Directing and promoting neuronal outgrowth and non-neuronal cell migration using phosphate glass fibres embedded in engineered neural tissue for peripheral nerve regeneration

Kulraj S Bhangra[1,4], Jonathan C Knowles[1], Rebecca J Shipley[2], David Choi[3] and James B Phillips[1,4]

[1]*Biomaterials & Tissue Engineering, UCL Eastman Dental Institute,* [2]*Mechanical Engineering, UCL Engineering,* [3]*Brain repair and Rehabilitation, UCL Institute of Neurology* [4]*Pharmacology, UCL School of Pharmacy*

Advances in biomaterials and tissue engineering have led to the development of Engineered Neural Tissue (EngNT) for peripheral nerve repair [1]. Experiments using EngNT with embedded Schwann cells to repair rat sciatic nerve injuries indicated sub-optimal growth of neurites from the proximal nerve stump into the EngNT [1, 2]. Phosphate glass fibres (PGfs) have been used in hard- and soft-tissue engineering applications [3, 4]. They are biocompatible and biodegradable and have emerged as a potential material to resolve soft-tissue engineering interface issues [5]. The aim of this study was to investigate whether PGfs could improve the interface between the proximal stump of a damaged nerve and EngNT in supporting neurite outgrowth.

Hemisected dorsal root ganglia (DRG) were placed in direct contact with EngNT incorporated with and without PGfs. DRGs attached to constructs were placed vertically into 1.5ml tubes and maintained in a tissue culture incubator (37°C/5% CO_2) for 72h. Following immunostaining, axonal growth and non-neuronal cell migration into the construct was imaged using an inverted fluorescent microscope. Image analysis was performed using ImageJ.

This study demonstrates that PGfs can be successfully incorporated into EngNT to encourage non-neuronal cell migration and neurite elongation in culture. Incorporating PGfs within EngNT permits non-neuronal cells to travel approximately twice the distance into EngNT. Furthermore, neurites are able to elongate approximately one and a half times the distance into EngNT that was modified with PGfs. Future work involves testing 'EngNT + PGf' constructs *in vivo* to investigate whether ingrowth of neurites from the proximal nerve stump is improved.

References

[1] Georgiou, M., et al., Biomaterials, 2013. 34(30): p. 7335-43.
[2] Georgiou, M., et al., Biomaterials, 2015. 37: p. 242-51.
[3] Bitar, M., et al. J Biomed Mater Res A, 2008. 87(4): p. 1017-26.
[4] Shah, R., et al. Biomaterials, 2005. 26(13): p. 1497-505.
[5] Ahmed, I., et al. Biomaterials, 2004. 25(16): p. 3223-32.