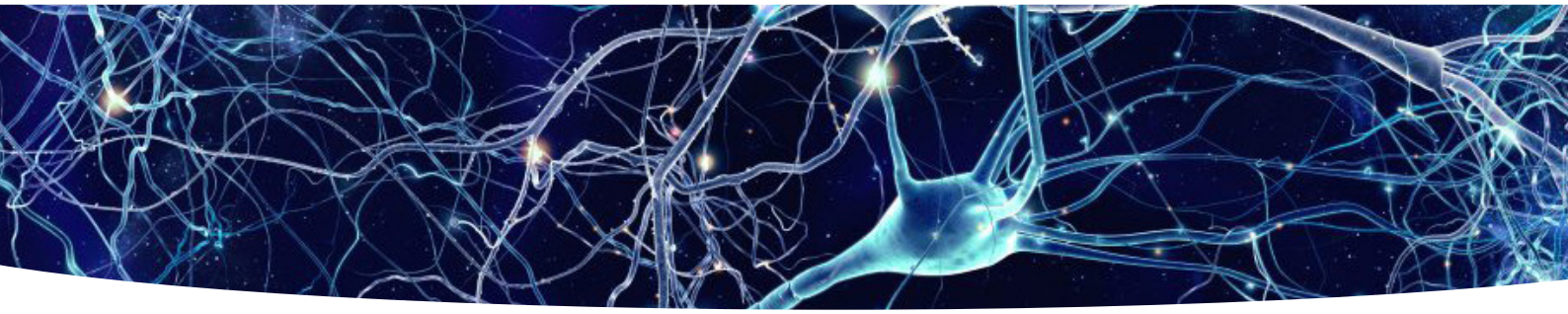
PD-MitoQUANT

Newsletter – August 2020



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

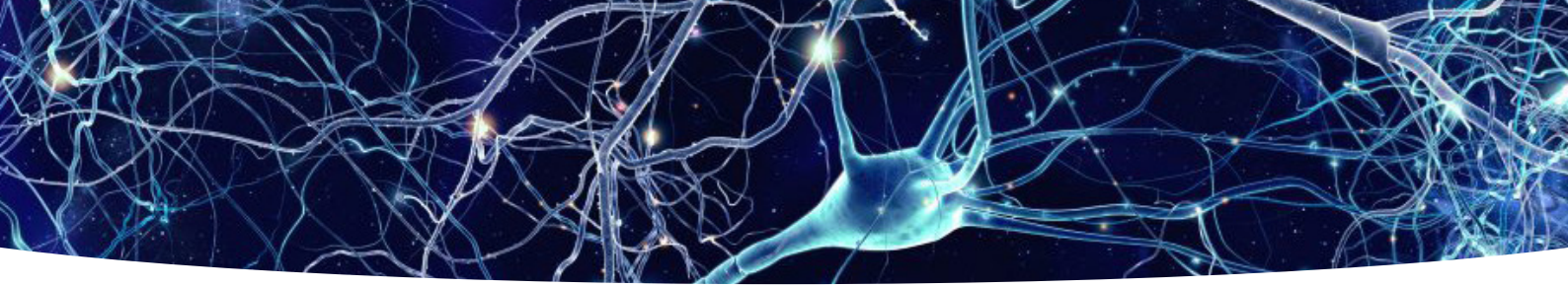
New, more effective treatments are urgently needed for the more than one million people living with Parkinson's in Europe today. PD-MitoQUANT (www.pdmitoquant.eu) is an Innovative Medicines Initiative (IMI) project investigating the role of mitochondrial malfunction in Parkinson's. Academic experts, 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

"We are now at the mid-point of the PD-MitoQUANT project, and excellent progress has been made on developing and standardising key models, protocols and assays. There have been delays due to the COVID-19 pandemic, but the consortium has worked together to reduce these delays and we're all delighted to be returning to our laboratories in a limited capacity. To date:

- *CNRS and Lundbeck have identified a novel form of α-synuclein (αSyn) that reliably induces neuropathology in models of Parkinson's. αSyn is a protein that is associated with disease pathology in nerve cells in Parkinson's, and comes in many different forms (monomers, oligomers, fibrils). A batch of the novel form of αSyn has been manufactured by CNRS and sent to partners across Europe.*
- *Robust protocols for primary and iPSC-derived in vitro neuronal cultures and seeding assays have been developed by Lundbeck and CNR, and shared with partners. Work in primary neurons has been started, including studies of how αSyn affects the production and use of energy in mitochondria (RCSI), whether it induces cell death (Lundbeck) and whether αSyn alters protein uptake into mitochondria or the degradation of damaged mitochondria (ICM, RUMC). We also study whether αSyn affects the transmission of signals from neuron to neuron (Teva), and how it changes the landscape of mitochondrial proteins (CNRS).*
- *Four in vivo models have also been established in ICM and DZNE. Two mouse models have been established in partner labs, where the levels of αSyn in the brain are increased by either injecting αSyn into the brain or by inserting a human αSyn gene in the brain. Models using fruit flies and roundworms have also been established by introducing αSyn genes."*



People with Parkinson's Share their Perspectives at PD-MitoQUANT meeting

PARKINSON'S UK
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PD-MitoQUANT is fortunate to have two people with Parkinson's, Richard Campbell and Paula Scurfield, involved in the project through our patient advocacy partner Parkinson's UK (www.parkinsons.org.uk). Recently, Richard wrote a blog entitled "Getting involved in an international research project on Parkinson's", where he spoke about joining the PD-MitoQUANT meeting in Israel.

"In November 2019, Paula and I accompanied Professor David Dexter, Deputy Research Director at Parkinson's UK, to a PD-MitoQUANT project meeting. The meeting was held near Tel Aviv in Israel, the base of Teva Pharmaceuticals — one of the commercial partners involved in the project.

We were there to give the point of view of people with Parkinson's and to make sure the scientific experts did not lose sight of the ultimate aim of the research — to improve treatments or even find a cure for Parkinson's.

We are not experts in the many scientific disciplines represented at the meeting, ***but we are experts in Parkinson's!*** *I suspect that we were the first people with Parkinson's that some of the experts had met, given that many of them spend their days working in laboratories. We reminded the experts that some of them, or members of their close family, would develop Parkinson's. We were also able to direct their attention to some of the problems of living with Parkinson's apart from the obvious and more well-known symptoms."*

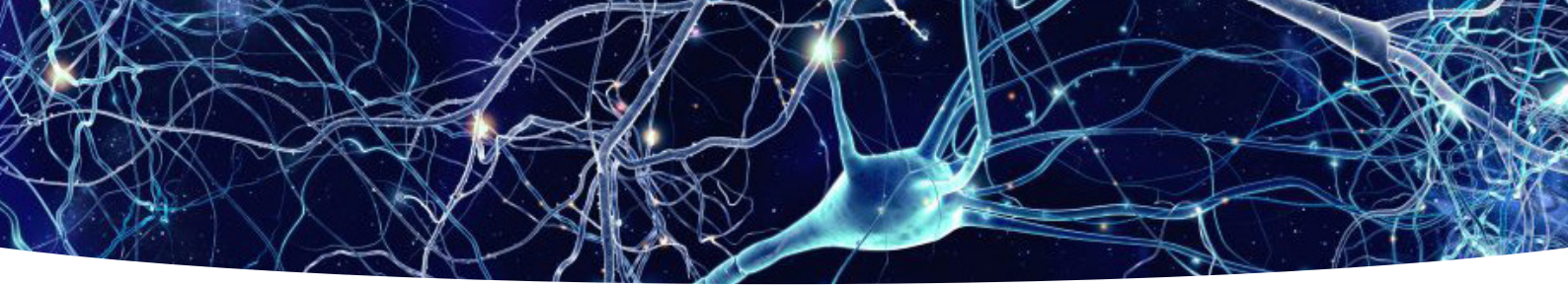
PD-MitoQUANT's Public Patient Involvement Representatives present at the Nov 2019 meeting

You can read Richard's full blog post to learn more about the perspective of people with Parkinson's on the project: https://bit.ly/3ebEYbU.

#newnormal as Laboratories Re-Open

Partner laboratories are re-opening following closures during restrictions for the COVID-19 pandemic across Europe. We're delighted to be resuming experiments and are adapting to the 'new normal' with measures to ensure social distancing in place.

Parkinson's UK are also going virtual for their 2020 Research Conference "Accelerating research and improving care" on 24 September 2020. You can register here to join: https://www.parkinsons.org.uk/events/online-research-conference-2020

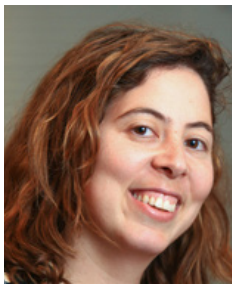


Partner Spotlight - Teva Pharmaceutical Industries Ltd

Teva Pharmaceutical Industries Ltd. (https://www.tevapharm.com/) is a global leader in generic medicines, with innovative treatments in select areas, including the central nervous system, pain and respiratory disease. The company has an established presence in generics, specialty drugs, as well over-the-counter and active pharmaceutical ingredient manufacturing, building on more than a century-old legacy. Teva also has a fully integrated R&D function, strong operational base and global infrastructure and scale. Headquartered in Israel, with production and research facilities around the globe, Teva employs approximately 40,000 professionals, committed to improving the lives of millions of patients worldwide.

Within PD-MitoQUANT, Teva will:

- conduct quantitative studies of mitochondrial bioenergetics *in vitro*, and
- examine the effects of αSyn fibrils on neuronal excitability *in vitro*.



Dr. Dana Bar-On

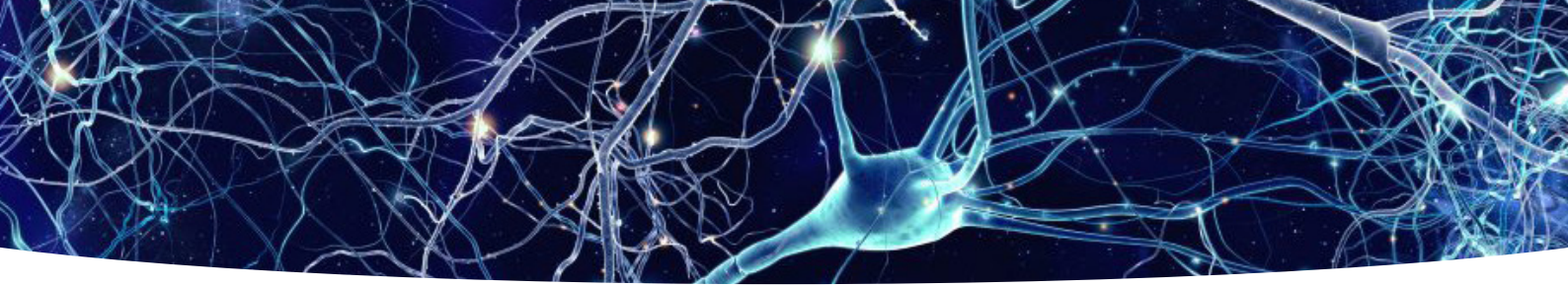
Dr. Dana Bar-On is the EFPIA Project Leader of PD-MitoQUANT, sharing overall leadership with the Coordinator. She is the director of Teva's Global R&D Academic Affairs and Networks team. Previous to her role in Teva, Dr. Bar-On was the head of the industry-academia cooperation at the Sagol School of Neuroscience in Tel Aviv University, the largest neuroscience school in Israel. Dr. Bar-On was the founder and head of BrainBoost and Minducate, two innovation and entrepreneurship centers aimed at creating and advancing new commercial academic ventures and start-ups in the field of brain disorders. She completed post-doctoral research in Tel Aviv University in collaboration with Cambridge University focusing on developing early diagnosis for Parkinson's via super-resolution microscopy. She finished her Ph.D. in Neurobiology focusing on advanced imaging methods, simulations and modelling of synaptic proteins.

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

Teva is focused on in-depth analysis and characterization of the αsyn fibrils and aggregation on neuronal cells by in vitro assays using neuronal primary cultures and later in iPSCs from PD patients developed by the consortium partners. Teva is implementing electrophysiological characterization and immunohistochemical measurement to test the effect of the fibrils on the neuronal activity.

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

I think the main benefit of this unique partnership is an open dialogue and stimulating interactions with leading academic partners and key opinion leaders (KOLs) in the field of Parkinson's. In addition, the exposure to cutting edge technologies, animal, *in vitro* and *ex-vivo* models in this field is very instrumental to Teva and coincides with Teva's unique expertise in the field of CNS therapeutics and Parkinson's specifically.



Q&A with RCSI's Dr. Niamh Connolly

RCSI Leading the world to better health

What is the main focus of your research in PD-MitoQUANT?

Dr. Niamh Connolly, RCSI

I am utilising data analysis techniques and mathematical models to investigate how the energy supply systems in our neurons are impacted in experimental models of Parkinson's. We recently published a paper where we applied some of these techniques to models of Alzheimer's (https://doi.org/10.1111/acel.12924), and we are now transferring this knowledge and interdisciplinary approach to the various models of Parkinson's developed in the PD-MitoQUANT consortium.

How can your work advance the treatment of Parkinson's?

Sophisticated data analysis techniques are vital to more thoroughly explore and interpret the huge amounts of experimental data we are now generating. Mathematical modelling can interrogate and elucidate the complex, non-intuitive signalling networks that exist in our neurons, providing insight that would not be possible with traditional 'wet-lab' methods alone. Together, these complementary approaches will help us to better understand the molecular mechanisms underlying Parksinon's, and pave the way for the design of new and improved therapies.

Why is PD-MitoQUANT an exciting project for RCSI?

The PD-MitoQUANT project is exciting for us in RCSI, and in the SFI-funded FutureNeuro research centre, as it enables us to apply our strong expertise in systems biology, bioenergetics and fluorescence microscopy to a vitally important area, namely a neurodegenerative disease that affects >1 million people in Europe, Parkinson's. PD-MitoQUANT also offers us the opportunity to collaborate with several experts across Europe, and I personally am enjoying it immensely and have already learned a huge amount!

Interested in learning learn more about Dr. Connolly's research? Check out this video from the Centre for Systems Medicine at RCSI: https://youtu.be/gRXMMlt4drc.

PD-MitoQUANT Partners

RCSI Leading the world to better health · ICM Brain & Spine Institute · DZNE German Center for Neurodegenerative Diseases within the Helmholtz Association · Consiglio Nazionale delle Ricerche · UCL · Radboudumc university medical center · cnrs · MIMETAS the organ-on-a-chip company · genexplain · Pintail · teva · Lundbeck · ucb · PARKINSON'S UK CHANGE ATTITUDES. FIND A CURE. JOIN US.

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