

**A novel bioactive multifunctional dendrimer-cell bone scaffold for polytraumatic large bone defects**

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Successful treatment of critical sized bone defects (CSD) still remains a major clinical problem in multidisciplinary cranio-maxillary-facial- und neurosurgical approaches. Due to diverse pathologic processes such as trauma, tumor, inflammation, infection and congenital malformations, critical size bone defects are defined as intraosseous wound in a particular bone and species that do not heal spontaneously during the patients lifetime if left untreated. The goal of our research is to evaluate the potential of an interdisciplinary approach to CSD healing based on novel dendrimer molecules which can present multiple binding sites for growth factors and cells (e.g. VEGF, RGDS, REDV), drugs (e.g. gabapentin-lactam (GBP-L)) or mineralizing function (e.g. phosphorylated serine). These dendrimers are applied in a construct consisting of biodegradable polyurethane foam (PU) saturated with autologous bone marrow derived mesenchymal stromal cells (MSC) in a crosslink hydrogel (e.g. plasma rich platelet, hyaluronan) with the aim of inducing rapid vascularization and jump-start new bone formation in a polytraumatic in vivo sheep model.

The research project consists in the in vitro evaluation of novel dendrimers containing peptide sequences able to bind VEGF and their abilities to stimulate endothelial cells and MSCs embedded within a hydrogel. Dendrimers containing phosphorylated serine or GBP-L will also be assessed in terms of new bone forming abilities defined on the basis of proliferation, metabolism, and differentiation of MSCs. Depending on the in vitro results, the most promising dendrimer/hydrogel construct will be tested using an in vivo animal model. The in vivo study will consist of an innovative combined maxillary and cranial critical size bone defect in sheep relevant to trauma patients.

The expected outcome is the assessment of a novel dendrimer technology for regenerative medicine, the development of a regenerative approach to CSD based on biodegradable smart materials and biological factors, together with an innovative combined in vivo study relevant for polytraumatized patients requiring an interdisciplinary team of CMF, trauma, and neuro-surgeons. Establishing a two-defect sheep model would not only be both more clinically and scientifically relevant, but it would also reduce animal experimentation and financial costs.