A Regeneration Niche-containing Nerve Graft Constructed with Low-immunogenic Xenogeneic Acellular Nerve Matrix and Adipose-derived Mesenchymal Stem Cells

Yong-jie Zhang 1,2, Hailang Luo 1, and Yan Jin 2

Corresponding Author: yanjin@fmmu.edu.cn

1Engineering technology center for tissue engineering of Xi’an, Xi’an, Shaanxi, China and 2Research and Development Center for Tissue Engineering, Fourth Military Medical University, Xi’an, Shaanxi, China.

Introduction
Trauma induced Peripheral nerve injuries affect about 2.8% of patients that required surgical intervention [1]. The performance of autologous nerve bridge, named ‘‘Gold Standard’’, is astricted due to some drawbacks. Consequently, a suitable autologous nerve substitute is necessary to support peripheral nerve regeneration [2]. Due to non-containing niche of natural nerve, numerous artificial nerve conduits could not substitute autologous nerve graft to repair long peripheral nerve defect. The goal of this study was to fabricate a kind of nerve graft containing regeneration niche, utilizing xenogenic ANM and neural differentiated autologous ADSCs.

Materials and Methods
We constructed a nerve regeneration niche-containing nerve graft through integrating xenogeneic acellular nerve matrix (ANM) with autologous neural differentiated adipose-derived mesenchymal stem cells (ADSCs). Xenogeneic ANM was processed by a protocol removing cells and myelin sheath completely, meanwhile preserving growth factors and extracellular matrix (ECM) microstructure of natural nerve, such as porous and basal lamina tube. After removal of a 5-cm segment of the right sciatic nerve, the graft was implanted into the gap.

Results
Cytocompatibility and immunocompatibility evaluation revealed that ANM could support cell attachment and proliferation, and did not stimulate vigorous host reject response. In vivo, neural differentiated ADSCs also presented glial cell characteristic and promote nerve regeneration post-transplantation. Six months after transplantation, dogs could stand upright on two hind limbs and the transplanted sides coordinate well with the normal limbs in movement. Electro-physiological recordings showed neural function recovering across the gap. Fluoro-Gold retrograde labeled neurons were found in the horn of grey matter ipsilaterally.

Discussion and Conclusions
These data suggest that transplanted mesenchymal stem cells differentiate into Schwann cells and reform myelin, which provides a potential therapy for long nerve defect and ADSCs is an ideal seed cell for nerve reconstruction. We conclude that constructed nerve graft, offering nerve regeneration niche, hold great promise to replace autologous in repair peripheral nerve defect.

References

Disclosures
Authors have nothing to disclose.