

OPDC wins £6M from Parkinson's UK to fund our research for another 5 years

Thanks to the renewal of generous funding from The Monument Trust, we are thrilled to announce Parkinson's UK is able to extend its partnership with the OPDC for a further 5 years with a grant of £6M. The next five years in Oxford hold enormous promise for delivering breakthroughs that could change the lives of people with Parkinson's.

By 2020 we hope to use the £6M to find new drugs to slow, or even stop Parkinson's, using a 'brain cell bank' we have developed to identify promising new drug targets. We also want to improve how to diagnose and monitor Parkinson's using cutting edge technology like smartphone apps.



OPDC Investigators: Top row L-R: Clare Mackay, Caleb Webber, Chris Ponting and Richard Wade-Martins. Bottom row L-R: Paul Bolam, Michele Hu, Laura Parkkinen and Peter Magill

“In the last five years we've made remarkable progress. We've built a study integrating work in the clinic and the laboratory like nowhere else in the world. Alongside this, our program to change cells from patients' skin into brain cells using cutting-edge stem cell technology has allowed us to gain completely new insights about Parkinson's and how it develops.

“We're delighted the new funding from Parkinson's UK will secure the future of this and other vital projects.”

Professor Richard-Wade Martins, OPDC lead researcher.



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News from the OPDC clinical study

The OPDC cohort, currently one of the largest of its kind in the world, is a longitudinal study, recruiting people with early Parkinson's, healthy control subjects without Parkinson's and participants at risk of developing future Parkinson's. We have now recruited over 1500 subjects to the cohort, including (as of March 2015) over 1000 people with early Parkinson's. In addition 300 healthy controls, and 180 Parkinson's at-risk individuals (73 with rapid eye movement (REM) sleep behaviour disorder (RBD) and 107 siblings of people with Parkinson's) have been recruited into the study. Only 10 % of our total cohort have been unable to continue with the 18 monthly follow-up visits despite best efforts.

Study recruitment plans

We will continue to recruit people with early Parkinson's diagnosed in the past three years up to October 2015. We have now stopped recruiting control subjects and siblings of people with Parkinson's, as we have reached our targets for these groups- many thanks to all those who contributed to this! We will continue to recruit RBD subjects over the next 5 years of this project, as we consider these individuals to be at high risk of conversion to future Parkinson's, and therefore a crucial group for our research.



Research aims for 2020

Over the next 5 years, our focus will move from identifying to targeting the early pathways to Parkinson's. We will use the wealth of data we collect in our participants including their stem cells, to develop more effective symptomatic treatments as well as treatments that slow down the progression of this condition. The android phone app developed by Dr Max Little has been effectively rolled out to all Discovery participants for the past year. This is one of several cutting-edge innovative technologies we are using to monitor symptom fluctuation and progression in our fight against Parkinson's. The need to develop bespoke treatments to improve life for people with Parkinson's, and the potential use of these novel technologies was recently highlighted by Dr Michele Hu at the Parkinson's UK annual Royal Institution lecture (see <http://bit.ly/BespokeTreatments> for video).

News in brief

- **Royal Institution Lecture : “Can bespoke treatments improve life with Parkinson's?”**

OPDC's Michele Hu delivered a free lecture at the world famous Royal Institution in November 2014. The talks focused on how our current research is leading us towards a new era of personalised treatment for Parkinson's that could be crucial to finally finding a cure. The talks were followed by a lively question and answer session.



Michele's talk and the Q and A session are available to view here: <http://bit.ly/BespokeTreatments>

- **Parkinson's UK Oxford Walk**

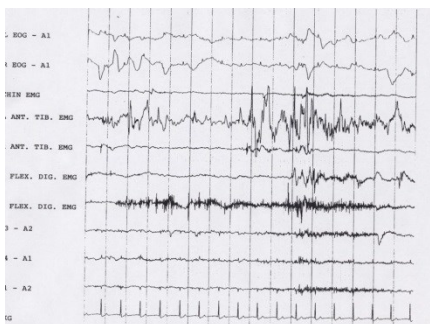
This October, a team of around 20 researchers and supporters from OPDC took part in the Oxford Parkinson's walk organised by the Oxford branch of Parkinson's UK.



The walk was started by OPDC Principal Investigator Richard Wade-Martins and was completed by members of Team OPDC and Parkinson's UK supporters and helped raise funds to continue our research. We would like to thank everyone who supported us and hope to see you again next time on October 25th 2015.

Expansion of OPDC sleep disorder study

Rapid eye movement (REM) sleep behaviour disorder (RBD) is a relatively rare sleep condition in which people act out their dreams during the REM stage of sleep. Dreams tend to be vivid and unpleasant, often involving shouting, fighting or running. RBD is thought to be related to abnormalities in a number of brain pathways which normally act to paralyse the body during REM sleep, therefore preventing potential injuries to the person and their bed partner. RBD may start suddenly, commonly in people in their 50's or 60's, with the frequency of episodes ranging between a few times a night and one every few days.



Parkinson's and sleep disorders

Over the past 15 years, a clear link between RBD and Parkinson's has emerged. Last year, we published a study showing that RBD is much more common in people with Parkinson's, and is often associated with more non-motor symptoms, like depression or memory loss. Importantly, RBD may sometimes be one of the first symptoms to emerge in people who will eventually be diagnosed with Parkinson's. Better understanding of RBD may help us to develop early diagnostic markers and allow us to introduce potential treatments even before the classical motor symptoms of Parkinson's appear.

Over the past two years, the OPDC has been recruiting patients from the sleep clinics in Oxford and Papworth. To date, we have seen over 70 patient with sleep study confirmed RBD, making it one of the biggest RBD patient cohorts in the world. We are pleased to announce that we will soon start recruiting from the sleep clinic in Sheffield, allowing us to increase numbers and gain more insights into this important condition.

Reference:

Rolinski et al., (2014) REM sleep behaviour disorder is associated with worse quality of life and other non-motor features in early Parkinson's disease. *Journal of Neurology, Neurosurgery, and Psychiatry*. 85(5):560-6

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3995329/>

News in brief

➤ OPDC Clinical Research Fellow wins Young Investigator Award for sleep research

OPDC's Dr Michal Rolinski has won a Young Investigator Award from the Parkinson Non-Motor-Study-Group and World Association of Sleep Medicine (WASM) in recognition on his work on REM Sleep Behaviour Disorders and Parkinson's.



Dr Michal Rolinski

The \$1,000 award recognises research efforts by new investigators in the study of sleep disorders. Dr Rolinski will give a presentation at the Young Investigator Award Symposium at the 6th World Congress on Sleep Medicine in Korea in March 2015.

➤ Parkinson's UK Oxford Carol Concert

On December 7th the Oxford branch of Parkinson's UK organised a Christmas Concert to raise funds for OPDC in Summertown. The concert featured Tom Poster on piano and carol singing with the 200 strong audience.

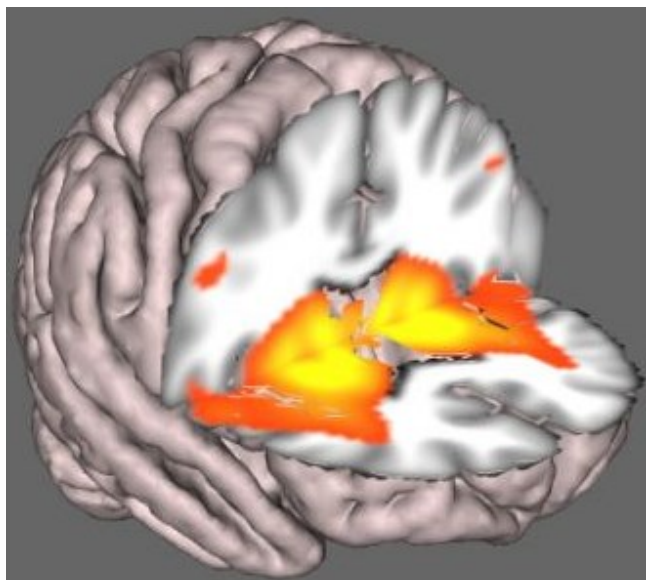


Richard Wade-Martins with Sally Bromley of Parkinson's UK,

OPDC Principal Investigator Dr Richard Wade-Martins spoke at the start of the concert and was delighted to accept a cheque from the branch for £30,000 to support OPDC's research.

OPDC researchers develop MRI technique that can detect people with early signs of Parkinson's

A brain-scanning technique that detects early signs of Parkinson's holds out the hope of tackling the disease before it starts to cause symptoms. OPDC have developed a simple and quick MRI technique that offers promise for early diagnosis of Parkinson's.



Conventional MRI cannot detect early signs of Parkinson's, so our researchers used an MRI technique, called resting-state fMRI, in which people are simply required to stay still in the scanner. They used the MRI data to look at the 'connectivity', or strength of brain networks, in the basal ganglia – part of the brain known to be involved in Parkinson's disease.

The team compared 19 people with early-stage Parkinson's disease while not on medication with 19 healthy people, matched for age and gender. The results, published in the journal *Neurology*, found that people with Parkinson's had much lower connectivity in the basal ganglia.

Dr Clare Mackay explains: **“Our MRI approach showed a very strong difference in connectivity between those who had Parkinson's and those that did not. So much so, that we wondered if it was too good to be true and carried out a validation test in a second group of patients. We got a similar result the second time.”**



Dr Clare Mackay



Dr Michele Hu

The MRI test was applied to a second group of 13 people with early-stage Parkinson's as a validation of the approach. They correctly identified 11 out of the 13 patients (85% accuracy). **“We think that our MRI test will be relevant for diagnosis of Parkinson's”.**

OPDC joint lead researcher Dr Michele Hu.

“We tested it in people with early-stage Parkinson's. But because it is so sensitive in these patients, we hope it will be able to predict who is at risk of disease before any symptoms have developed. However, this is something that we still have to show in further research.”

To see if this is the case, OPDC is now carrying out further studies of the MRI technique with people who are at increased risk of Parkinson's.

Reference: Szewczyk-Krolikowskiet al., (2014) Functional connectivity in the basal ganglia network differentiates PD patients from controls. *Neurology*. 83(3): 208-214

<http://www.ncbi.nlm.nih.gov/pubmed/23861334>

Looking for the early warning signs of Parkinson's in the blood

Blood-based biomarkers, are changes in the blood that if detected can be used to diagnose or monitor the progression of a condition. There is already promise for biomarkers to help with early diagnosis of Alzheimer's and we hope that similar success may also be possible in Parkinson's. Finding biomarkers of Parkinson's in the blood could speed up the development of new drugs that correct these biomarkers back to normal healthy levels and prevent progression of the condition.

Blood extracted from volunteers in studies

Blood analysed for proteins in people with Parkinson's that are not found in controls

Proteins compared across blood and brain tissue of people with Parkinson's

Outcome of Study:

Proteins found in blood and brain of people with Parkinson's could help us develop drugs that correct these proteins back to normal healthy levels and possibly prevent Parkinson's developing

A new study taking place here at the University of Oxford called "**Mapping Proteomics to Parkinson's Disease**" (MAP2PD), funded by Parkinson's UK, aims to detect proteins in the blood that could be used to diagnose and track progression starting in the earliest stages of the condition. We have just completed Phase 1 of the study where we measured 1129 proteins in the blood (using a technology from SomaLogic, Inc) from 161 people with Parkinson's (disease duration < 3 yrs) and 66 healthy controls. The results showed a total of 55 proteins that were present at different levels in the blood of people with Parkinson's compared to controls.

We then looked at whether combinations of these proteins may also differ in people with Parkinson's and discovered a subset of 22 proteins that together could predict Parkinson's with greater accuracy than the individual proteins. This promising development leads us to Phase 2 of the study to see if these differences are seen in even larger sample sizes of people with Parkinson's and controls. If so, we will assess whether these same protein biomarkers are present in the brains of people with Parkinson's and try to understand how these proteins might cause the condition.

Dementias Platform UK

OPDC is proud to be part of the new MRC Dementias Platform UK (DPUK). DPUK is a multi-million pound public-private partnership, developed and led by the **Medical Research Council**,

to accelerate progress in, and open up, dementias research across a range of neurodegenerative conditions, including Alzheimer's, Parkinson's and Motor Neurone Disease. DPUK's aims are early detection, improved treatment and ultimately, prevention, of dementias. The platform will create the world's largest study group for use in dementia research and is led by John Gallacher who recently moved to Oxford. It will allow researchers to examine dementia in a whole new way, investigating not just what is going wrong in the brain, but at the brain in the context of the whole body.



**Dementias
Platform^{UK}**
Medical Research Council



OPDC's role in DPUK

OPDC will contribute to a large clinical cohort of over two million people in the UK over the age of 50. In addition, several OPDC Investigators are playing a major leadership role in the DPUK. Richard Wade-Martins is leading the Dementia Stem Cell Network to develop six Dementia Stem Cell Centres across the UK, including one at Oxford. Simon Lovestone leads the informatics theme that will create the infrastructure to support new ways of collaborating to make the best use of data. Clare Mackay leads imaging informatics, which enable data sharing and accelerate the translation of imaging technology to real patient benefit.



For a short video introduction to the Dementias Platform UK visit <http://vimeo.com/116058818>

“We are delighted to have OPDC on board. By bringing cohort data together, DPUK will make it easier for scientists to access data, which will ultimately accelerate progress in research”. Professor John Gallacher, DPUK director.

OPDC welcomes new researchers to the project

In the past year we are happy to have been joined by exciting new researchers.



Professor Simon Lovestone heads up a group looking for markers in the blood linked to diseases such as Alzheimer's and Parkinson's and, specifically, concentrating on biomarkers which can be used in clinical trials. There is more about his work in the "biomarkers" story on page 5.

Dr Max Little is a mathematician at Aston University's Department of Engineering and Applied Science. Max's contribution to the OPDC project involves supervising the analysis of smartphone data collected from the participants, and advising on the use of machine learning techniques in general. You can read about his research on page 2.



Dr Natalie Connor-Robson is one of OPDC's new Career Development Fellows. She is investigating changes that occur early on in Parkinson's. She concentrates on using genetically altered models of Parkinson's to understand molecular alterations and changes in behaviour.



As part of our celebrations for the renewal of our funding, we held our OPDC Discovery Participant's Open Day this March at the Medical Sciences Teaching Centre.

This free event for those taking part in the study included talks from our researchers to update on both the clinical and lab based aspects of OPDC.

Speakers include Dr Michele Hu, Dr Max Little, Dr Claudio Ruffmann, Dr Michal Rolinski, Dr Fahd Baig and Dr Richard Wade-Martins with representatives from Parkinson's UK.

The talks have been filmed to be made available on our website.

New International/EU Research Projects

> Michael J. Fox Foundation Biomarker Grant



Dr Laura Parkkinen will lead a new study on the development of potential diagnostic biomarkers in Parkinson's using samples collected in OPDC. Dr Javier Alegre-Abarrategui, Dr Richard Wade-Martins and Dr Michele Hu are co-Investigators on this award.

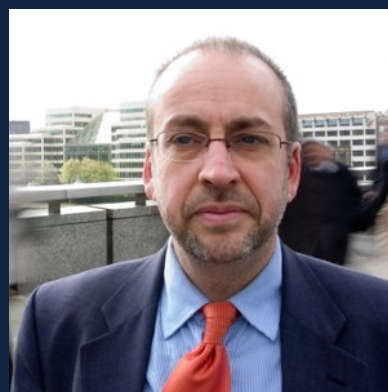


Dr Laura Parkkinen

> Alzheimer's Research UK Oxford Drug Discovery Institute



OPDC's Professor Simon Lovestone is one of the Oxford University project leaders on this new initiative funded by Alzheimer's Research UK. The research team at Oxford will develop multiple projects to identify new therapeutic targets in Alzheimer's, Parkinson's and motor neuron disease. Dr Richard Wade-Martins will be the Parkinson's research lead on this £10 million project.



Professor Simon Lovestone

OPDC launches new website and twitter account

We have been working on a new improved website where we hope to keep you updated with all the news and events from OPDC. The website address will remain www.opdc.ox.ac.uk but we hope the new site will be easier to use for all.



You can also keep updated by following us on twitter @oxfordPDcentre.



Find out more:



Funded by



Information on all our current research activities can be found on our website www.opdc.ox.ac.uk and in the 'OPDC' section of Parkinson's UK website <http://www.parkinsons.org.uk/content/oxford-parkinsons-disease-centre>

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