ABSTRACT SUBMISSION

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Heparan Sulfate enhances BMP2-mediated osteogenic differentiation

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ABSTRACT

The use of bone morphogenetic protein 2 (BMP2) in bone regeneration is clinically approved but the negative side effects, due to a lack of control in amount and localization specificity, demand for new insights about the interaction between cells and BMP2. It has been shown that the extra-cellular matrix (ECM) molecule heparan sulfate (HS) enhances the bioactivity of BMP2 [1] but it is not sure if the activation of integrins presents a pre-condition, referring to the BMP receptors–integrin crosstalk [2].

A biomimetic approach is chosen to study the effect of ECM components on osteogenic differentiation, e.g. heparan sulfate, which naturally binds BMP2, and the adhesion peptide cyclic RGD or RAD – the latter having a 400-fold lower affinity to integrins than RGD. This allows to study the effect of HS on osteogenic differentiation with and without the specific activation of integrins.

A Streptavidin (SAv) monolayer on gold-sputtered glass surfaces is used as a versatile platform to (co-)immobilize matrix molecules via the SAv-biotin binding and the molecular adsorption of each component is precisely quantified with surface sensitive techniques. These biomimetic platforms are supports for cellular differentiation studies. In particular we quantify the level of p-SMAD 1/5/9 (BMP2 signaling cascade) and Osterix (osteogenic marker) of mice myoblast C2C12 cells.

P-SMAD1/5/9 is 3-4 times up-regulated on RGD platforms compared to RAD for all BMP2 conditions but not the expression of Osterix, where a difference between RGD and RAD platforms is not significant. Furthermore HS enhances BMP2 activity also on RAD platforms compared to soluble and immobilized BMP2. Therefore HS has a strong effect on the osteogenic differentiation independently of the specific activation of integrins by RGD and represents a strong candidate for future surface treatment of bone implants. Silencing integrins via siRNA transfection is expected to confirm these results.

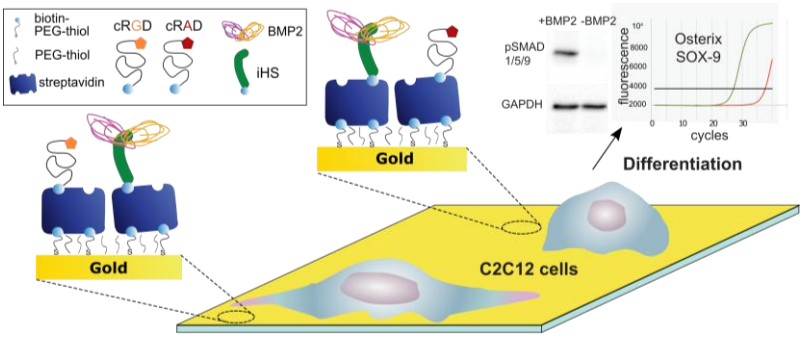

Figure 1: Scheme of the biomimetic platform and cells responding to different surface conditions.

[1] E. Migliorini *et al.*, Advanced Biosystems (2017), 1, 1600041, doi:10.1002/adbi.201600041
[2] L. Fourel *et al.*, The Journal of Cell Biology (2016), 212 (6), 693–706, doi:10.1083/jcb.201508018