ECMBoneRegen

Tissue engineering of young bone extracellular microenvironment to enhance bone defect regeneration during aging

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Keywords			

Projektbeschreibung

Regeneration of bone deficiencies resulting from trauma, tumor resection and bone diseases represents one of the most pressing health problems in the aging European population. Current treatments of bone defects include the transplantation of autologous bone grafts, allogeneic bone grafts and bone substitutes from various natural and synthetic biomaterials, and bone growth factors to induce bone formation. However, these treatments are associated with significant drawbacks, including severely decreased bone quality in the aged patients, complications at the tissue harvesting site, risk of infections, inappropriate material properties etc., resulting in revision surgeries in 10-30% of the cases. Moreover, these treatments depend on a functional population of bone-forming cells and vasculature to mediate the process of bone regeneration. Aged bone tissue is subjected to the regulation by aged systemic environment and damaging effects of various systemic conditions. Often, the function of bone-forming cells is severely compromised as a result of multiple interacting cell-intrinsic and cell-extrinsic mechanisms. Therefore, the success of bone regeneration in elderly patients is in most cases limited.
The aim of our project is to develop a new multidisciplinary approach to enhance the regeneration of bone defects in the elderly, based on recent advances in cellular reprogramming and functional bone tissue engineering with human stem cells. We hypothesize that bone-forming cells derived from reprogrammed adult/aged somatic cells can synthesize a “rejuvenated”, embryonic-like bone microenvironment with high regenerative capacity and enhance the bone healing processes mediated by aged endogenous cells. We propose to investigate the extrinsic microenvironment components synthesized by the fetal/embryonic-like osteogenic cells derived from human induced pluripotent stem cells (hiPSCs), and test their potential to enhance the regenerative potential of aged bone and vascular cells. We will focus our studies on the cells from patients unable to benefit from the current therapies. Using bioengineering approaches, we will then develop novel acellular bone tissue substitutes with enhanced capacity to induce bone regeneration during aging, and evaluate their safety and functionality in preclinical rodent models of tissue regeneration and repair.
Our studies will provide new understanding of extrinsic mechanisms governing bone cell biology during aging and provide basis for new therapeutic possibilities for elderly patients currently lacking successful outcomes. Bioengineered off-the-shelf bone substitutes could provide a new possibility for inducing bone fomation during aging, a treatment strategy that is currently limited as compared to a number of treatments options aimed at decreasing bone resorption. In addition, our novel bioengineered bone substitutes will offer an advanced tissue model for future basic biology and translational research

studies.

Projektpartner

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