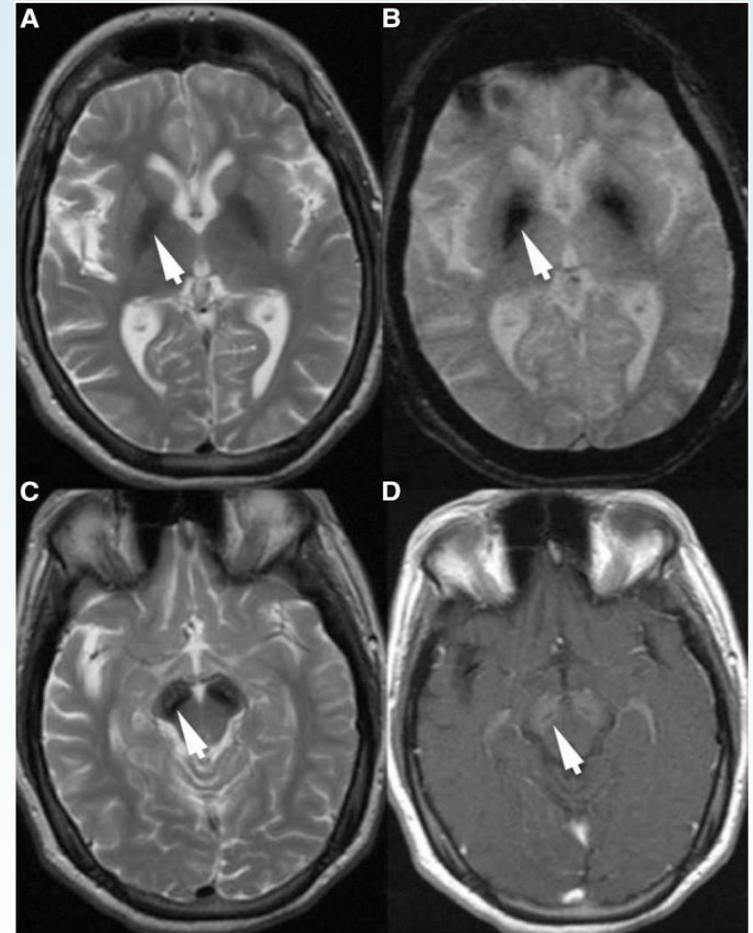


Investigation of disease mechanisms and screening for treatments in beta-propeller protein-associated neurodegeneration (BPAN)

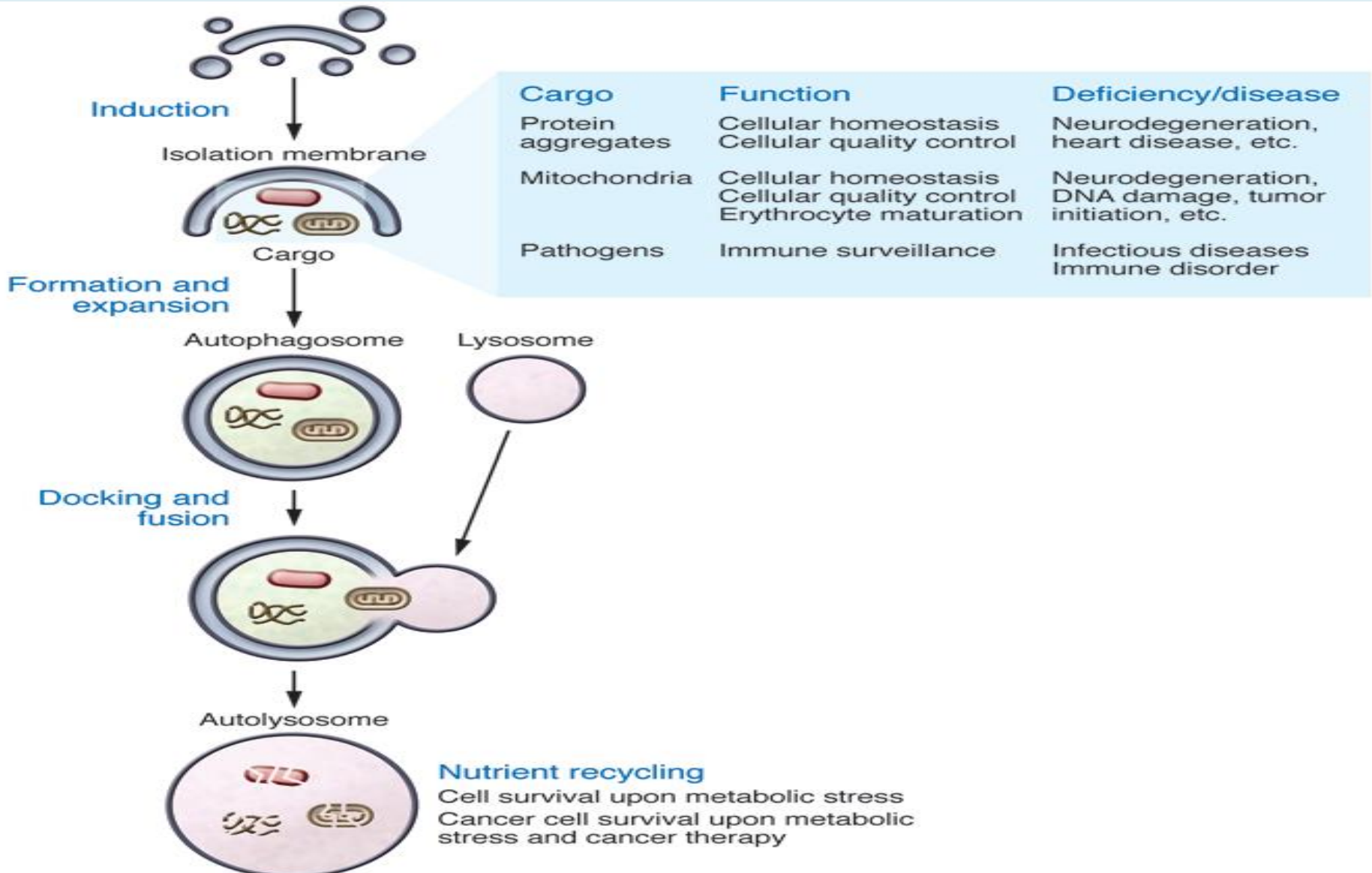
Dr Apostolos Papandreou, London, UK

Background

- WDR45: present in all cells, but problems primarily neurological
- MRI findings: areas of the brain involved in movement control



Autophagy



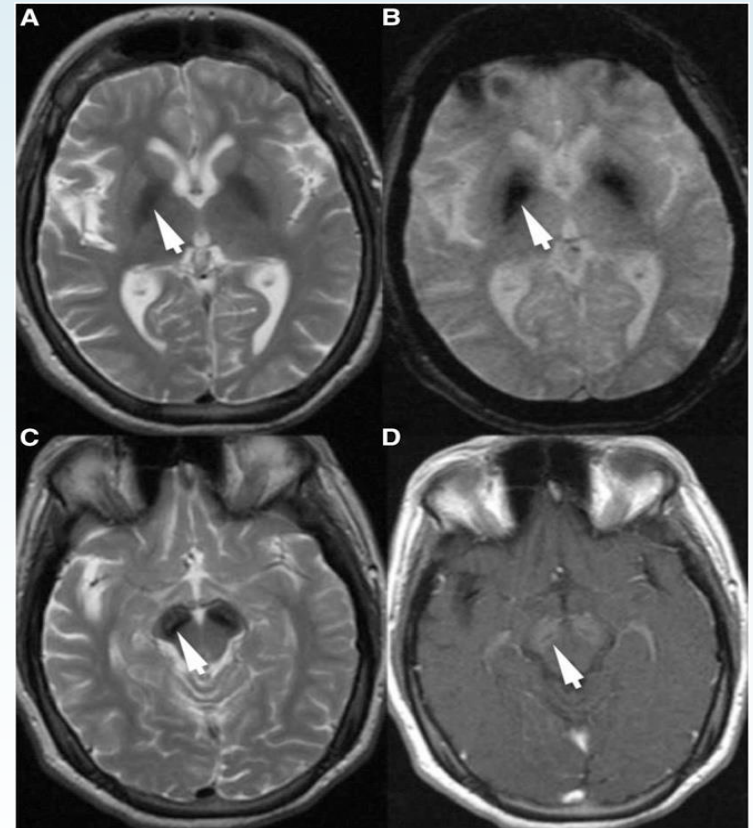
Overall Aim

- Progressive course
- No drugs currently available that can improve or cure BPAN
- Lack of understanding of disease mechanisms

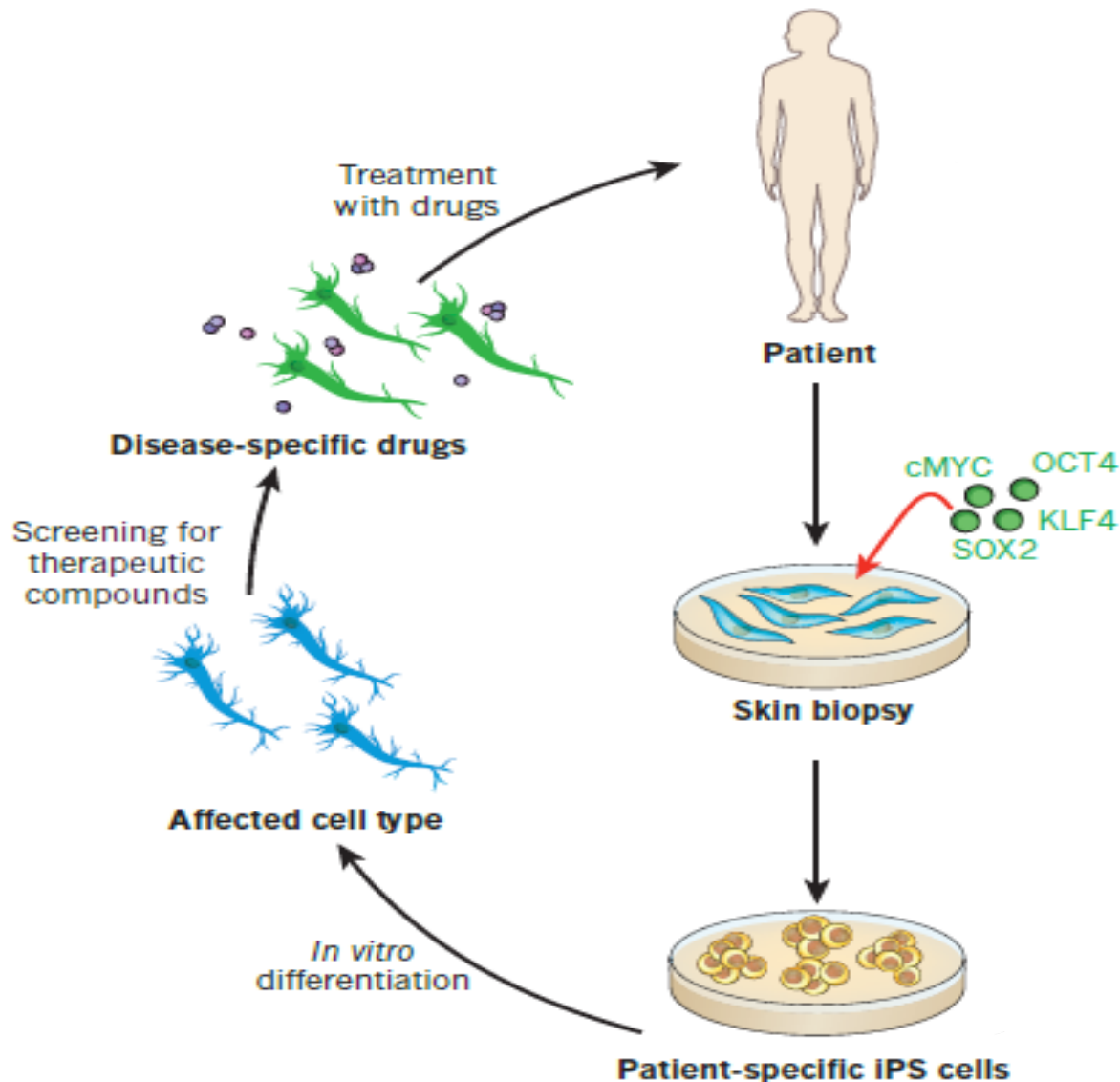
Aim: to establish a cell model for BPAN and use it to advance i) understanding of disease pathophysiology and ii) treatment development.

What type of research model?

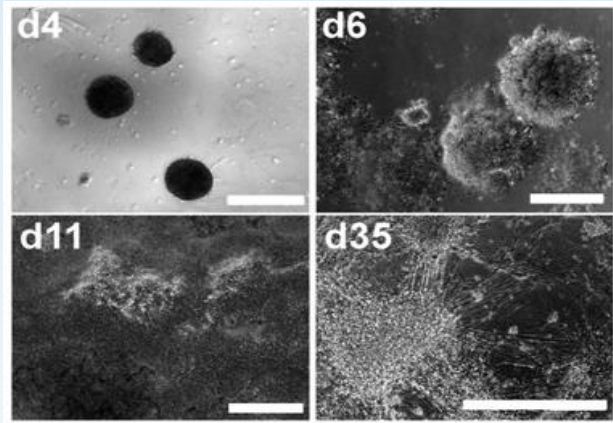
- We want to study nerve cells, as symptoms primarily neurological
- Dopaminergic neurons
- A model that 1) allows us to study patient-derived cells with known mutations; 2) has capacity for regeneration and differentiation



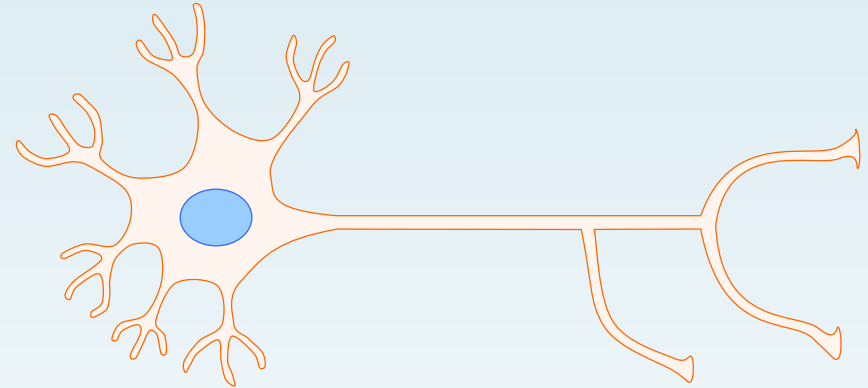
Induced Pluripotent Stem Cells (iPSc)



Neuronal Cell Differentiation

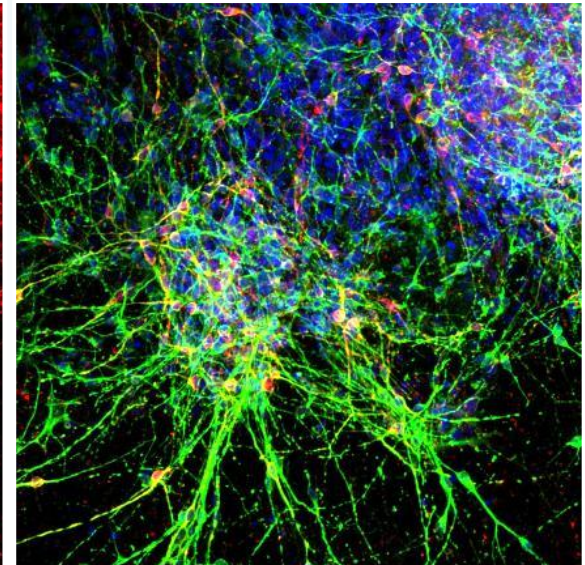
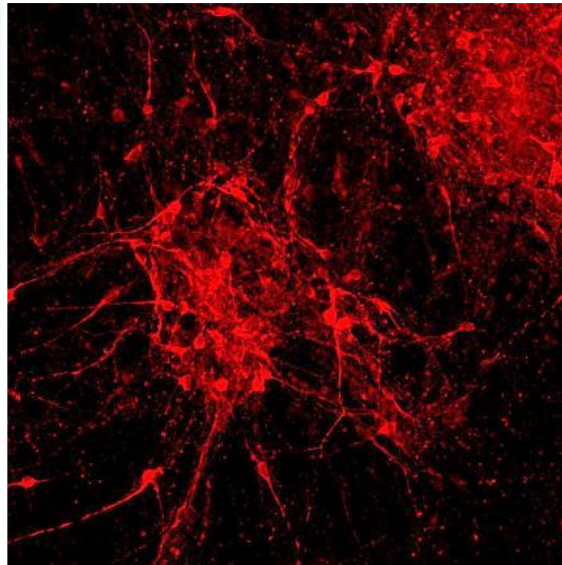
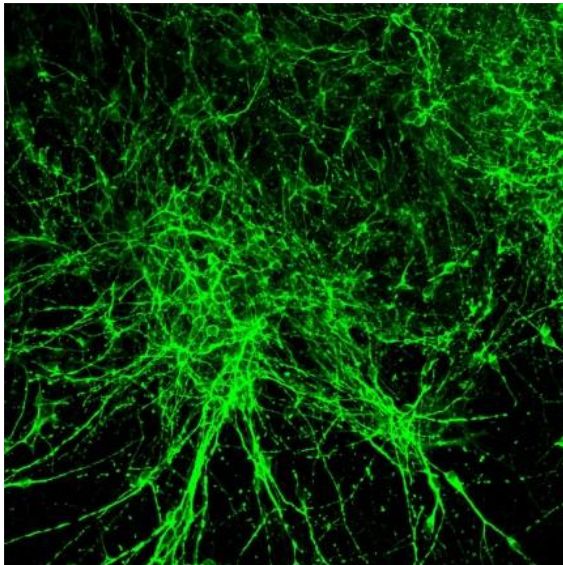


MAP2



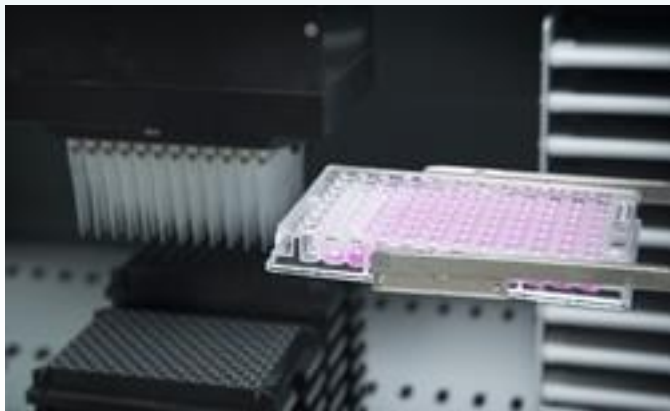
TH

merge



Further Experiments

- Eventually: brain cells that
 - carry disease-causing mutations
 - do not have mutations and are expected to be functioning normally



- **Identify** defective cell functions and processes
- **Test** thousands of chemicals for the ability to 'cure' the cells



Potentially effective chemicals: further testing, aiming to take the best compound forward for a future clinical trial.

Progress so far

- Early stages
- 2 patients recruited so far
- iPSc ready from one patient, being generated from the 2nd
- Aiming to perform experiments on cells deriving from at least 5-6 patients in total (ideally with different mutation types)

Benefits of our approach

- Regeneration and differentiation capacity
- Studies on human nerve cells
- Large number of drug screening experiments in a short time period
- Potential for drug repurposing

Timelines and Laboratory Realities

Time Consuming experiments

Genetic make-up of our nerve cells?

Studies on cells vs networks of nerve cells/ the whole brain

Acknowledgements

UCL- Institute of Child Health, Developmental Neurosciences Programme, London

MA Kurian
E Meyer
S Barral
J Ng
A McTague
A Ngoh
K Kramer
R Privolizzi

UCL-Laboratory of Molecular Cell Biology

R Ketteler lab
D Little

ICH-Genetics and Genomic Medicine Unit

P Gissen
PB Mills
PC Clayton
K Mills
F Mazzacuva
E Sirka
C Pollard

