



Joint MD/PhD Fellowships Groningen-Oldenburg Outline PhD Project

Working title of project	Importance of mitochondria in neuronal and retinal diseases
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Short Summary of PhD project (mx. 500 words), incl. research question(s), methods, approx. schedule (incl. times in Groningen/Oldenburg)

Significance of Mitochondria: Mitochondria, often referred to as the cell's powerhouses, generate ATP, which serves as the primary energy source for cellular processes. Primarily, energy-demanding cells and organs are affected by mitochondrial impairments and an increasing number of neuronal diseases, including retinal degeneration, have been associated with defective mitochondria. The retina, a part of the central nervous system (CNS), is highly organized and shares many similarities with the brain and spinal cord.

Retinal Diseases: The visual system is crucial as it provides the majority of environmental information to the human brain. Consequently, visual impairments can significantly impact patients' quality of life. Our research has identified mitochondrial defects in retinal degenerative diseases. To validate our findings, we have generated patient-derived cell lines and used CRISPR technology for genome editing to induce targeted mutations in isogenic cell lines.

Research Plan: In this MD-PhD project, we aim to investigate the pathogenic mitochondrial processes that lead to neuronal and/or retinal degeneration. We will conduct mitochondrial measurements at functional and morphological levels to determine factors such as oxygen consumption (OCR), reactive oxygen species (ROS), and mitochondrial network formation in patient-derived and CRISPR-edited cell lines.



1. We will initiate the training of the MD-PhD candidate on mitochondrial measurement, high-resolution imaging, and cell culture technologies (approx. 6 months, UMCG).
2. We will proceed to analyze the patient-derived and mutated cell lines and characterize the mitochondrial defects in detail (approx. 6 months, UMCG).
3. We will utilize high-throughput RNA sequencing technologies to characterize the molecular-level consequences of the mitochondrial defect (6 months, UMO).
4. We plan to further apply CRISPR technology to induce new defects in candidate genes to better understand the implications of the detected mitochondrial defects. Additionally, we will test therapeutic approaches aiming to ameliorate the mitochondrial defects (approximately approx. 2 years, UMO).

Training and Development: The MD-PhD candidate will gain a deep understanding of the role of mitochondria in human health and disease, with a focus on retinal degeneration. The project will equip the MD-PhD candidate with training on mitochondrial measurements, cell culture, microscopic analysis, and genome-editing technologies, offering an excellent opportunity to develop a research profile within medical sciences. The MD-PhD candidate will follow the local PhD training options (e.g. GSMS, BCN trajectory, courses to further develop soft skills).

PhD Candidate Profile/desired qualifications

The ideal MD-PhD candidate should be highly motivated to contribute to research and scientific progress, aim to enhance understanding of retinal diseases and their therapeutic approaches, and possess experience in studying genetic diseases and relevant laboratory technologies (e.g., cell culture, molecular biology).