Official Journal of TESMA
Regenerative Research
www.regres.tesma.org.my
E-ISSN 2232-0822
Tissue Engineering and Regenerative Medicine Society of Malaysia

Regenerative Research 7(1) 2018 19

REGENERATION OF CENTRAL NERVOUS SYSTEM (CNS) BY TISSUE ENGINEERING TECHNIQUE

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ARTICLE INFO

Published: 26th August 2018
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KEYWORDS

Scaffold;
Ice particle-freeze drying method;
Schwann cells;
Olfactory Ensheathing Cells;
Spinal cord regeneration

SUMMARY

Purpose: The spinal cord (SC) plays a crucial role in controlling the reflection behavior and connecting the brain and peripheral nervous system. The spinal cord injury (SCI) is generated by the physical injury, virus, cyst, tumor, and etc. The movement and sensory function are lost according to the extent of the spinal cord damage. The regeneration of SC is critical but is difficult to regenerate neurologically. In the case of the model for SCI, the substances that hinder the generation and function of the secondary damage which is caused by glial scarring must be studied in addition to the apoptosis control. In this study, we designed scaffolds not only for Schwann cells (SCs) and Olfactory Ensheathing Cells (OECs) replacement but also to provide enhanced biological environment for specific matrix-integrin interaction of cells with synthesis of natural ECM. **Materials and Methods:** In this study, we proposed application of nerve channel scaffold by employing tissue-engineering principles for the repair of SCI. We fabricated nerve channel (PLGA, DBP/PLGA, HA/PLGA et al.) scaffolds by an ice particle-freeze drying method. SCs or OECs were seeded on a nerve channel scaffold. The cell adhesion and proliferation on scaffolds was examined by SEM. The cellular viability was assayed by MTT. RT-PCR was conducted to confirm mRNA expression by using SC specific marker S-100, Glial fibrillary acid protein (GFAP) and neurofilament protein (NF). Moreover, the spinal cord was completely transected horizontally at two levels (T7 and T8) for in vivo study. The nerve channel scaffold cultured with cells was implanted in the lesion. We analyzed the defect area by the Basso, Beattie and Bresnahan (BBB) scoring, sensory test and chamber movement test after 8 weeks post-injury. We confirmed axonal regeneration by immunochemical staining. **Results:** In this study, we observed that scaffolds enhanced the cellular proliferation, cell attachment, maintain phenotype, and migration of nerve regeneration. We also verified that the implantation of the scaffolds containing SCs or OECs into a completely defected spinal cord model supported significant improvement in the axon and the central nervous system. In particular, implantation of SCs or OECs seeded DBP/ PLGA nerve channel scaffold into a complete spinal cord transection model promoted significant recovery in functional outcome when measured by the behavioral tests. Furthermore, NF and Neuron Glial Antigen 2 (NG2) staining showed a higher axonal regeneration in the scaffolds with cells group compared to the scaffolds with no cells group. In conclusion, the in vivo experiment was successful by SCs or OECs incorporated nerve channel scaffold transplantation. **Conclusions:** This study suggest that the fabricated nerve channel scaffold has a positive effect on SC regeneration and possess prospective application for SCI therapeutic usage.