Joint MD/PhD Fellowships Groningen-Oldenburg

Outline PhD Project

Working title of project	**Exploring Therapeutic Approaches using Patient-Derived Induced Stem Cells and Organoids**
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Short Summary of PhD project

Significance of Stem Cell Research: Stem cell-derived organoids serve as potent tools for studying diseases within a culture situation that closely mimics in vivo conditions. These organoids represent cutting-edge technology for investigating pathogenic processes and testing potential therapeutics.

Retinal diseases: We have previously established primary cell lines from patients suffering from Retinitis pigmentosa, a blinding disease caused by genetic alterations. As the visual system provides the majority of environmental information to the human brain, visual impairments significantly impact the patients' quality of life.

Research Plan: We have successfully generated pluripotent stem cells from patients, which can be differentiated into various cell types, including neurons and retinal organoids. In this MD-PhD project, we aim to study the pathogenic processes leading to neuronal and/or retinal degeneration using these stem cell-derived retinal organoids.

(i) We will initiate the training of the MD-PhD candidate with the generation of stem cells from patient-derived primary fibroblasts (3 months, UMCG). Genome editing using the CRISPR-technology may also be applied with the aim to engineer isogenic cell lines and/or reporter cell lines. (3-9 months, UMCG).

(ii) We will proceed to differentiate and characterize the induced stem cells towards a neuronal cell fate to determinate differentiation potential of the primary iPSCs and their CRISPR-engineered counterparts.

(iii) We will develop the differentiation towards retinal organoids and utilize these organoids to study pathogenic processes and test therapeutic approaches (2 to 2.5 years, UMO).

Training and Development: Organoid technologies hold promising future perspectives as vehicles for drug testing and, in the near future as for regenerative therapies in the human context. This project will thus provide the MD-PhD candidate with a broad foundation to develop a research profile within medical sciences.

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).