clickECM – a new approach to click-modify the human cell-derived ECM

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The extracellular matrix (ECM) is a complex network of biomolecules that surround the cells in a human tissue. Primary cells are capable of producing an ECM in vitro which can be isolated after several days of culture [1]. Due to the high biological activity, different types of ECM are able to promote cell adhesion, proliferation, and differentiation in a tissue specific manner [2]. Because of its diverse functions, the isolated ECM is a promising material for the use in tissue engineering and regenerative medicine. Therefore, we performed metabolic oligosaccharide engineering (MOE) to introduce click groups into the glycan structures of the ECM. As a prove of principle for the chemical reactivity and the accessibility of these incorporated click groups we tested, whether they can be used to form covalent bonds with alkyne-functionalized surfaces to generate a long-term stable coating with high biological complexity.
Therefore substrates were functionalized with activated alkynes to covalently immobilize the ECM on surfaces via copper-free click reaction [3] resulting in a significant increase in coating stability compared to a physisorbed ECM coating The bioactive properties of these coatings were evaluated by quantifying the cell proliferation. Histochemical and immunofluorescence analysis were performed to characterize the biological composition of clickECM.
We could for the first time show that MOE can be used to introduce click groups into the ECM of human dermal fibroblasts. This clickECM consists of glycans, collagens, and non-collagenous proteins whereby the ratio of these biomolecules is the same in clickECM and unmodified ECM. Cell proliferation was significantly enhanced on the clickECM-coated surfaces compared to uncoated substrates. These results demonstrate that the covalent immobilization mediates an increased stability while preserving the high biological activity of the human dermal ECM.

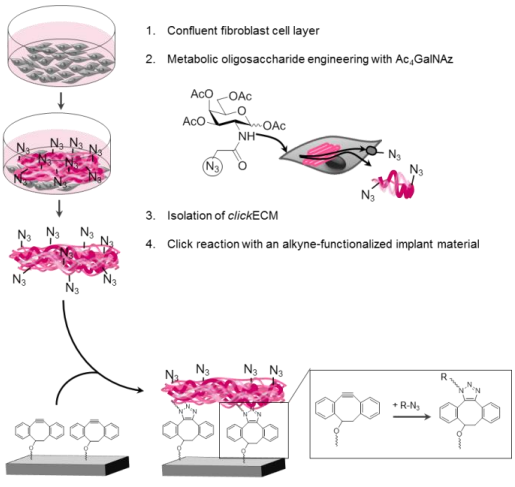

Figure 1. Preparation of a coating with clickECM

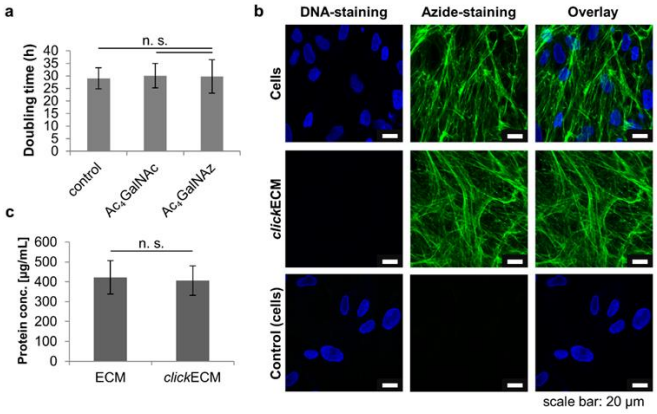

Figure 2: Click modification of ECM via MOE

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[2] Lu, H. et al., *Biomaterials,* 2011, **32**, 9658.
[3] H.C. Kolb, M.C. Finn and K.B. Sharpless, *Angew. Chem. Int. Ed. Engl.,* 2001, **40**, 2004.