

Pathophysiology of demyelinating neuropathies

The peripheral nervous system is a prime example of a tissue with a strong regenerative potential, however, full functional recovery is rare. Indeed, the clinical outcome of acute nerve injuries and chronic peripheral neuropathies usually remains poor and constitutes a significant clinical and economic burden.

Nerve repair is mainly mediated by Schwann cells, which orchestrate nerve de- and regeneration after acute nerve injury. This process is associated with a complex glial molecular reprogramming and includes, among others, auto- and paracrine growth factor stimulation. Moreover, we recently found a dynamic glial metabolic adaptation and an activation of mitochondrial respiration to be required for efficient peripheral nerve repair.

Notably, the acquisition of a glial repair phenotype is not restricted to traumatic nerve injuries, but we identified Schwann cells in glial-mediated peripheral neuropathies to undergo changes that resemble the cellular response observed after acute injury. However, the repair-like phenotype of neuropathic Schwann cells can exert either protective or detrimental effects on nerve integrity and function, depending on the disease characteristics of the respective type of neuropathy. We therefore suggest that untangling the multifaceted functions and dynamics of the Schwann cell repair response in peripheral neuropathies may provide novel therapeutic targets for these largely untreatable diseases.