



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

“We've now reached the end of year 3 of PD-MitoQUANT, having been granted a 6-month extension due to the COVID-19 pandemic. The impressive collection of datasets from both cultured cells and pre-clinical models generated by the consortium are now being put to use to identify and validate potential targets and signatures of alpha-synuclein (α Syn) toxicity, including bioenergetics and mitochondrial quality control, plasma membrane ion channels and new neuronal signalling molecules. This has been a great achievement of all our partners, demonstrating the necessity for an integrated approach. Advanced bioinformatics and network analyses of our in silico academic and industrial partners were used to identify potential targets and signatures to inform target selection, with inputs from all partners. We have started validation studies for the targets and signatures in model organisms (DZNE, ICM), 3D 'Organ-on-a-Chip' models (Mimetas), directly reprogrammed neurons (CNR), and in vivo models (DZNE, ICM), which we will complete in the remaining months of the project.”



Coordinator,
Prof. Jochen Prehn

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You can also meet some of our early- and mid-stage researchers in our [Researchers profiles](#).



Partner Spotlight - Radboud University Nijmegen Medical Centre

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The Radboud University Nijmegen Medical Center (RUMC, www.radboudumc.nl/) is one of the main academic hospitals in the Netherlands. Mitochondrial research is embedded within the research theme: "Metabolic Disorders", the Radboud Institute for Molecular Life Sciences (RIMLS) and the Radboud Center for Mitochondrial Medicine (RCMM). The RCMM is a top-ranking international center hosting more than 100 mitochondrial experts on clinical care, diagnostics and fundamental research.

In PD-MitoQUANT, RUMC will conduct a detailed analysis of mitochondrial morphological and functional readouts ("morphofunction") in PD cell models using quantitative high-content and super-resolution microscopy.

Together with Dr. Merel Adjobo-Hermans (Dept of Biochemistry), Dr. Werner J.H. Koopman (Dept of Pediatrics) heads the Cellular Bioenergetics group. Research focuses on understanding the connection between mitochondrial (ultra) structure and function, with the aim to better understand the pathomechanism of human mitochondrial diseases and drive rational intervention development.



Dr. Koopman



Dr. Adjobo-Hermans.

What do you find most interesting about mitochondria?

The Cellular Bioenergetics group is fascinated by the stunning dynamics mitochondria display and aims at unravelling the intricate regulation of mitochondrial morphofunction. A proper quantitative understanding of how the cell influences mitochondrial morphofunction and vice-versa is still lacking. Moreover, the role of mitochondrial morphofunction in health and disease has only recently become a topic of more intensive research. We expect our unique approach, combining patient-derived neuronal cell differentiation and advanced multidimensional fluorescence microscopy with robust image analysis, to yield important new insights into alpha-synuclein-induced Parkinson's.

2021 Par-Con Research Support Network Conference

When it comes to sharing accessible research results, people with Parkinson's are often excluded, as the language of journals is mystifying to a non-scientist. Explaining the significance of research findings, and thus offering hope, often falls to Parkinson's charities. This is possibly why the most recent Parkinson's UK three-day conference for the Parkinson's community, held in October 2021 via Zoom, was such a huge success. Around 2,500 people signed up to attend. The conference was organised by a group of people affected by Parkinson's, who helped to shape 12 conference sessions. 39 expert speakers included academics, neurologists, people with Parkinson's and media personalities.

A video library of the talks is available (bit.ly/33y9ddu) - have a look!



Partner Spotlight - UCB S.A.



UCB, Brussels, Belgium (www.ucb.com) is a global biopharmaceutical company focused on the discovery and development of innovative medicines and solutions to transform the lives of people living with severe diseases of the immune system or of the central nervous system. With approximately 8,400 people in nearly 40 countries, the company generated revenue of € 5.3 billion in 2020. UCB is listed on Euronext Brussels (symbol: UCB).



Within PD-MitoQUANT, UCB is involved in:

- bioinformatics and network analyses of 'omics data, and
- validation of novel mitochondrial signatures in *in vivo* models and samples from Parkinson's patients.

Veerle De Wever is a principal research scientist in the *In Vitro* Pharmacology department at UCB. Our department is at the center of the pre-clinical research. We develop screening assays, explore biology models and implement cutting-edge technologies to drive our research to better solutions for patients. Previous to UCB, Veerle's academic research focused on the identification & regulation of key enzymes for cell cycle & stress regulation in human cells & model organisms.



Dr. De Wever

Alexandre Brenet just obtained his PhD in neuroscience from the University of Paris. During his PhD, he characterized a new epilepsy model in zebrafish larvae and focused on studying the involvement of microglial cells in epileptogenesis and epileptic seizures. He has freshly joined the *In Vitro* Pharmacology Department at UCB, where he will contribute to assays development on various targets and protein binding & interaction studies.



Dr. Brenet

What is the main focus of UCB's research in PD-MitoQUANT?

UCB is committed to validating novel signatures via protein studies in human samples & *in vivo* models, created by the consortium. UCB will employ genomic & phenotypic association studies to bootstrap and explore novel mitochondrial signatures for their links to Parkinson's.

What are the main benefits of Public Private Partnerships like PD-MitoQUANT for UCB?

The direct contact between patients, academia and pharma brings together a world of expertise which is a great opportunity for UCB to continue their commitment to Parkinson's patients. We can learn what matters most to patients & work together with academic partners towards novel, improved solutions.



Dissemination Highlights

Our researchers have been busy presenting recent project results at virtual conferences:

- Dr. Shruti Desai (RUMC) presented 'PD-MitoQUANT: Quantification of Mitochondrial Morphofunction in Neuronal Cells' at the 2021 Neuronet public event during the 31st Alzheimer Europe conference (December 2021).
- Prof. Ronald Melki (CNRS) gave a plenary talk at the Young Scientist Symposium on Protein Quality Control (September 2021), which aims to provide early-career scientists with an interactive platform for discussion of research in the field of protein quality control.
- Dr. Niraj Khemka (RCSI) attended the virtual Neuroscience Ireland meeting (September 2021), where he showcased PD-MitoQUANT in a poster 'Multi-omics profiling of fibril-induced α Syn aggregation in primary neurons as model for Parkinson's disease'.
- Dr. Sinéad O'Sullivan (DZNE) presented 'Modelling α Syn pathology in vivo' at the August NeuroConnect meeting of the Neuroscience Ireland Early Career Researcher Network.



Latest Project Publication

DZNE and CNRS published 'Microglia jointly degrade fibrillar α Syn cargo by distribution through tunneling nanotubes' in Cell (doi.org/10.1016/j.cell.2021.09.007). To break down toxic proteins more quickly, immune cells in the brain can join together to form networks when needed. However, with certain mutations that can cause Parkinson's, this cooperation is impaired. This collaborative work with Michael Heneka's group from the University of Bonn showed that microglia share the burden of fibrillar α Syn through the directed transfer of the fibrils from affected to naive cells and mitochondria from naive to affected cells.



For a full list of project papers, visit our [Publications page!](#)



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