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Poster P11

Unraveling the macrophage – Schwann cell crosstalk in Charcot-Marie-Tooth disease type 1A

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Charcot-Marie-Tooth disease type 1A (CMT1A), the most common inherited peripheral neuropathy, is caused by a duplication of the PMP22 gene in myelinating Schwann cells. Growing evidence points to a significant involvement of the immune system in CMT1A pathogenesis, with macrophages increasingly being implicated in driving disease progression. Despite these associations, the functional role of macrophages and the specific mechanisms by which they interact with Schwann cells to influence disease progression remain poorly understood.

Here, we aimed to investigate macrophage biology and the complex crosstalk between Schwann cells and macrophages to better understand the underlying disease mechanisms of CMT1A. We stimulated macrophages derived from peripheral blood mononuclear cells with human myelin extracts to induce myelin uptake and activate their lipid metabolism. Compared to healthy controls, macrophages of a CMT1A patient showed a significant increase in lipid droplets, suggesting altered lipid handling. In parallel, we have been developing a 2D co-culture system to explore direct and indirect interactions between Schwann cells and macrophages in CMT1A. Co-cultures of Schwann cells and blood-derived macrophages from CMT1A patients and healthy controls were maintained for 24 to 72 hours to investigate intracellular communication. Various media compositions were tested, and a 50% mix of Schwann cell and macrophage media supported their viability and typical cell morphology. Moreover, a close interaction was observed between both cell types and myelin-related gene expression was upregulated in Schwann cells, suggesting an impact on differentiation and maturation.

In summary, our co-culture system offers a powerful platform to unravel the molecular mechanisms driving Schwann cell–macrophage interactions in CMT1A. These findings, coupled with a deeper understanding into macrophage biology, may uncover novel therapeutic strategies targeting immune responses in CMT1A.