Question/Biological Problem

Peripheral nerve injury (PNI) is very prevalent affecting more than 1 million people a year worldwide [1]. Although peripheral nerves have an intrinsic ability to heal and regenerate, the process is complex and is only successful in ideal conditions. The gold standard for clinical treatment of PNI is the use of autografting. However, autografting is limited to gaps of 5cm or less. Autografting is also limited by shortage of donor source, donor site morbidity and loss of function, as well as increased operating time [1]. An alternative treatment for PNI is the use of nerve conduits to guide and promote axonal growth. In addition, a conduit will provide mechanical stability during healing and a barrier between the healing nerve and the surrounding inflammation [1].

AIM: To build a model to investigate a novel bioactive BDNF seeded resorbable nerve guide conduit for nerve regeneration
To build a model to investigate nerve regeneration promoted by BDNF or BDNF + VEGF seeding of a nerve guide conduit.

Research Model and Plan

- A rat sciatic nerve injury model will be used for this study.
- A scaffold made with poly (lactide-co-glycolide), PLGA, will be under investigation for this study. PLGA is biocompatible, biodegradable, and has good mechanical strength [2]; by using different manufacturing techniques or combining with other materials can change the properties of the material, it. PLGA scaffolds have also been reported to support better cell migration and wound healing [3]. In this study, a hybrid PLGA structure as outlined by Peng et. al will be used for its demonstrated increased migration rate of cells and growth in the desired direction [4].
- In this study, the focus will be to evaluate the performance of a conduit that is seeded with factors that promote axonal growth and regeneration; BDNF and a combination of BDNF and VEGF will be investigated. Using neurotrophic factors such as BDNF has shown an increased myelination and size of regenerated tissue as well as BDNF secretion [5]. On the other hand, plasmid DNA delivery of a combined VEGF and NGF shows significant increase in myelin sheath and higher density of microvessels formation.
- A rat sciatic nerve injury model will be utilized for this study. Rats will be divided into three groups; (1) Non-seeded conduit, (2) BDNF seeded conduit, (3) BDNF + VEGF seeded conduit. The rats in each group will be sub-divided with different nerve injury lengths; 3, 5, and 7cm.
- Rats will be followed for 8 weeks following conduit transplantation. Enzyme-linked immunosorbent assay (ELISA) method will be used to measure BDNF secretions. Histological analysis using TEM scanning and H&E staining will be conducted to determine myelinated axons and cross-sectional area of regenerated nerves. Angiogenesis will be assessed using DAPI double-immunofluorescence assay. To determine proper return of function following nerve regeneration, functional gait analysis will be performed at prior to surgery as well as at 2,4,6, and 8 weeks following transplantation. Finally, statistical methods will be utilized to analyze differences between groups and within subgroups (injury gap) of the same group.

References:

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