#### What we have achieved

- Expanded our study into one of the largest and best-characterised cohorts of people with Parkinson's in the world.
- Developed brain imaging methods to detect changes in the early stages of Parkinson's and are working on finding biomarkers in the blood to correlate with specific clinical features.
- Our successful programme generating dopaminergic neurons from stem cells derived from skin samples of people with Parkinson's is the largest of its kind in Europe.
- We have made over 100 induced pluripotent stem cell (iPSC) lines from subjects with genetic and sporadic forms of Parkinson's, and healthy controls.
- Established a world-leading centre for the generation and characterisation of rodent models of early Parkinson's.
- Developed a new line of mice engineered to produce high levels of the human alphasynuclein, a protein thought to play an important role in Parkinson's.

# Our investigators are involved in major international & EU research projects



HE MICHAEL J. FOX FOUNDATION FOR PARKINSON'S RESEARCH

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PARKINSON'S" CHANGE ATTITUDES. FIND A CURE. JOIN US.

Funded by PARKINSON'S<sup>UK</sup> CHANGE ATTITUDES. FIND A CURE JOIN US. Oxford Parkinson's Disease Centre



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Oxford University Hospitals NHS Trust



Clinical Research Network Thames Valley and South Midlands

Oxford Biomedical Research Centre Enabling translational research through partnership

University of Oxford MEDICAL SCIENCES DIVISION



#### About OPDC

The Oxford Parkinson's Disease Centre (OPDC) at the University of Oxford is funded by an £11M award from Parkinson's UK for 2010-2020.

Our programme targets the molecular pathways of Parkinson's in order to:

- Understand disease progression;
- · Predict the onset of Parkinson's;
- Identify potential drug targets;
- Develop new treatments that will prevent the development of Parkinson's in at-risk individuals.

### **OPDC Discovery Cohort**



We have developed one of the largest and bestcharacterised cohorts of people with Parkinson's in the world; we have recruited over 1500 subjects, including over 1000 people with Parkinson's. We will continue to recruit people with rapid eye movement (REM) sleep behaviour disorder (RBD), as we consider these individuals to be at high risk of conversion to Parkinson's in the future.

We will continue to monitor members of our cohort to better understand Parkinson's progression. We use clinical assessments, MRI imaging, blood tests, new phone-based movement and speech tests to further our understanding of how Parkinson's develops over time and affects people in different ways.

### **Cellular basis of Parkinson's**

To uncover the pathological mechanisms of Parkinson's, we have to understand why vulnerable brain cells, or neurons, die.

We reprogram skin cells taken from our Discovery Cohort participants into stem cells and generate dopamine neurons, which are most vulnerable in people with Parkinson's.

- We use genetic modelling to increase power to detect Parkinson's genes.
- In-depth characterisation of our rich resource of Parkinson's neurons will provide rationale for target discovery.
- Phenotypes revealed in genetic and sporadic Parkinson's will be used to identify novel targets and repositionable drugs.



### **Rodent models**

We have generated rodent models of early neuronal dysfunction to mimic what goes wrong in the brain early on in Parkinson's. These offer robust and physiologically-relevant models for addressing our research priorities, such as:

- Understanding why certain types of neuron are more vulnerable in disease;
- Identifying how damage and loss of dopamineproducing neurons impacts on their targets elsewhere in the brain;
- Providing *in vivo* testing platforms to evaluate novel therapeutic interventions designed to slow, halt or even reverse disease progression.

### Working together

Clinicians and scientists in the OPDC interact regularly through meetings. Bringing together the neuroscientists, stem cell experts, brain imagers, neurologists, biochemists, geneticists and pathologists to discuss complex themes in Parkinson's allows us to link up work in areas of overlapping interest.



#### **Our team**



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Dr Clare Mackay

Dr George Tofaris

Dr Caleb Webber

Dr Max Little

**Co-Investigators** 

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## Career Development Fellows

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