Schwann Cells Promote Peripheral Neuropathy Through Upregulation of the Extracellular Matrix Protein Periostin

Chronic inflammatory demyelinating polyneuropathy (CIDP) is a debilitating autoimmune disease in humans characterized by sensorimotor impairment, demyelination, and inflammation via macrophage infiltration into the peripheral nervous system (PNS). The dysfunction of Schwann cells, as a major component of the PNS, is thought to contribute heavily to the observed motor impairment in CIDP. Here we investigate the role of Schwann cells in the development of CIDP. Since extracellular matrix (ECM) proteins are known to play a role in the inflammatory response, we examined the differences in ECM protein expression in the sciatic nerves of wild-type (WT) mice and mice with spontaneous autoimmune peripheral polyneuropathy (SAPP), a mouse model for human CIDP. We found that the ECM protein periostin (Postn) is upregulated by Schwann cells in SAPP mice. Immunofluorescence showed that Postn infiltrates the endoneurium, the connective tissue encapsulating Schwann cells, in SAPP mice whereas it is only expressed on the periphery of the endoneurium in WT mice. We also found that Postn elicits the migration of macrophages into the PNS, suggesting that Postn upregulation indirectly causes inflammation and nerve damage via macrophages. Additionally, we identified a novel population of cells in the PNS of SAPP mice that express the marker CD49b along with classical markers for Schwann cells. qPCR and immunofluorescent staining show that these CD49b+ cells are a form of dedifferentiated Schwann cells, exhibiting lack of myelination, which is a possible explanation for the motor impairment seen in CIDP patients. Understanding the mechanisms behind the upregulation of Postn and CD49b+ cells and inhibiting their upregulation and/or signaling could lead to treatments that suppress inflammation and neurodegeneration for CIDP patients.