The Function of APOE During Remyelination

Multiple Sclerosis (MS) is characterized by lesions of the Central Nervous System (CNS). These lesions are characterized by an inflammatory response, marked by an increase in macrophages and microglia to help clear the accumulating lipids in myelin debris. Apolipoprotein E (APOE) aids in mediating lipoprotein metabolism. There are three isoforms of APOE present in the human population (APOE2, APOE3, and APOE4) and, due to structural variations, these isoforms have differences in binding to lipids and cell receptors. Therefore, we speculate that these isoforms contribute to the pathogenesis of MS and regulate remyelination differently. Our LFB-PAS staining shows significantly impaired remyelination in APOE3 and APOE4 mice. Further, APOE3 macrophages ingested significantly fewer apoptotic cells in comparison to their WT counterparts. These findings suggest that the presence of APOE3 plays an inhibitory role in remyelination. Finally, from secretome analysis, we found upregulated candidates in APOE3 post-phagocytosis macrophages that promote neural conduction and clearance of myelin debris, suggesting a compensatory mechanism for remyelination in the presence of APOE3.