Development of a 2D Co-Culture System to Uncover Schwann Cell-Macrophage Interactions in CMT1A

Van Brussel M (1), Bekaert B (1), in't Groen S (1), Kleinewietfeld M (2), Van Den Bosch L (3), Wolfs E (2), Vangansewinkel T (1), Timmerman V (1)

(1) University of Antwerp, Antwerp, Belgium.
(2) UHasselt, Hasselt, Belgium.
(3) VIB/KU Leuven, LEUVEN, Belgium

Charcot-Marie-Tooth (CMT) disease is the most common inherited peripheral neuropathy, with the majority of cases being caused by a duplication of the peripheral myelin protein 22 (PMP22) gene. PMP22 is an integral membrane glycoprotein of compact myelin, which is strongly expressed by Schwann cells (SCs). Increasing evidence indicates a critical role of the immune system in the disease pathology, and especially macrophages have been linked to CMT1A disease progression. However, the specific mechanisms by which macrophages interact with Schwann cells and influence the disease remain unknown. Therefore, we aim to investigate the intricate interplay between Schwann cells and macrophages to elucidate the underlying disease mechanisms of CMT1A. Currently, we are optimizing a 2D co-culture system to explore direct and indirect interactions between Schwann cells and macrophages in CMT1A. To clarify cell-cell interactions, Schwann cells and blood-derived macrophages from CMT1A patients or healthy controls are co-cultured for 72 hours. In addition to the co-culture experiments, macrophages are also stimulated with conditioned culture medium of healthy and CMT1A Schwann cells to study indirect signaling effects. Our focus will be to identify potential key targets and mechanisms involved in Schwann cell and macrophage interaction and communication. In summary, the establishment of a 2D co-culture system will provide a powerful platform to unravel the molecular mechanisms driving Schwann cell / macrophage interactions in CMT1A. Insights gained from this study will advance our understanding of neuro-immune crosstalk in peripheral neuropathies and may uncover novel therapeutic strategies targeting immune responses in CMT1A.