The role of TLR7/8 signaling in the pathogenesis of neuromyelitis optica

Neuromyelitis optica (NMO) is a neuroinflammatory autoimmune disorder associated with extensive inflammation of optic nerves and spinal cord. In NMO, pathogenic autoantibodies against the water channel aquaporin-4 (AQP4) expressed on the surface of astrocytic endfeet mediate the destruction of astrocytes, leading to secondary demyelination and neuronal damage.

In an immunological mechanism called antibody-dependent cellular phagocytosis (ADCP), macrophages phagocytize and digest cells tagged by autoantibodies, eventually triggering further inflammation by antigen presentation to cytotoxic immune cells. This process is regulated by intracellular pattern recognition receptors toll-like receptor 7 and 8 (TLR7 and TLR8).

The aim of this project is to evaluate the significance of TLR7 and TLR8 signaling for macrophage-mediated pathomechanisms in NMO. For this, an established in vitro-model for phagocytosis in NMO will be used: Human embryonic kidney (HEK) cells expressing a green fluorescent AQP4 protein will be co-cultured with human macrophage-like cells from healthy donors in the presence of NMO patient serum. After treatment with TLR7/8 agonists or antagonists, phagocytic activity and expression of activation markers in macrophage-like cells will be investigated using flow cytometry. Furthermore, the production of pro-inflammatory cytokines will be analyzed by ELISA measurements in cell culture supernatants.