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Short Bowel Syndrome and Tissue Engineering: a preliminary study towards the development of a new regenerative approach in paediatric patients

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Pediatric Short Bowel Syndrome (SBS) is a malabsorption state following massive surgical resections of the small intestine. The current therapeutic options issues (i.e. parental nutrition, surgical lengthening, transplantation) have prompt the research in Tissue Engineering. Thus, our aim was to preliminary investigate in vitro/in vivo two composite scaffolds for engineering the small intestine without resorting to autologous intestinal epithelial organoid units which, to date, are the cell source mainly considered for this purpose. In particular, we developed composite supports consisting of a novel biocompatible/resorbable cryogel that is oxidized polyvinyl alcohol (OxPVA) [1] crosslinked with intestinal mucosa whole (wIM/OxPVA) or homogenized (hIM/OxPVA). After evaluating the scaffolds by histology and Scanning Electron Microscopy (SEM), we assessed their interaction with adipose mesenchymal stem cells. Thereafter, the in vivo behavior of scaffolds was studied implanting them in the omentum of Sprague Dawley rats. At 4 weeks, explants were processed by histology and immunohistochemistry (CD3; F4/80; Ki-67; desmin; α-SMA; MNF116). Considering the in vitro evidence, both histological and SEM results proved the effectiveness of the decellularization, and allowed to appreciate the preservation of intestinal villi of the wIM as well as the characteristic features of the hIM. At 7 days from cell seeding, MTT assay showed that hIM/OxPVA scaffolds could support cell adhesion/proliferation even if the wIM/OxPVA ones seem to significantly increase cell growth ($p < 0.01$). Considering in vivo data, around the cryogels was recognizable a continuous and relatively organized tissue wall; its thickness was greater in wIM/OxPVA scaffolds than in wIM/OxPVA and OxPVA (control) ones. The presence of Ki-67$^+$ elements, proving cell proliferation, was mainly ascribable to lymphocyte-macrophage populations and in minority to connective and myofibroblastic ones; primarily on the outer sides, CD3$^+$ and F4/80$^+$ cells were found. Moreover, the outer layer of the tissue wall showed a connective appearance partially immunoreactive for both anti-Desmin and -αSMA, which are related to myofibroblastic features and smooth muscle cells. In the parietal thickness, vascular structures with organized endothelium were found. Towards the polymer, cubic/cylindrical cells partially positive for anti-MNF116 were recognizable and they were ascribable to epithelial cells. Both scaffolds, albeit with some difference, are promising, nevertheless further analysis will be necessary.

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