AB020. 3D scaffolds for optic nerve regeneration

Joel Edin, Nicole Scalet, May Griffith

Department of Ophthalmology, Maisonneuve-Rosemont Hospital Research Centre, University of Montreal, Montreal, Quebec, Canada

Background: Regeneration of nerves or nerve bundles is problematic mainly due to issues of nerves finding their target tissues. A very clear example of this is the lack of treatments for traumatic injury to the optic nerve, something that is associated with surgery or trauma to the skull. Nerve guides have been used to support this for the better part of the last century, unfortunately the clinical improvements in patients receiving this sort of treatment is poor. Large improvements to the type of nerve guides used are needed to make this a viable solution for repair. It has been shown that electrostimulation of cells on conductive polymers can have positive effects on nerve regeneration. There are several material innovations that improve on speed of nerve regeneration; conductive polymer coatings being one example. There are constant improvements on solutions for nerve regeneration in many fields, unfortunately combining these different solutions is often slow. We combine electrospinning, 3D printing and surface modification. Electrospinning allows control over fibrous structures. We tune the surface properties using conductive polymer coatings. The conductive fibrous structure can be integrated in a larger 3D printed scaffold that takes the role of guiding the nerve bundle.

Methods: For manufacture of aligned fibers, PCL in chloroform was electrospun on a rotating mandrel. Random fibers were collected on a flat stationary collector. Dip coating was performed by submerging the fibrous scaffold in a solution of PEDOT:PSS in water and isopropanol. An outer layer of PEDOT:tosylate was added using vapor phase polymerization (VPP). 3D printing was performed using an ink consisting of 0.25% alginate and 8.75% gelatin. The ink was cross-linked after printing using 0.4% $CaCl_2$. Cell cultures were performed using chick dorsal root ganglia and a mouse neuroblastoma cell line. Ganglia and cells were seeded on the fibrous scaffolds. Electrostimulation was performed using a custom set up at constant DC current and slow pulsed DC current (1 min on off cycle) Materials were imaged using scanning electron microscopy. Cell cultures were stained using ICC and imaged with fluorescence microscopy.

Results: All of the materials supported cell growth and neurite extension to some degree. The materials that were coated with PEDOT:tosylate and a combination of PEDOT:tosylate + PEDOT:PSS outperformed the PSS only group. Stimulation with a slow pulsed or constant DC current increased neurite extension on the negative pole, while there was inhibition of neurite growth on the opposite pole. The 3D printed outer layer serves as a biocompatible, bioactive support and guide for the bundle of neurites.

Conclusions: The nerve guides can guide nerve growth. The 3D printed scaffold is cell friendly. The construct allows electrostimulation to increase speed of regeneration.

Keywords: 3D printing; nerve regeneration; electrospinning

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