ABSTRACT

A 3D in vitro co-culture to model peripheral nerve remyelination after injury

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Peripheral nerve injury is common, results in significant disability for patients and imposes a heavy financial burden on healthcare services. Recent research identifying novel strategies to improve nerve regeneration is hindered by the lack of a standardised model. This work sought to develop a versatile in vitro construct to model remyelination after nerve injury.

Novel macroporous poly(ε-lysine) scaffolds with additional chemical groups were characterised in a 3D Schwann cell culture model. Immunohistochemistry, proliferation assays, LIVE/DEAD staining and scanning electron microscopy (SEM) modalities were utilised in order to select the most promising scaffold. A scaffold functionalised with IKVAV peptide was then used as a basis for co-culture experiments utilising rat Schwann cells or adipose-derived stem cells (ASCs) and neurons. Myelin formation was identified on SEM and gene expression quantified using included real-time PCR.

We demonstrated that cultured Schwann cells and neurons maintain their phenotype and morphology in this novel 3D scaffold. Compared to amine scaffold variants, the IKVAV scaffold encouraged 2 times more cell viability ($p < 0.05$ and 0.01) and 2.6 times higher proliferation ($p < 0.05$). Schwann cells and differentiated ASCs were seen to arrange linearly along neurites. Gene expression of myelin basic protein, peripheral myelin protein and protein zero were all upregulated in Schwann cell groups. Differentiated ASCs produced more myelin-based gene expression than undifferentiated ASCs.

This study demonstrates that IKVAV poly(epsilon-lysine) is a promising construct to model remyelination.

Furthermore, this high-throughput tool could be utilised for the study of potential therapies for nerve injury.

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