TERMIS poster presentation

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Investigating the use of engineered neural tissue to generate peripheral nerve repair constructs populated with neurons.

Following peripheral nerve injury, the motor axons in the distal nerve between the injury site and the muscle degenerate. Recovery of function following proximal injuries is a clinical challenge since neuronal regeneration rate is limited, resulting in muscle atrophy due to the delay, even where the 'gold standard' autograft is used. Much research focuses on improving repair conduits that mimic the autograft and promote host neurite regeneration, whereas here we propose to improve long gap repair by populating constructs with neurons. With a ready-to-implant construct populated with glial cells supporting neurons with elongated neurites, the gap between proximal stump and muscle could potentially be reconnected promptly. Immediate innervation of the muscle would help reduce atrophy as regeneration progresses. The overall aim here therefore is to prepare a construct containing neurons with elongated neurites with a view to rapid bridging of a nerve injury site and restoration of innervation to muscle. The objective of this initial study was to investigate the potential for using Engineered Neural Tissue (EngNT) as the basis for establishing robust constructs containing functional neurons with elongated aligned neurites.

EngNT is formed from simultaneous self-alignment of Schwann cells and collagen fibrils in a tethered gel, followed by stabilisation with plastic compression resulting in an anisotropic tissue-like structure. Various types of neurons including NG108-15 cell line and primary rat motor neurons, were maintained in co-culture with EngNT at different densities for 1, 4 and 7 days. Neurite growth was assessed by immunostaining for ßIII-tubulin followed by fluorescence microscopy and image analysis. The results showed that NG108-15 neurites aligned parallel to Schwann cells, with 85% of neurites exhibiting less than 30 degree deviation from the alignment axis. Neurite length increased with time in culture to 210.38 ± 80.97 μm after 7 days. Neurite growth from neurons in EngNT was longer than neurite growth in control cultures without Schwann cells. Moreover, the neurite length of NG108-15 cells in EngNT was considerably greater than reported previously using other culture conditions. These results indicate that EngNT may be an appropriate substrate for generating long neurites in vitro with a view to generating therapeutic constructs containing long functional neurons.