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The Impact of PMP22 Over-expression on Peripheral Nervous System (PNS) Myelination in vitro

Charcot-Marie-Tooth disease is the most common inherited neuropathy and a duplication of the peripheral myelin protein 22 gene (PMP22) causes the most frequent subform Charcot-Marie-Tooth 1A (CMT1A). It is a slowly progressive dysmyelinating and demyelinating peripheral neuropathy and leads to distal muscle atrophy. Previous studies had reported that Pmp22-transgenic rats showed a peripheral hypomyelination, Schwann cell hypertrophy (onion blub formation), and muscle weakness. Moreover, reduced nerve conduction velocities closely resemble recordings in human patients with CMT1A. To establish a reliable in vitro system for novel therapeutic treatment evaluation, we co-cultured E13.5 dorsal root ganglion (DRG) neuron and Schwann cells overexpressing PMP22. We noticed a remarkable, but yet not significant, reduction in the number of myelinated segments in transgenic co-cultures compared to the wild type controls. Interestingly, by we observed a striking reduction of the intermodal length in the Pmp22-transgenic cultures. As both observed phenotypes are recapitulating the in vivo situation, we suggest that this co-culture system may provide a model system for testing treatment options for the still incurable CMT1A disease.