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03-P071 3D Differentiation of human Adipose-derived stem cells/hTERT in Methacrylate Gelatin Hydrogels with Different Stiffness

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Methacrylamide-modified gelatin (Gel-MOD) hydrogels represent an attractive source for biofabrication of three-dimensional (3D) tissue-engineered constructs, as they have tunable mechanical properties, are compatible with different types of cells and resemble elements found in natural cell-matrix environments. It has been demonstrated that Gel-MOD properties can be altered depending on the degree of methacrylation. In our study we investigated how 5%, 7.5% and 10% (m/V) Gel-MOD hydrogels (degree of methacrylation 63%) affect proliferation and differentiation of human adipose-derived stem cells/hTERT (hASC/hTERT) after their encapsulation in microspheroid form and their 3 or 5-week exposure to osteogenic or chondrogenic differentiation medium, respectively. Employing confocal microscopy we observed that all experimental conditions supported hASC/hTERT viability during the entire testing period. Morphological evaluation and gene expression analysis of selected genes *SOX9*, *ACAN* and *COL2A1* proved that compared to the 3D control (undifferentiated) sample, chondrogenic differentiation of hASC/hTERT was successfully achieved in all three different formulations of Gel-MOD and was most prominent in 5% gel. Interestingly, when selected osteogenic genes (*RUNX2*, *BGLAP*, *ALPL*, *COL1A1*) were analyzed in 3D control or osteogenically differentiated samples and were compared to the expression obtained from hASC/hTERT after their monolayer expansion (prior encapsulation – day 0), their expression in 3D increased to a similar extent in both conditions. This could suggest that Gel-MOD alone (without any induction medium) is able to shift the behavior of of hASC/hTERT towards osteogenic lineage. The acquired preliminary data indicate that Gel-MOD shows very promising potential in the field of osteo-chondral tissue engineering.

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03-P072 Reconstruction of Large bone defect in sheep with customized 3D printed calcium phosphate scaffolds

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The reconstruction of large bone defects resulting from severe trauma or resection of tumors remains a challenge for orthopedic and plastic surgeons. Today, a vascularized bone is taken from the patient and grafted into the defect. However, this transplantation adds morbidity and requires extensive micro surgery to adapt to both the vasculature and the skeleton. We propose an alternative approach consisting of manufacturing patient specific biomaterial scaffolds through 3D printing. This study aims to demonstrate the feasibility of regenerating large bone defects with 3D printed anatomically accurate biomaterial scaffolds in sheep.The left posterior limb was scanned by computed tomography (CT), and a contrast agent was injected in order to visualize the metatarsus and the vasculature. CT data were imported into medical imaging software and converted to STL files. The metatarsus bone of sheep was 3D printed with PLA filament from the CT scans. It allowed surgical planning with the placement of an osteosynthesis plate and screws. A cutting guide was also designed and 3D printed in order to create a segmental defect of 35 mm in the metatarsus. A specific biomaterial was produced by 3D printing using a calcium phosphate /pluronic paste that hardens into a porous scaffold. Three groups were considered: empty defects, and defects filled with either a customized biomaterial scaffold, or the biomaterial scaffold with a vascular pedicle running through it. After surgery, bone regeneration and vascularization were followed by CT at 30, 60 and 90 days. Sheep were euthanized and a vasculature contrast agent (Microfil) was injected into the femoral artery. Metatarsus were dissected, and analysed by microCT and histology study.The scaffold had interconnected porosity to favor bone regeneration. CT scans indicated that the empty defect remained non-bridged after 3 months. A limited bone healing was observed with the 3D scaffold. The vascular pedicle going through the scaffold was functional without thrombosis. The vasculature favored bone regeneration of the critical size metatarsus defect.

This pre-clinical study demonstrated the feasibility of 3D printing patient specific biomaterial scaffolds for regeneration of large bone defects resulting from severe trauma or resection of tumor.

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