

## CAMBRIDGE CENTRE FOR BRAIN REPAIR & ADDENBROOKE'S HOSPITAL

### 2015 PARKINSON'S DISEASE NEWSLETTER



#### Roger Barker: Introduction

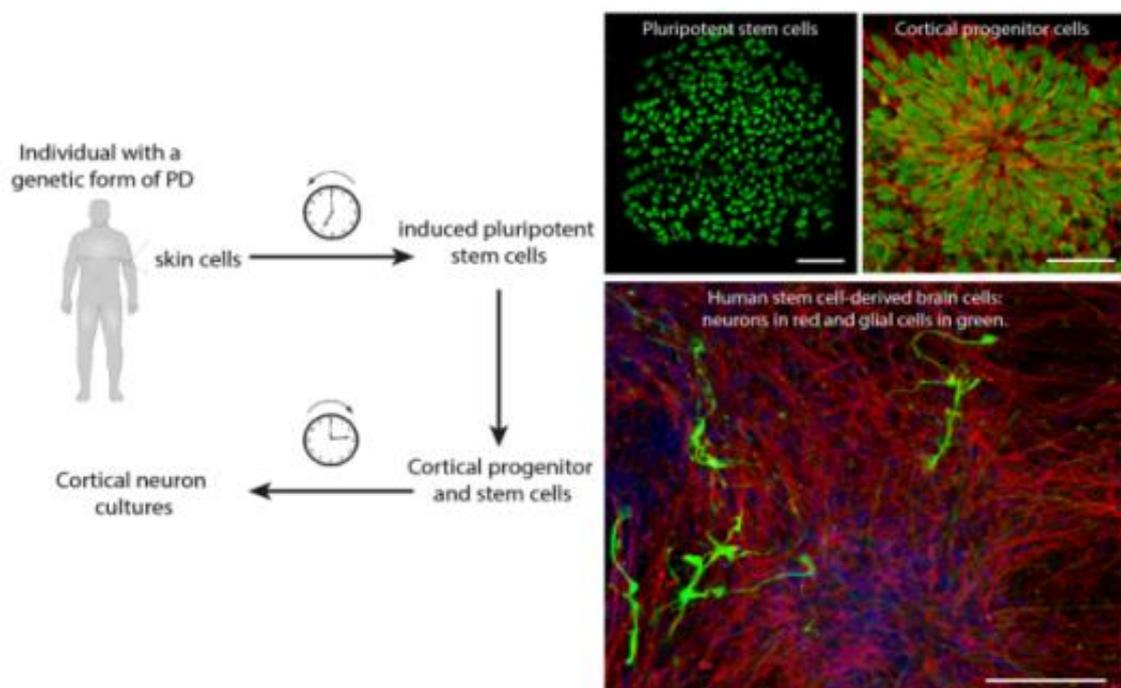
Welcome to our 2015 Parkinson's Disease Newsletter. We hope you enjoy reading about all the work we are currently doing both in the clinic and laboratory. As you can see we have continued to investigate Parkinson's disease from a number of different perspectives with the overall aim to better understand what goes wrong in PD and how we can better treat it. I want to thank you all for your help and support as we seek to find a cure for Parkinson's disease.

#### Philipp Berg – Human stem cell models to study PD



The discovery of Lewy bodies (LBs) in the brains of people with Parkinson's disease (PD) was made more than 100 years ago. LBs are made up of aggregates of a protein called alpha-synuclein and it is thought its aggregation is key to the disease process. Indeed PD starts many years before it is actually diagnosed and even though we know that at a later stage in the disease LBs have formed and a significant number of brain cells have died, we still have a very poor understanding of why and how the disease starts and how this could potentially be prevented.

wellcome<sup>trust</sup>

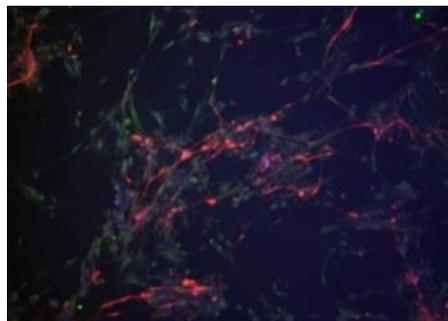


While the majority of PD cases occur for no obvious reason, there are rare genetic forms of the disease, for example caused by mutations in the alpha-synuclein gene. It is clear that these mutations give rise to PD and we are trying to make use of these genetic forms of PD to study disease initiation in human brain cells. In collaboration with Rick Livesey and the Gurdon Institute, we used reprogrammed induced pluripotent stem cells iPSCs (iPSCs – cells that have the capacity to develop into any cell type in the body) generated from skin cells of people with this genetic form of PD. We then used these cells to produce human brain cells to study the effect of the PD alpha-synuclein mutation and found that this genetic change resulted in an immediate change in the amount of protein in these cultured brain cells. We are now investigating what the consequences of this are and by so doing we expect to learn about the initial phases of PD long before LBs start to form and cells have been lost.

### **Lucy Collins – Developing a new personalised model of Parkinson’s Disease**



We have been working on developing a new personal cell model to better understand the underlying cause of Parkinson’s in patients with a particular form of PD that relates to inheriting part of a gene causing a related rare condition, Gaucher's disease. This is done by creating nerve cells directly from the normal cells found in a small skin sample and we can use them in the lab to investigate what goes wrong in brain cells in PD. This technique also allows us to test various drugs as potential new therapies. The image is an example of neurons (in red) made from a skin sample from a patient.



### **Romina Vuono – Understanding the role of tau and alpha synuclein in PD pathology**

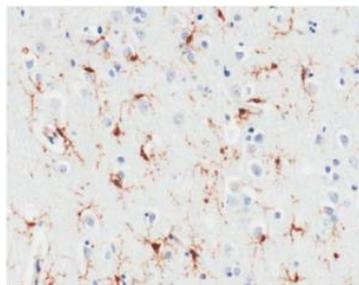
A lot of recent work has shown that a particular form of alpha synuclein and another protein called tau are critical to the development of PD. We are therefore now looking to see whether there are specific toxic species of tau and alpha synuclein present in the brains of PD patients which have an impact on the disease features and progression and which will hopefully lead to better therapies and markers of disease.

### **Caroline Williams-Gray – Inflammatory markers in the blood predict disease progression in PD**

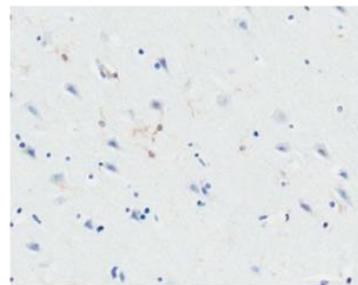


Parkinson's disease progresses at different speeds in different individuals, with some having a rapid disease course and developing debilitating memory and balance problems within a few years of diagnosis, and others having a more benign course with relatively little disability for many years. Recent research suggests that inflammation in the brain may be a driver of disease progression, and so anti-inflammatory drugs may help slow it down. In order to take this idea forward into successful clinical trials, it is important to find a practical way to measure disease-related changes in inflammation in patients. We have recently conducted a study to look at this in blood samples. This was done in collaboration with colleagues at the University of Newcastle. 230 patients with Parkinson's disease were included from Cambridge and Newcastle and compared to samples, from 93 people of similar age without the disease. We found that higher 'pro-inflammatory' scores in these blood samples predicted faster progression of movement problems and lower memory scores over the subsequent 3 years while higher 'anti-inflammatory' scores were protective. This is the first study to demonstrate that levels of inflammatory molecules in blood samples relate to the future progression of Parkinson's, and suggests they may be helpful in selecting the most appropriate patients for anti-inflammatory drug trials. Further work is now being done to investigate how these inflammatory markers change in patients over time, and whether they might be useful to track changes in inflammation as Parkinson's disease progresses.

**PD with dementia**



**PD without dementia**



### **Kirsten Scott – The B cells of the immune system and PD**



I am looking at the role of one particular immune cell, the B lymphocyte, in Parkinson's Disease. B lymphocytes are known for producing antibodies that recognise infections we have been in contact with previously. We also now know that they influence the behaviour of other immune cells and there is evidence to suggest that they may have an effect in PD. I am therefore studying them in patients and also experimentally to see whether we can alter their function in mouse models of PD and what then happens if we do this.



### **Ruwani Wijeyekoon – The innate immune system in PD**



I am working together with Caroline Williams-Gray and Kirsten Scott on a study investigating the immune system in Parkinson's disease. Several studies have indicated that the 'innate' part of the immune system may have an important role in Parkinson's disease. I am co investigating changes in the peripheral innate immune system, particularly in the properties and function of monocytes (a type of innate immune cell in the blood), in different groups of patients with Parkinson's disease.

### **Antonina Kouli – The inflammatory pathology of PD**



I am a new PhD student working with Caroline and I am specifically studying post mortem brains of individuals with Parkinson's who have kindly donated their brains for research following their death. We are examining the distribution of inflammatory changes throughout the brain, determining whether these changes are more pronounced in PD compared to non-PD brains. Then, we will evaluate the relationship between these changes and the patient's clinical course in life.

### **Simon Stott – Birax2 / Parkinson's UK Breath Analysis Study**



Starting in December, we will be recruiting subjects to be involved in a new breath analysis study into markers of PD. In collaboration with Professor Hossam Haick from Technion in Israel (who invented and developed the breath analysis technology), we are hoping to collect multiple breath samples over the three year study from 200 subjects with PD and 100 age-matched controls. We will also be recruiting approximately 50 subjects who have recently been diagnosed with PD to compare patients with early versus more established PD. The goal of the study is to determine if there are combinations of chemical compounds in the breath that can be used to differentiate PD and controls and also possibly different types of PD. We also hope to further investigate whether these chemicals have any possible role in the disease, in order to better understand the condition and the development of novel therapies.

### Sarah Mason – Hallucinations in PD



We have just started recruiting for a new project that is looking to better understand why some people with PD go on to develop hallucinations as part of their disease while others do not. In particular we are looking to see whether there are any similarities in the risk factors that make people more likely to hallucinate across different diseases, specifically Parkinson's disease, Macular Degeneration (a form of eye disease) and some forms of dementia. To do this we are interested in testing patients with Parkinson's disease REGARDLESS of whether they have ever experienced any hallucinations on a series of short tests of memory and attention. We will use the information collected from patients who have not previously hallucinated as a comparison. This is a collaborative project between ourselves, Kings College London and Newcastle University. If you are interested in participating please contact Sarah Mason ([slm64@cam.ac.uk](mailto:slm64@cam.ac.uk) or 01223 331160).

### Natalie Valle Guzman – Transeuro, Control Participants and Smart-PD



**Transeuro** -Transeuro is a European research consortium with the principal objective of developing a cell-based treatment for patients with early stage Parkinson's disease. The study is a unique initiative which brings together some of the world's leading Parkinson's researchers, aiming to reduce further delays in using cells to treat Parkinson's disease. The initiative focuses on refining cell-based therapies, which replaces the diseased cells with healthy cells. The first patient received a cell transplant in May in the UK and we expect to complete the transplants by the summer of 2016.

**Control Participants** - We are very grateful to the hundreds of patients with Parkinson's disease (PD) that have helped us in the past, and are currently helping us with our research. We are very interested in comparing this information with that of healthy controls, to confirm which of the changes we have found are due to PD, and which are due to normal aging. We are therefore currently assessing control volunteers with the same thinking assessments that we use in our patients, in order to answer this question.

**SMART-PD** - The SMART-PD trial investigates the use of a smartphone app that reminds patients with PD when to take their medication as well track their symptoms over time. We have now finished the first phase of the trial and currently the feedback of the patients is being used to improve the application.



### **Nick Blair**



I am a new member of the team, having trained as a neurologist in Sydney Australia and studying PD through stem cell models. I am now working within a new network in the UK, that is a regenerative medicine platform using stem cells. This has enabled us to develop new collaborations with the University of Lund. As a result we have started to plan for a new first in human stem cell dopaminergic neuronal transplant trial which will be done between the team of Malin Parmar in Lund and ourselves. As part of this we are using the new protocols developed in Sweden by Malin, to study the dopamine cells in Cambridge. It is hoped that we will have completed all the necessary work and secured the required funding for a trial in 2018/2019.



### **Jenny Wilson – Brain Bank**



You are probably familiar with organ donations of the heart, kidneys or eyes to sustain the health or even the life of people in need. Brain donation for research is a precious and unique gift. Scientists can learn and understand more about disease processes when they are able to work on donated tissue. Ultimately, we hope that scientific work of this kind will lead to better and more effective treatments and that future generations will benefit from your help and this includes Parkinson's disease. The donation of a brain and other parts of the CNS is a big decision and needs to be discussed with family and friends. Advice is available from the Cambridge Brain Bank research nurse Jenny Wilson who would be very happy to discuss any concerns or questions you or your family may have. Telephone number 01223 217336 or email [brbank@addenbrookes.nhs.uk](mailto:brbank@addenbrookes.nhs.uk) for further information as well as visiting the website: [www.cuh.org.uk/tissue-bank](http://www.cuh.org.uk/tissue-bank)



### **Parkinson's Disease Open Day**

We had a Parkinson's Open Day, on the 7<sup>th</sup> November 2015 that brought together people with the condition, their carers, researchers and clinicians from all over East Anglia. The morning session provided an exciting series of short lectures, presented by both lab members and invited guest speakers. The first speaker, Prof Maria Grazia Spillantini (who made the seminal discovery in 1997-1998 that alpha-synuclein is the main component of Lewy bodies and Lewy neurites – the pathological hallmarks of Parkinson's disease) talked about the role of alpha synuclein in PD. Next Dr Caroline Williams-Gray (who has done so much work on the CamPaIGN study) presented data on the natural history of idiopathic PD and a possible role for the immune system in driving aspects of this condition. Ms Julie Wilson from Parkinson's UK then discussed the strategy of Parkinson's UK for the next 5 years as they strive to support people with the condition through local activities such as exercise, dance and so on. These talks were followed by a Q&A session led by Roger Barker. The afternoon session provided an opportunity to see on-going research in the lab by talking to group members and reading posters summarising their work.



### **Dance Ensemble presents 'Take a step' – The story of Parkinson's**

Dance Ensemble is a community dance group founded by a member of our group Dr Romina Vuono together with her colleague Jeanette Simpson. Over the past two years, in an effort to raise awareness of Parkinson's disease they have been building a unique and original production – Take a Step – that weaves the science of the condition together with a series of dance pieces that ultimately builds to show the positive affect of fund raising towards finding a cure. 'Take a step' will be performed in Cambridge at the Cambridge Junction ([www.junction.co.uk/take-a-step](http://www.junction.co.uk/take-a-step)) in early January. The three performances are already filling up, but some tickets are still available for those who would like to come and support. All proceeds from the show will go to Parkinson's UK, a charity offering support to those with the condition and also funding research to find a cure. The group has a fund raising page for those that cannot join the production but would like to pledge their support. It can be found at <http://uk.virginmoneygiving.com/team/danceensemble>

**Websites of interest:**

Barker lab website: <http://thebarkerlab.co.uk/>

Parkinson's UK: <http://www.parkinsons.org.uk/>

GForce –PD: <http://www.gforce-pd.com/>

Transeuro: <http://www.transeuro.org.uk/index.html>

Cambridge Brain Bank: <http://www.cuh.org.uk/for-public/cambridge-brain-bank>

Facebook: <https://en-gb.facebook.com/people/Barker-Lab/100010790558064>

**Donations**

If you would like to donate to any of our research projects, then please do contact us on 01223 331160 or send any donations (payable to the University of Cambridge) to:

Prof Roger A Barker, Cambridge Centre for Brain Repair,

E.D. Adrian Building, Forvie Site, Robinson Way,

Cambridge, CB2 0PY.

**Contact us**

If you have a query or any concerns about PD, please feel free to contact us on 01223 331160.