Development of a Stably Aligned, Schwann Cell Seeded Composite Biomaterial that Supports Neurite Outgrowth for Neural Tissue Engineering Applications

by

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ABSTRACT

Spinal cord injury (SCI) is a devastating condition due to trauma, sports-related injuries and disease resulting in varying degrees of paralysis, reducing a patient's quality of life and lowering life expectancy. Despite the capacity for regeneration, there is no functional treatment for SCI due to the hostile microenvironment of the spinal cord following injury. A host of variables inhibit nerve regeneration such as glial scarring, cell death, removal of myelin, lack of a permissive substrate and an inadequate level of growth factors. Due to the complexity, there is likely not one single therapeutic intervention that will solely control regeneration. Rather, the synergistic combination of various guidance cues (e.g. soluble factors, substrate composition, cellular, chemical, electrical, mechanical, or topographical) will be necessary to promote nerve regeneration and develop a clinically effective therapy for SCI.

Investigation of various guidance cues in a 3D model is necessary to carefully investigate neuronal and glia response prior to *in vivo* experimentation. The goal of this thesis is to present the development and characterization of a novel, stably aligned composite biomaterial to serve as a platform to investigate guidance cues on neurite outgrowth. One aim of this work was to develop a biomaterial concurrently supportive of both Schwann cells (SC) and neurons. This was accomplished by combining collagen I and Matrigel™ at a 65/35 volume/volume ratio. SC viability was consistently high and cells were able to spread in this composite biomaterial. Also, this composite biomaterial is supportive of both neurite outgrowth and Schwann cell migration. A second aim was to stably align the cellular and matrix components of these scaffolding materials. Alignment is useful in directing neurite outgrowth and was accomplished through the use of fibroblast (FB) mediated compaction. Following the removal of constraint, stable alignment of SC, FB, and collagen I was observed for at least 7 days in culture. Finally, neurite outgrowth within these constructs was examined and aligned matrices have the ability to direct this outgrowth in 3D space.

Future studies will involve combining guidance cues such as soluble factors or electrical stimulation with these aligned and unaligned SC loaded collagen I-Matrigel™ biomaterials. Relative strengths of each cue, as well as synergistic effects, may be examined to aid in the development of a therapeutically viable SCI implant.