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In situ tissue engineering concept for enhanced bone defect regeneration– functionalization of biomimetic scaffolds with an autologous growth factor mix from hypoxia-exposed hBMSC

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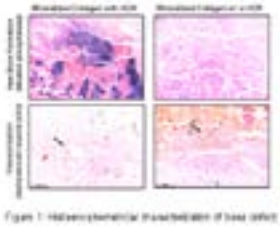
The potential for self-regeneration of bone tissue is not sufficient to regain the original function in the case of extensive lesions, osteoporosis, injury or tumor resection. Hence, the main goal of bone tissue engineering has been the generation of biological substitutes which remodel into native tissue to replace affected bone. *In vivo* tissue regeneration depends on migration of stem cells into injured areas, their differentiation into specific cell types and their interaction with other cells that are necessary to generate new tissue. Therefore, optimized biomaterials are needed which allow survival and growth of mesenchymal stem cells, a subset of bone marrow stromal cells (BMSCs), which can migrate and differentiate into osteoblasts in bone tissue. Hypoxia-conditioned media (HCM) has a high chemo attractive capacity for BMSCs, as it harbors high concentrations of growth factors which are important to stimulate angiogenesis and cell migration. It can be derived from BMSCs but also from skin fibroblasts which can be easily obtained from patients in individualized therapy approaches. Scaffold functionalization with a central growth factor depot enhances hBMSC infiltration as well as ingrowth of tubular endothelial structures providing a strategy to stimulate *in situ* colonization with cells from the surrounding tissue. For *in vivo* testing, a 4 mm wedge shaped osteotomy of the distal metaphyseal area was generated in the femur of osteoporotic rats. Six weeks after implantation of mineralized collagen scaffolds loaded with HCM, bone defect healing was characterized histomorphometrically revealing an enhancing effect on vascularization and new bone formation. In our work, we demonstrated that allogenous growth factor mix derived from HCM is suitable to attract cells with regenerative potential, induces vascularization *in vitro* and has been shown to enhance bone defect healing *in vivo*.



Recent Publications

1. Quade M, *et al.,* (2018) Strontium-modification of porous scaffolds from mineralized collagen for potential use in bone defect therapy. Materials Science & Engineering C Materials Science & Engineering 84:159-167.
2. Gabrielyan A, *et al.,* (2017) Metabolically conditioned media derived from bone marrow stromal cells or human skin fibroblasts act as effective chemo attractants for mesenchymal stem cells. Stem Cell Research &Therapy 8(1):212.
3. Quade M, *et al.,* (2017) Central growth factor loaded depots in bone tissue engineering scaffolds for enhanced cell attraction. Tissue Engineering Part A 23(15-16):762-772.
4. Gabrielyan A, *et al.,* (2014) Hypoxia-conditioned media allows species-specific attraction of bone marrow stromal cells without need for recombinant proteins. BMC Veterinary Research 10(1):56.
5. Alt V, *et al.,* (2013) A new metaphyseal bone defect model in osteoporotic rats to study biomaterials for the enhancement of bone healing in osteoporotic fractures. Acta Biomaterialia 9(6):7035–7042.

Biography

Anastasia Gabrielyan studied Biology at TU Dresden and is currently a PhD student at the University Hospital Carl Gustav Carus, Dresden. Her research has been published in reputed journals.

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