Universität Basel

Research Project

Vascularization of tissue engineered grafts

Third-party funded project

Project title Vascularization of tissue engineered grafts
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Rationale: Vascularization of engineered tissues of clinically relevant sizes is central for cell survival and successful engraftment. In the field of bone regeneration, several studies have established that bone marrow stromal cells, expanded in culture and loaded into porous ceramic scaffolds, are able to form bone tissue, both ectopically and orthotopically. Despite the report of few clinical cases, however, no convincing successes have been achieved in humans, most likely because of lack of sufficient vascular supply, resulting in immediate cell death after implantation. Recent reports in the context of other tissues suggested that addition of vascular cells inside the graft, such as endothelial cells, could improve vascularization and engraftment. Towards this prospective, we have shown that the generation of osteogenic-vasculogenic constructs starting from a single human cell source containing both osteogenic and endothelial cells, namely adipose tissue, is possible. Overall goal: To modulate the relative fractions and level of maturation/organization of human adipose tissue-derived endothelial cell progenitors (EP) and osteoprogenitor cells in a 3D co-culture system and to use the model to investigate the role of a network of EP on the engraftment and bone formation of the resulting engineered construct. Hypothesis: The presence of EP in tissue engineered bone grafts generated by adipose-derived nucleated cells improves and accelerates vascularization of the construct after in vivo implantation, thereby increasing the amount and uniformity of bone tissue formation. Specific aims: 1. Modulate the level of maturation/organization of adipose-derived endothelial cells and osteoprogenitors inside a 3D co-culture system. 2. Investigate the role of an EP network on the vascularization and bone formation of the resulting engineered construct. 3. Investigate the effect of EP in critically sized engineered constructs on cell survival and bone formation in the central core of the grafts. 4. Develop a serum-free medium to support a reproducible and clinically compliant engineering of the defined construct properties. Relevance of the expected results: This project will provide fundamental knowledge on the yet unresolved process by which EP can organize vascular networks and connect to the vasculature of the host in vivo. In the more general field of tissue engineering, it will provide a way to efficiently overcome one of the most critical limitations in current tissue engineering applications, namely vascularization and engraftment of implanted constructs. Finally, this project is very likely to define the starting point for a pilot clinical study using vasculogenic, autologous bone grafts in the treatment of critical size bone defects such as spine fusion or talus reconstruction. A better engraftment, by accelerating the bone healing process, will obviously have a major health and economical significance.

Keywords tissue engineering, bone repair, vascularization, endothelial progenitors, bioreactors
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