CSC-RUB PhD Project Proposal

Title: The role of mitochondria at neuro-immune interfaces

Sector of research: Molecular and Cellular Neuroscience

Degree awarded: PhD in Neuroscience

Keywords: mitochondria, innate and adaptive immunity, neurodegeneration, neuroinflammation, microbiome, gut-brain axis, bioenergetics, cellular signaling, super-resolution microscopy

Supervisor of PhD project:

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Research focus of supervisor:

The major aim of our research is to uncover molecular mechanisms underlying neurodegenerative diseases, which is a prerequisite to develop causative therapeutic strategies for these disorders. Specifically, we are studying the role of the proteostasis network in preventing protein aggregation and in promoting degradation of misfolded proteins linked to neurodegeneration. Another focus of our work are mitochondria as key organelles in orchestrating cellular signaling, interorganellar communication, and in regulating viability and bioenergetics. There is increasing evidence that mitochondria play an important role not only in neurodegenerative but also in neuroinflammatory diseases, such as Multiple Sclerosis. We therefore are studying which mitochondrial pathways are implicated in neuroprotective and anti-inflammatory signaling.

We have a longstanding expertise in cell biology, molecular biology, protein biochemistry, and advanced cellular imaging, including super-resolution microscopy and live cell imaging.

Publications:


**Summary of research plan**

**Background:**
Mitochondria are essential organelles for the maintenance of neuronal integrity, based on their manifold functions in regulating cellular metabolism and coordinating cell death and viability pathways. Accordingly, mitochondrial damage, dysfunction, or ineffective mitochondrial quality control is associated with neurological disorders and can occur as a cause or consequence of pathological processes. Moreover, mitochondria play a central role in orchestrating both innate and adaptive immune responses, thereby providing a link between neurodegenerative and neuroinflammatory processes. We recently found that specific metabolites from gut microbiota decrease disease progression and neurodegeneration in Multiple Sclerosis by restoring mitochondrial function in regulatory T cells (Ducha et al., Cell, 2020).

**Study objective:**
The aims of the project are
- to study which mitochondrial aspects are affected by gut microbe metabolites in neurons and immune cells and which signal transduction pathways are mediating these effects
- to get insight into mechanisms of how mitochondria influence neuroinflammation and neurodegeneration.

**Expected Results:**
By identifying the molecular targets of protective metabolites from gut microbes and the pathways mediating their effects we expect insights into mechanisms implicated in both neuroinflammatory and neurodegenerative diseases. These targets may be exploited for therapeutic strategies to suppress neuroinflammation and to halt neurodegenerative processes.
At least one research article and one review article should be published based on this project.

**Methods:**
Advanced cellular imaging (super-resolution microscopy, live cell imaging), state-of-the-art techniques in cell biology, biochemistry, molecular biology, such as CRISPR/Cas genome editing, mitochondrial bioenergetics, ELISA, cellular signaling assays, immunoprecipitation, immunoblotting, immunocytochemistry, immunohistochemistry, reporter gene assays, mass spectrometry.

**Candidate Requirements:**
We are seeking a highly motivated, enthusiastic candidate with good communication skills, fluency in English and the ability for teamwork.

**Motivation for CSC application** (max 250 words):
We offer a stimulating international research environment with numerous national and international collaborations, integration in research centers (RESOLV Cluster of Excellence, DFG Research Unit 2848, Parkin Consortium of the Michael J. Fox Foundation, International Max Planck Research School for Living Matter), and admission to the Ruhr University Research School for interdisciplinary skills development and mentoring. Laboratory work is supplemented by seminars, summer schools, elective workshops, career development training and participation in national and international conferences.