

Influence of artificial and native extracellular matrices on adhesion and differentiation of mesenchymal stem cells and osteoblasts

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Artificial extracellular matrices (aECM) consisting of collagen and sulfated glycosaminoglycan derivatives (sGAG) promote the osteogenic lineage commitment of human mesenchymal stromal cells (hMSC). This effect was seen with sGAG in 2D (substrate coatings) and in 3D (modified fibrillary collagen networks, B10).

In addition to the pro-osteogenic effects, sGAG and aECM alter significantly the endogenous (native) ECM (nECM) of hMSC. sGAG derivatives interact with hMSC-derived matrix vesicles, they co-localize with numerous nECM proteins (e.g. fibronectin) and become incorporated in the complex nECM network. Thus, sGAG induce changes in the nECM composition, assembly, cross-linking, remodelling, and mineralisation (cooperation with Z4 (proteomics), A3 (SPR analysis), A7 (molecular modelling), and Viola Vogel's group, ETH Zurich FRET, fiber stretch assay).

For better understanding how EZM characteristics influence osteogenic differentiation we will investigate sGAG-induced alterations of nECM structure, composition and physico-chemical properties as well as the phosphorylation status of particular ECM proteins more detailed (cooperation with A3, A6, B10, Z4). Our working hypothesis is that the pro-osteogenic effect of sGAG derivatives and aECM is mainly caused by sGAG-induced altered nECM. Therefore, the so altered nECM itself should be used for the modification of biomaterial surfaces. Our studies showed further an intracellular enrichment of sGAG and suggested that the endocytotic receptor LRP-1/CD91 (low density lipoprotein receptor-related protein-1) could be involved. Pull-down experiments and SPR analyses (cooperation with Z4 and A3) are planned to identify intracellular target molecules.

According to the strategy of the consortium we investigate whether sGAG and ECM reveal beneficial effects for hMSC from different sources and patients with compromised bone healing (cooperation with B5 and the Savkovic group).

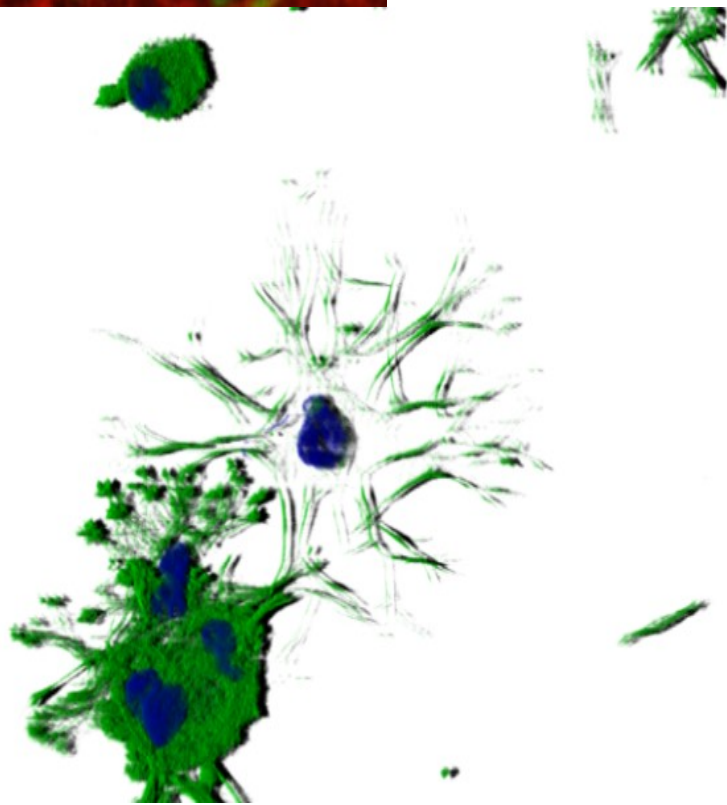
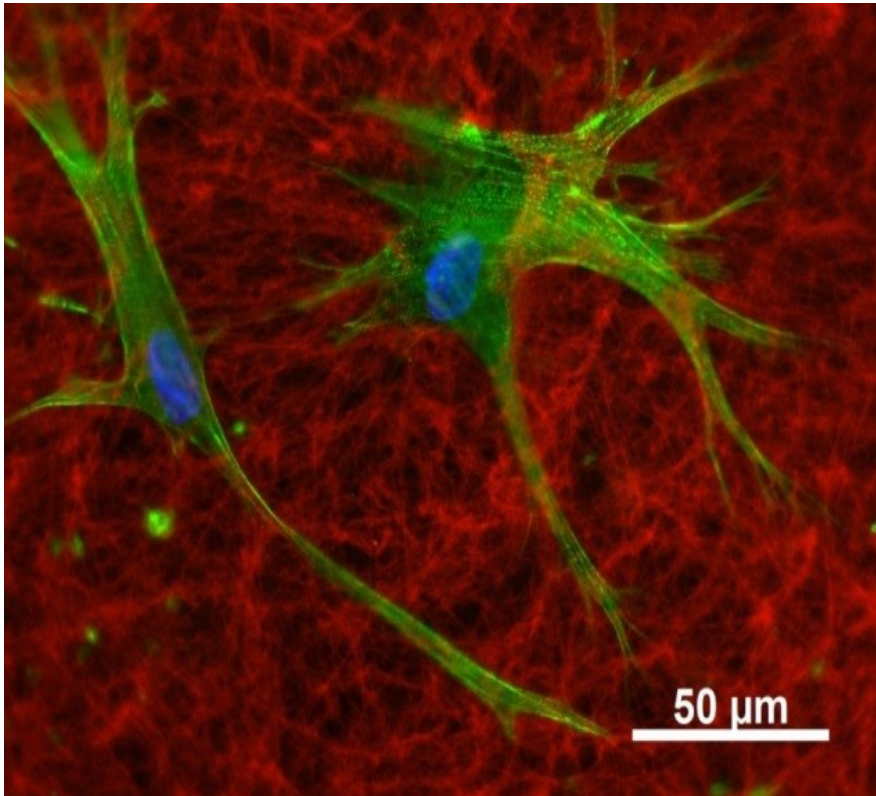


Figure 1. Collagen | F-Actin Morphology of hMSC on (left) and in (right) a 3D collagen network, 24 h after plating

Project-related Publications

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