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Title : Biomimetic materials presenting extracellular matrix components to study bone morphogenetic protein bioactivity

Jean Le Pennec, Julius Sefkow-Werner, Adria Sales, Paul Machillot, Catherine Picart and Elisa Migliorini

BACKGROUND AND PURPOSE: The extracellular matrix (ECM) is a complex 3D microenvironment around cells composed of structural and adhesion proteins, proteoglycans-carrying glycosaminoglycans (GAGs) that bind and release growth factors to cellular receptors. In particular, bone morphogenetic protein 2 (BMP2) is bound to GAGs on the ECM and cell surface. 3D biomaterials are a good approximation to the real in vivo microenvironment, they allow cells to maintain their original shape, have higher stability and longer lifespan by showing a less altered genotype. On the contrary, 2D culture is not representative of the chemical and physical properties of the ECM. However, precise chemical functionalization of 3D biomaterials is still a challenge, and high-throughput methods for designing and functionalizing 3D biomaterials are rare. In addition, the analysis of cellular responses in 3D is more complex than in 2D.

METHODS: For these reasons, we propose "2.5D" biomaterials with controlled chemical and mechanical properties that can be functionalized by a liquid handling robot followed by automated cellular readout based on immunofluorescence. Thanks to these 2.5D biomaterials, we have demonstrated the existence of a bidirectional cross-talk between BMP2 and integrin adhesion ligands. We have also shown that the glycosaminoglycan (GAG) heparan sulfate (HS) has a positive role on BMP2-mediated signaling when presented to the cell by a biomaterial, compared to the other GAGs chondroitin sulfate and hyaluronic acid. On the contrary, cell surface CS has a positive effect on BMP2 signaling, whereas HS seems to inhibit short-term BMP2 signaling.

CONCLUSIONS: We are developing well-characterized biomimetic materials for high-throughput in vitro cell culture studies. In the future, we expect to use these materials as coatings for 3D scaffolds.