Portrait et Abstract de Yi Ling

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Yiling Tsang started her PhD in 2021 at the University of Münster, working in Lydia Sorokin's lab on a project titled "Modeling the Cellular and Basement Membrane Constituents of the Blood-Brain Barrier." Her research focuses on the blood-brain barrier (BBB) and the roles of its cellular and basement membrane components. She is developing a 3D BBB model using a dextran-hydrogel system. In this model, induced pluripotent stem cell (iPSC)-derived brain endothelial cells (iBECs) are combined with astrocytes and perivascular cells within the dextran gel, enabling the study of the basement membrane's role in leukocyte transmigration.

Modelling the Cellular and Basement Membrane Constituents of the Blood-Brain Barrier

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Basement membranes (BMs) are integral components of the vascular wall that contribute to the structural/functional specialization of blood vessels including the limited permeability of brain blood vessels to soluble molecules and cells, known as the blood-brain barrier (BBB). In addition to the endothelial monolayer and its underlying BM, brain blood vessels are ensheathed in an astrocyte endfeet layer and associated parenchymal BM, so-called as it marks the border to the CNS parenchyma. The endothelial layer and its BM are similar in several tissues, hence, considerable information is available on this barrier; however, little is known about the parenchymal barrier. This is because it is specific to the BBB and cannot be easily reconstructed in vitro. Data also suggest that the parenchymal barrier impacts on the endothelial barrier and vice versa. To understand the BBB and the role of its cellular and BM constituents, we are generating a 3D BBB model using a dextranhydrogel that allows independent control of gel stiffness and adhesiveness. Induced pluripotent stem cells (iPSCs) are differentiated to brain-like endothelial cells (iBECs), which are combined with astrocytes and perivascular cells in the dextran gels. We demonstrate that the extracellular matrix (ECM) affects iPSC differentiation to iBECs in 2D and 3D cultures and expression levels of the junctional molecules claudin-5 and occludin. Culturing of iBECs in dextran-hydrogels results in polarized deposition of endothelial-specific BM components and attachment of astrocyte endfeet. Our studies reveal stiffness and adhesiveness of the dextran gels to be critical factors in iPSC differentiation to iBECs