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Poster P13

Schmidt-Lanterman Incisure number supports Schwann cell function in Charcot-Marie-Tooth disease 1A (CMT1A)

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Schmidt-Lanterman Incisures (SLIs) are funnel-shaped cytoplasmic channels in the compact myelin internode of peripheral nerves. Although first described over 150 years ago, their functional role remains largely unknown. In demyelinating diseases such as Charcot-Marie-Tooth disease (CMT1A), caused by duplication of the PMP22 gene, increased numbers of SLIs are observed in both human patients and mouse models. A Schwann cell specific knockout of Vcl, which encodes the actin-binding protein vinculin, results in a reduced number of SLIs, while radial myelination, motor behavior or electrophysiological measurements are unaltered. Thus, vinculin conditional knockout mice (VclcKO) provide a useful model to study the relevance and function of SLI in physiological and pathological conditions. While a reduced number of SLIs has no effect on the phenotype of healthy Schwann cells, deletion of vinculin in the context of PMP22 overexpression deteriorates the CMT1A disease pathology, indicating a critical role for SLIs under demyelinating conditions.

Following peripheral nerve crush injury an increase in the number of SLIs can be observed. However, VclcKO mice fail to upregulate SLI formation following injury and show a delayed regeneration. Based on these findings we hypothesize that increased SLI numbers are beneficial during chronic and acute nerve injury.