Investigation of Directed Neurite Outgrowth Mediated by Schwann cell Extracellular Matrix and Adhesion Molecules

by

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ABSTRACT

The regenerative capacity of the Peripheral Nervous System (PNS) can be in part attributed to the ability of peripheral glia (Schwann cells) to assist in the clearance of myelin debris from the injury site, provide neurotrophic support, create an extracellular matrix, and express surface molecules which are axonally regulated. After a crushed nerve injury, tubes of basal lamina remain intact and serve as a conduit to support migrating Schwann cells (SCs) which in turn serve as a foundation to guide regenerating neurons through the injury site. In nerve transections, reinnervation is more challenging because the basal lamina tubes are no longer intact. While synthetic guidance channels have been engineered to bridge nerve gaps and support regeneration, the optimal conduit has yet to be developed. Schwann cells have been identified as a key component for enhanced axonal elongation into guidance channels; however, the mechanisms by which SCs direct neurite outgrowth are still unclear. This doctoral thesis presents the methods for an *in vitro* SC-neuron co-culture system and development of supporting image analysis techniques that will allow the investigation of directed neurite outgrowth and de-coupling of potential mechanisms responsible for directing outgrowth. Specifically, we will address the role of SC-derived extracellular matrix and related substrate adhesion (e.g. integrins) and cellular adhesion (e.g. L1 and NCAM) molecules in SC mediated guidance of neurite outgrowth. The knowledge gained from these studies can be directly applied to the design of more functional nerve guidance channels for peripheral nerve repair applications.