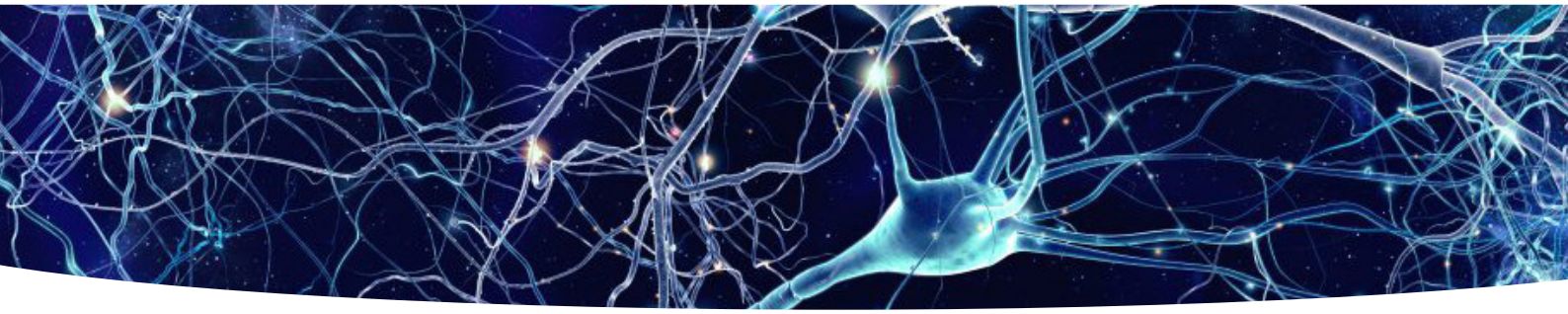
PD-MitoQUANT

Newsletter – January 2020



Learning more about the role of mitochondrial dysfunction in Parkinson's to help develop better therapies

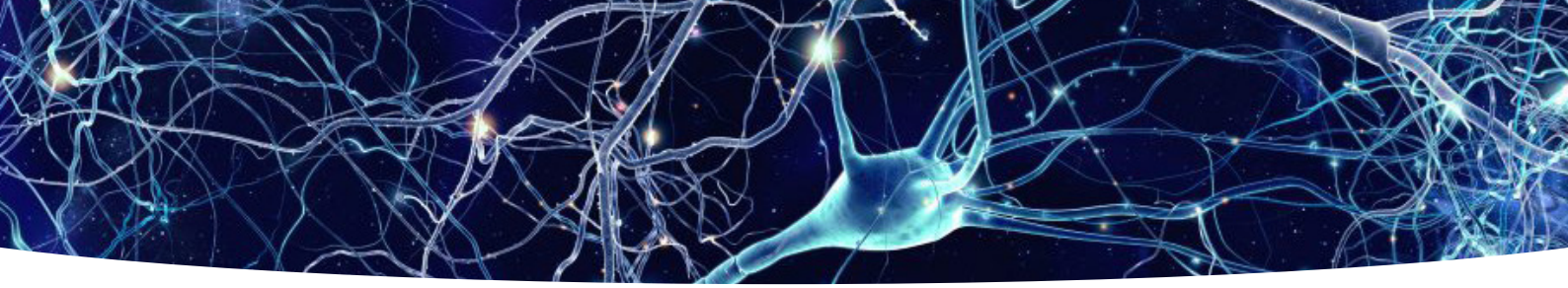
New, more effective treatments are urgently needed for the more than one million people living with Parkinson's in Europe today. PD-MitoQUANT (www.pdmitoquant.eu) is an Innovative Medicines Initiative (IMI) project investigating the role of mitochondrial malfunction in Parkinson's. Academic experts, Small/Medium Enterprises (SMEs), pharmaceutical companies from the European Federation of Pharmaceutical Industries and Associations (EFPIA) and the patient advocacy organisation, Parkinson's UK have assembled in this project to: (i) improve our understanding of mitochondrial dysfunction in Parkinson's, (ii) validate molecular drivers and mechanisms, (iii) develop improved models for study, and (iv) discover novel therapeutic targets for future therapies.

Message from Coordinator Prof Jochen Prehn

Coordinator, Prof. Jochen Prehn

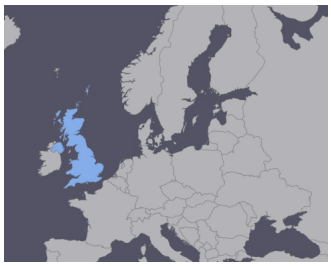
"PD-MitoQUANT began work in February 2019. All partners have contributed to ground-breaking work.

- *CNRS and Lundbeck identified a novel form of the protein α-synuclein that produces disease pathology in nerve cells, which will be studied throughout the project. α-synuclein is a major contributor to Parkinson's. However, it comes in different forms (monomers, oligomers, fibrils), as described in the PD-MitoQUANT publication in the Journal of Neurochemistry (α-synuclein oligomers and fibrils: a spectrum of species, a spectrum of toxicities; June 2019; 150(5); https://bit.ly/2PDPCit). The identification of a form that reliably induces neuropathology in models of Parkinson's represents a significant achievement for the consortium and the field in general.*
- *CNR, ICM and SME MIMETAS expanded on the delivery of translatable models of Parkinson's by establishing models and protocols for generating neurons originating from cells of people with Parkinson's. Lundbeck and RCSI have harmonized cell culture regimens to streamline analysis throughout PD-MitoQUANT. DZNE and ICM developed tools to study α-synuclein toxicity in Drosophila and C. elegans. Here, the effects of genes and master regulators of α-synuclein toxicity can be analyzed in high throughput. RCSI, TEVA, UCL, RUMC and ICM established stringent protocols for the evaluation of mitochondrial dysfunction in these models.*
- *Industry partners UCB and SME GeneXplain and RCSI co-created stringent data management and bioinformatics platforms that will be adopted by the entire consortium.*
- *Finally, Parkinson's UK developed PD-MitoQUANT's communication plan, continually involving our patient representatives."*



Meet PPI Volunteer Paula Scurfield

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



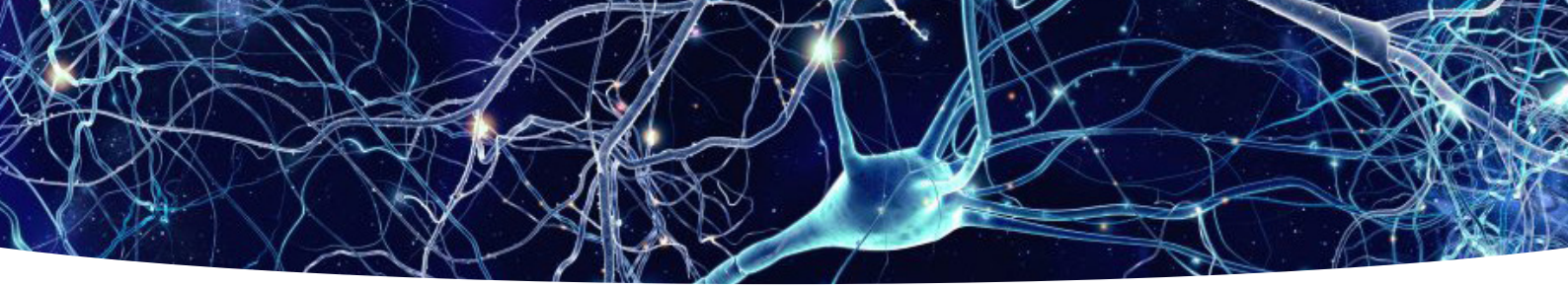
The public, including patients, can and should be involved in all aspects of research, including study design, communication, and ethics. Patients bring unique knowledge and skills to projects, which can improve the quality of research. The IMI (https://www.imi.europa.eu/) encourages public and patient involvement (PPI) in all of its projects. PD-MitoQUANT is fortunate to have two people with Parkinson's involved in the project through our patient advocacy partner Parkinson's UK (https://www.parkinsons.org.uk). In our last newsletter, we introduced Richard Campbell. Here, we meet Paula Scurfield.

PPI Volunteer Paula Scurfield

Paula was diagnosed with Parkinson's in March 2014 and is the fourth person in her family to have the condition. Before retirement 10 years ago, Paula worked as a geography teacher and part-time university lecturer in Hong Kong, Washington DC, Beijing, the Maldives, and the UK. She believes that volunteering and taking part in clinical trials is empowering, enabling her to meet the challenges of living with an incurable neurodegenerative disorder head-on. When not travelling, gardening, exercising, and spending time with her family - including six grandchildren, one dog, and one rabbit - Paula volunteers for Parkinson's UK as a lay reviewer of research grant applications, taking part in PPI tasks, chairs the Research Support Network Development Team, is a First Steps presenter (a two day programme for newly diagnosed People with Parkinson's), and a volunteer educator. She is fascinated by the aetiology of PD and is particularly keen to learn more about the underlying biochemical pathology of mitochondrial malfunction and α-synuclein misfolding. Paula is greatly looking forward to being involved as an expert patient in the PD-MitoQUANT project and to doing everything she can to assist the research team.

Highlights of the PD-MitoQUANT Plenary Meeting

In sunny Herzliya, Israel, the consortium gathered for the 2nd plenary meeting. Hosted by Teva Pharmaceutical Industries, researchers presented their work developing models of Parkinson's to investigate the impact of α-synuclein fibrils on mitochondrial function. The emotional opening talks by our PPI volunteers Paula and Richard set the tone, describing the challenges of life with Parkinson's and underscoring the importance of an outlook toward patient benefit even in basic research. Themes for debate were the best approaches to model the multi-year, progressive degenerative process of Parkinson's within the laboratory setting, the role of non-neuronal cells in neuronal demise, and the processes for optimizing reproducibility of experimental models across participating research labs. The meeting concluded with insights from the Scientific & Ethics Advisory Board.



Meet PD-MitoQUANT PI Dr Olga Corti

Olga Corti, PhD is a Research Director at the Institut du Cerveau et de la Moelle épinière (ICM, https://icm-institute.org/en/) located in Paris France. Olga is an expert in the functional analysis of protein products of Parkinson's genes with a focus on mechanisms of mitochondrial quality control. We asked Olga some questions about her research and ICM's role within PD-MitoQUANT.

Within Parkinson's research, which cell types and mechanisms are most interesting to you at the moment and why?

Parkinson's is due to the gradual loss of specific neuronal populations that produce the neurotransmitter dopamine. We still do not understand why these neurons die, and it is essential that we do if we want to find out how to prevent this degenerative process.

Until recently, scientists were only able to study degenerative mechanisms and dopamine-producing neurons on brains dissected post-mortem. But thanks to remarkable discoveries, it is now possible to generate human neurons in a laboratory, starting from any cell type of the body. Now we can create and study lab-made dopaminergic neurons from people affected by Parkinson's. These neurons are studied in parallel with neurons from non-affected individuals, from types of neurons that are not affected by Parkinson's and from mice carrying mutations in genes responsible for familial forms of the condition. We use these tools to try to understand what goes wrong in Parkinson's.

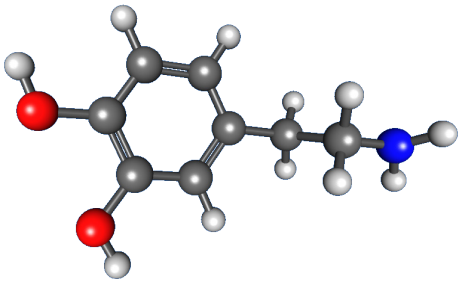
Olga Corti, Ph.D. Research Director, ICM

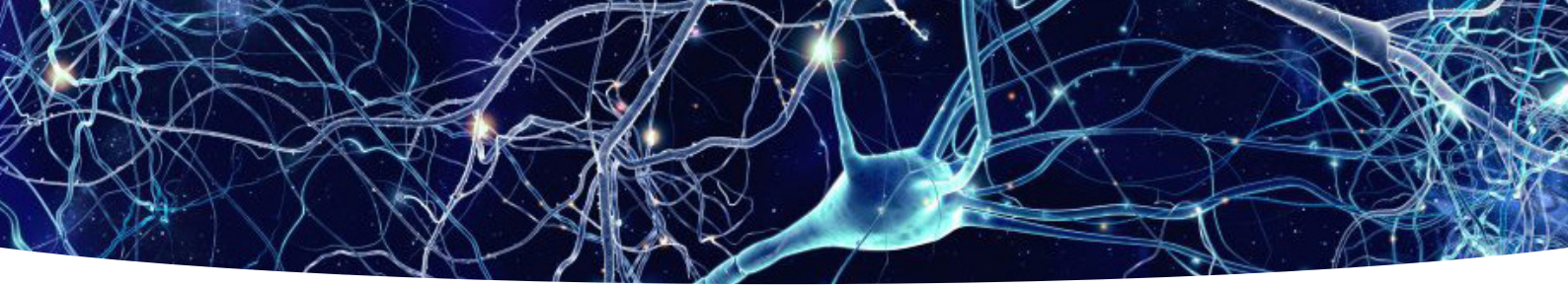
My team at ICM investigate the mechanisms related to mitochondria – the parts of neurons responsible for producing enough energy to sustain the neurons and ensure neurotransmission. There is increasing genetic evidence for the involvement of mitochondria in Parkinson's. We are interested in understanding how mutations responsible for familial forms of Parkinson's affect the mitochondria, and the consequences on the neurons' function

See the full interview with Olga here https://www.pdmitoquant.eu/2019/10/ocortiinterview/.

Learn the Lingo

Dopamine is a neurotransmitter involved in controlling motion. A neurotransmitter is a chemical that passes messages between nerve cells (neurons). Parkinson's involves the loss of neurons that release dopamine, resulting in symptoms like tremors or slow movement.





Partner in the Spotlight: MIMETAS

Everyone wants better medicines for Parkinson's. To make this possible, researchers need better disease models that are fully human and physiologically-relevant. These tools need to be informative and compatible with a variety of compounds and high-throughput readout equipment. Meet our partner MIMETAS whose vision is to create "the simplest device for the most complex 3D biology".

Remko van Vught, Director of Business Development.

MIMETAS is a privately-owned biotech company, headquartered in Leiden (NL), that provides organ-on-a-chip products for compound testing, screening and fundamental research. Its flagship product, the OrganoPlate® (https://mimetas.com/page/technology), supports 3-D cell culture under continuous perfusion, with membrane-free co-culture and epithelial and endothelial tubules. The company develops and validates customized disease, toxicology and transport models. MIMETAS has developed tissue models to bridge the translational gap between in vitro and in vivo models and humans. Within PD-MitoQUANT, MIMETAS builds on existing expertise in central nervous system models and relevant assays to conduct a targeted evaluation of the effect of α-Syn fibrils on laboratory-made, brain tissue, by integrating relevant cell types (neurons and glia) in their 'Organ-on-a-Chip' platform.

"It's exciting to be part of PD-MitoQUANT to improve the understanding of mitochondrial dysfunction in Parkinson's. The project enables us to further advance our models, develop analysis tools and support discovery of innovative therapeutic targets",
Remko van Vught, Director of Business Development.

PD-MitoQUANT Partners

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