their future ventures.

Dr Tharuka Herath,
OUH PD Fellow



Navin Cooray,
Postdoctoral Researcher

Dr Cristina Campos,
OPDC Clinical Research Fellow

OPDC participate in the annual Walk for Parkinson's in Oxford

In September 2021, a team made up of OPDC researchers and supporters took part in the annual 'Walk for Parkinson's' event in Oxford, organised by Parkinson's UK. The walk (either 2 mile or 6 mile) went through woodland at Wytham Woods to raise awareness and funds for Parkinson's Disease research. Everyone received a medal on completion, which is well deserved considering a huge £18, 812 was raised! Massive thank you to Katy Slade, Parkinson's UK Regional Fundraiser and her team for their organisation and ongoing efforts to make the event a success.

OPDC researchers and supporters from the Wade-Martins Research Group after finishing the walk

New Laboratory Facilities!

In the last newsletter, we gave an update that new lab facilities were underway, and we can confirm that Researchers from the OPDC and Wade-Martins Group have officially moved into their new facilities at the Kavli Institute for NanoScience Discovery! The facilities provide state of the art laboratory space for research as well as areas designated to facilitate interdisciplinary working. It took months of meticulous effort to successfully plan and arrange the relocation. It was a huge team effort to move and transfer the numerous pieces of specialist large equipment into new laboratory space, ensuring that the impact on our daily research was minimised.

External view of the Kavli Institute-largest laboratory structure the university has ever constructed!

'I am delighted that we have now moved into our laboratories in the new Kavli Institute for Nanoscience Discovery (KIND) on the South Parks Road Campus. The institute will provide outstanding opportunities for new cross-disciplinary programs with other cell biologists, as well as with physical sciences, chemists and advanced microscopy. It will be a great place to do our science: we are all very excited!'- **Professor Richard Wade-Martins**

Inside the new Lab.

Some Current OPDC research work…

Alongside running the Discovery cohort, the OPDC team are also working on some other research projects, such as…

- **PPMI**: Parkinson's Progression Markers Initiative by the Michael J. Fox Foundation is about working towards critically needed biological markers of Parkinson's onset and progression. It is recruiting worldwide and OPDC are really excited to be working on it. We have so far recruited 12 participants (5 prodromal, 5 controls, and 2 PD).
- **Exenatide:** A clinical drug trial using an already approved diabetes drug, hoping to see if it can slow down or even stop the degeneration of PD. It is recruiting nationally, and we have recruited 24 out of 25 so far.
- **Wearable technology**: We are using the OPDC smartphone app and axivity devices across various projects. This enables us to gather huge quantities of longitudinal data. We will also be restarting our sleep wearables study in Oxford. We are giving our sleep kit a little bit of a revamp (to improve both participant experience and data quality!).
- **Discovery sub-studies**: Over the years our participants for Discovery have been incredible and extremely willing to take part in our research. Whether this be doing cognitive tests, having brain scans, lumbar punctures, giving blood (to name just a few things!), and we are beyond grateful. We are going to be expanding the data we collect to also include skin swabs and faecal samples. These are avenues that have the potential to show new findings, which haven't necessarily been explored before…

New findings with potential real-life application

Scientists at the OPDC, funded by Parkinson's UK, have potentially found a pioneering new clinical test that could be developed to diagnose Parkinson's correctly in its early stages.

The highly sensitive method, called α-Synuclein real-time quaking-induced conversion (αSyn-RT-QuIC) observes the clumping of alpha-synuclein in cerebrospinal fluid. The clumping of alpha-synuclein is associated with the death of dopamine producing nerve cells, which consequently causes symptoms associated with Parkinson's.

A recent study done on people with Parkinson's, showed that more than a quarter were misdiagnosed with a different condition before getting their current Parkinson's diagnosis. This if often due to an overlap of signs and symptoms with other conditions (such as multiple system atrophy (MSA) and essential tremor). The findings using αSyn-RT-QuIC could be used to be able to distinguish between these conditions, but also measure disease progression.

'The most exciting finding of the study is that the detected clumps of alpha-synuclein differed between different clinical Parkinson's subtypes and between people with Parkinson's and MSA. These differences could represent distinct 'strain profiles' which could not only provide a way to distinguish between different neurodegenerative disorders but also provide a way to distinguish variations within a single condition. How the 'strain profiles' vary within Parkinson's and how they relate to clinical subtypes will need to be investigated further'-**Dr Laura Parkkinen**

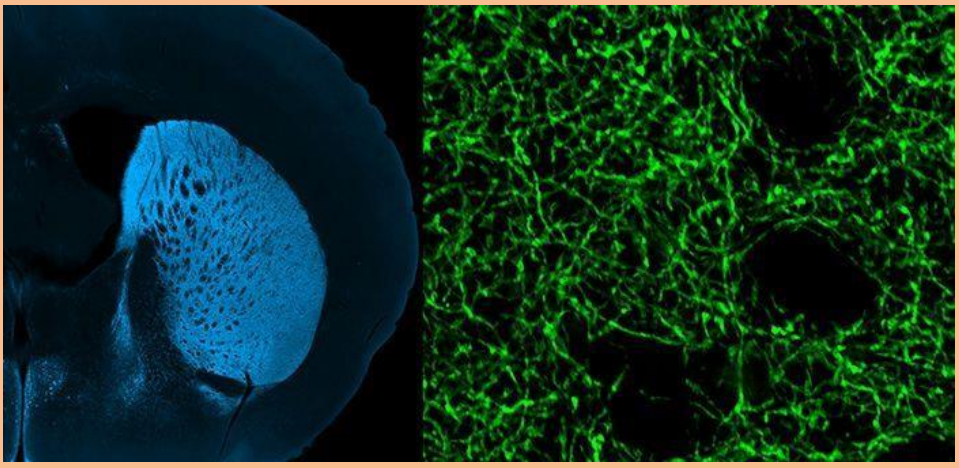
Oxford awarded two major new grant programs for Parkinson's

Mapping unchartered networks in the progression of Parkinson's

We have been awarded $9 million from the Aligning Science Across Parkinson's (ASAP) initiative and the Michael J. Fox Foundation to fully map out a key set of the neuronal circuitry relevant to Parkinson's. This project is a landmark collaboration between Stephanie Cragg, Richard Wade-Martins and Peter Magill at OPDC; Mark Howe at Boston University in the USA and Dinos Meletis at the Karolinska Institute in Sweden, as well as collaborators Yulong Li at Peking University and Michael Lin at Stanford University. ASAP mission is to accelerate the pace of discovery and inform the path to a cure through collaboration, research-enabling resources, and data sharing.

The team will assess how circuit activity changes during progression of Parkinson's in vulnerable compared to resistant circuits and define how circuit dysfunction in vulnerable circuits relates to disease symptoms. In particular, the team will focus on studying the circuits that govern dopamine output.

To find out more about this project, go to https://www.dpag.ox.ac.uk/news/mapping-unchartered-networks-in-the-progression-of-parkinsons



Fluorescently labelled dopamine axons in the mouse striatum

'We Know dopamine neurons die, and that the messages they transmit on to other cells are lost in Parkinson's, but we don't really understand how all the other interacting circuits contribute to that and either make it worse or attempt to offset it, so we are looking to identify what the sequence of dysfunction is''-**Professor Stephanie Cragg**

Oxford awarded two major new grant programs for Parkinson's (cont.)

Oxford Parkinson's research team obtains £3.8 million Wellcome Trust Collaborative Award to study the role of calcium in dopamine neurons

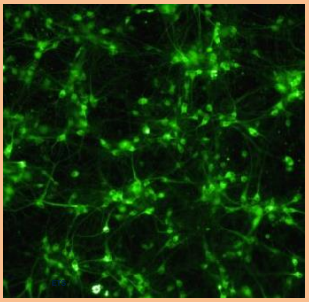
Researchers at the Oxford Parkinson's Disease Centre led by Professor Richard Wade-Martins with Professor Stephanie Cragg and Professor Peter Magill, have recently been awarded a
£3.8 million Wellcome Trust Collaborative Award in Science to study the critical role of calcium in the biology of dopamine neurons. Richard, Stephanie, and Peter are joined by Professor Birgit Liss from the University of Ulm in Germany, and Professor Josef Kittler from University College London, to create new and international team of scientists to provide new and detailed information about how dopamine-producing nerve cells operate in health and in Parkinson's.

Professor Richard Wade-Martins

Professor Stephanie Cragg

Professor Peter Magill

The development of improved therapies for Parkinson's requires new knowledge of why certain types of neuron dysfunction and die. Nerve cells producing the chemical dopamine are essential for many behaviours. These nerve cells are also particularly vulnerable in Parkinson's Disease, but we do not know exactly why. However, we think the ways these cells deal with calcium ions is a vital piece of the Parkinson's puzzle. Working with human stem cell-derived dopamine neurons in a dish in the laboratory and in the whole brain, we will study different 'compartments' along the complete length of these nerve cells. We will reveal how calcium enters cells and is handles by them to generate electrical and chemical signals, and how these and other processes linked to calcium go awry in Parkinson's. Our multidisciplinary and collaborative approach will tell us more about why these nerve cells are vulnerable and how we might be able to stop them dying.



Tracking calcium signalling (in green) in human dopamine neurons grown from stem cells in the laboratory.

Giving to OPDC

At the OPDC we are working hard to understand Parkinson's and to develop new treatments. As we look to the future, we want to ensure that our work is sustainable, and that it can continue for years to come.

If you would like to support **patient-facing cohort work** on Parkinson's at the University of Oxford, please contact Lorraine Johns, Oxford Parkinson's Disease Centre, Level 6, West Wing, John Radcliffe Hospital, Oxford, OX3 9DU. Telephone number is 01865 223166.

A Legacy gift will help the OPDC to continue vital research programs, to find a cure and to improve the lives of everyone affected by Parkinson's. Large or small, your support will really make a difference to our work. If you would like to know more about leaving a gift to the OPDC Cohort in your will, please contact us on 01865 223166 or email Parkinsons.discovery@nhs.net.

If you would like to specifically support **discovery science laboratory research projects** working on Parkinson's at the University of Oxford, you can make a one-off donation or set up a regular payment to OPDC on our website: https://www.dpag.ox.ac.uk/opdc/donate. Alternatively, please contact the OPDC Administrator, Oxford Parkinson's Disease Centre, Department of Physiology, Anatomy and Genetics, Kavli Institute for NanoScience Discovery, South Parks Road, Oxford, OX1 3QU.

If you would like to support the work done nationally by Parkinson's UK, please visit www.parkinsons.org.uk/donate.

Funded by
PARKINSON'S UK
CHANGE ATTITUDES. FIND A CURE. JOIN US.

Information on all our current research activities can be found on our website

@OxfordPDCentre **www.opdc.ox.ac.uk**

Oxford Parkinson's Disease Centre

facebook.com/OxfordPDCentre

Oxford Biomedical Research Centre
Enabling translational research through partnership

THE MICHAEL J. FOX FOUNDATION FOR PARKINSON'S RESEARCH

NHS National Institute for Health Research
Clinical Research Network Thames Valley and South Midlands