

Project Title: 3D U-Net Analysis of Myelinating Oligodendrocytes in Human Brain Organoids: Exploring Myelin Disorders and Therapeutic Pathways

Marie-Kristin Schreiber, Dr.rer.nat., Institute of Pharmacology and Toxicology, University Medical Center Göttingen

Myelin disorders, including Pelizaeus-Merzbacher Disease (PMD), are characterized by disruptions in oligodendrocyte function and impaired myelination. Yet, the development of effective therapies remains constrained by the absence of human-specific models. Human brain organoids, specifically bioengineered neuronal organoids (BENOs), provide a promising platform to study these disorders in a biologically relevant context. However, current imaging methods are limited, typically capturing partial organoid slices and failing to represent the complete 3D cellular architecture. This proposal addresses this gap by developing the 3D Oligodendrocyte Morphometrics (3DOM) image analysis tool for whole-organoid microscopy stacks of BENOs, providing unprecedented insights into human-derived oligodendrocyte morphology and myelination within a complete 3D context. Preliminary work with a 2D version of 3DOM has demonstrated its effectiveness in revealing distinct phenotypic variations in PMD patient-derived organoids. Building on this foundation, the proposed 3D model leverages a 3D U-Net architecture to preserve the full spatial organization of oligodendrocytes while incorporating a neuronal channel to quantify myelination. This 3D approach enables a more detailed analysis of branching patterns and cellular interactions, which is essential for understanding the complexities of myelin disorders. Support from this fellowship will enable me to build critical expertise in bioimage analysis, foster interdisciplinary collaboration, and establish 3DOM as a valuable open-source tool for the research community. This project aims to advance research in human-specific myelin disorders and generate foundational insights that could guide the development of future therapeutic strategies.