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In vitro and *in vivo* study of a novel biodegradable synthetic conduit for injured peripheral nerves

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In case of peripheral nerve injury (PNI) with wide substance-loss, surgical reconstruction is still a challenge. Bridging the gap by autologous sensory nerves as grafts is the current standard; nevertheless, the related issues have prompted the research towards the development of effective artificial synthetic/biological nerve conduits (NCs). Here, we manufactured a novel NC using oxidized polyvinyl alcohol (OxPVA) that is a biodegradable cryogel recently patented by our group [1]. Thus, its characteristics were compared with neat polyvinyl alcohol (PVA) and silk-fibroin (SF) NCs through in vitro/in vivo analysis. Considering in vitro studies, a morphological characterization was performed by Scanning Electron Microscopy (SEM). Thereafter, cell adhesion and proliferation of a Schwann-cell line (SH-SY5Y) were evaluated by SEM and MTT assay. Regarding in vivo tests, the NCs were implanted into the surgical injured sciatic nerve (gap: 5 mm) of Sprague-Dawley rats, and the functional recovery was assessed after 12-weeks. The NCs were then processed for histological, immunohistochemical (anti-CD3; -β-tubulin; -S100) and Transmission Electron Microscopy (TEM) analyses. In particular, morphometric analyses (section area, total number and density of nerve fibers) were performed at the level of proximal, central and distal portions with respect to NC. In vitro results by SEM showed that PVA and SF supports have a smoother surface than OxPVA scaffolds. Moreover, unlike SF scaffolds, PVA-based ones do not support SH-SY5Y adhesion and proliferation. Regarding the in vivo study, all animals showed a functional recovery with normal walk, even though only animals implanted with PVA and SF NCs sometimes showed spasms while walking. On the contrary, animals implanted with OxPVA NCs exhibited a normal movement. Anti-CD3 immunohistochemistry assessed the absence of severe inflammatory reactions in all the grafts. A strong positive immunoreaction for β-tubulin and S100 demonstrated the good regeneration of nervous fibers. TEM highlighted regeneration of myelinated/un-myelinated axons and Schwann cells in all the grafts. However, morphometric analysis demonstrated that OxPVA assure a better outcome in nerve regeneration in terms of total number of nerve fibers. Our results sustain the potential of OxPVA for the development of NCs useful for PNI with substance loss with the advantage of biodegradation.

References

[1] Stocco et al. (2015) Partially oxidized polyvinyl alcohol as a promising material for tissue engineering. J Tissue Eng Regen Med doi: 10.1002/term.2101.

Keywords

Peripheral nerve injury, substance loss, nerve conduit, oxidized polyvinyl alcohol, peripheral nerve regeneration

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