

Preclinical Studies for Evaluation of New Therapy for Reconstruction of Alveolar Process by Mesenchymal Stem Cells Seeded onto Bio-Oss® Collagen

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Objective: Orofacial clefts are one of the most common disorders in newborns. In cleft lip and palate missing part of the bone in alveolar process must be filled to enable of proper growth of the jaw and cutting teeth. In transplantology for the purpose of filling the extensive bone cavity commonly autological graft or graft from the deceased are used. Sources of the bone graft are ala of ilium, rarely skull or mandibular symphysis. Usage of Bio-Oss® Collagen will reduce number of surgeries during reconstruction of alveolar process compare to autologous bone grafting and overcome controversies in parents in case of allogenic transplantation. Mesenchymal stem cells by its secretion of angiogenic factors, recruitment of other MSCs or differentiation into osteoblasts may have positive influence on tissue regeneration after surgery.

Materials and methods: Mesenchymal stem cells derived from Wharton's jelly from umbilical cord (WJ-MSC) were cultured in low glucose DMEM supplemented with heparin, 10% platelet lysate, glucose and antibiotics. In *in vitro* studies WJ-MSC were seeded on Bio-Oss® Collagen and cultured in StemPro® Osteogenesis Differentiation Kit. In days 1, 7, 14 and 21 viability (confocal microscopy) and seeding capability (electron microscopy) of WJ-MSC on Bio-Oss® scaffolds were analyzed as well as gene expression (qPCR) and secretion of proteins (Luminex). In *in vivo* studies on rats the gaps after the cranium trepanation were filled with Bio-Oss® scaffolds with WJ-MSC and the computed tomography were performed after 7, 14 and 21 days after the surgery.

Results: WJ-MSC in *in vitro* studies shows ability to attach and proliferate on Bio-Oss® scaffolds. Results obtained from qPCR and Luminex indicates that WJ-MSC possess the ability to differentiate into osteoblasts/osteoclasts, may induce angiogenesis and mobilization of host MSCs. In *in vivo* studies usage of Bio-Oss® with WJ-MSC reduced time needed for healing of the skull.

Conclusions: The current study gave promising results for improvement in the reconstruction of the alveolar process by using bone substitute supported by mesenchymal stem cells.