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Host laboratory:

BioSanté, <https://biosante-lab.fr/en>

Host group/team:

BRM: Biomimetism and Regenerative Medicine

Title of the M2 research internship:

Control of mesenchymal stem cell differentiation using biomimetic films: the early steps

Project summary:**Context**

Cells in our tissues are embedded in an extracellular matrix that provides physical and biomechanical signals. Among these signals, bioactive proteins of the bone morphogenetic proteins (BMP) family have major physiological roles in morphogenesis and tissue regeneration [1] and in pathological processes, including musculo-skeletal, cardiovascular, pulmonary diseases and cancers. Their specific role in the initiation of cell fate decisions are still poorly known. Our team has developed bioactive surface coatings presenting proteins at the basolateral side of cells in a controlled manner [2] [3]. These coatings can be deposited in microplates for high content studies of cell adhesion and differentiation [4, 5]. Controlling cell differentiation using biomaterials is of great interest in view of drug testing for the development of medical treatments, notably in the case of cancers where BMP proteins are involved.

Project description

The aim of the project is to study the differentiation of stem cells in response to several BMP proteins bound to the biomimetic films of controlled stiffness. We will more particularly focus on the early steps of differentiation to bone, fat and cartilage tissues. We will focus on the signalling at the plasma membrane and on protein internalization, up to signaling in the nucleus. To reach this objective, the candidate will learn to use the liquid handling robot, (mesenchymal) stem cell culture, immuno-fluorescence stainings, biological assays and high content microscopy.

Keywords:

health engineering, cell signaling/ receptors, mesenchymal stem cells

Relevant publications of the team:

Migliorini, E., et al., Learning from BMPs and their biophysical extracellular matrix microenvironment for biomaterial design. *Bone*, 2020. 141: p. 115540.

Gribova, V., R. Auzely-Velty, and C. Picart, Polyelectrolyte multilayer assemblies on materials surfaces: From cell adhesion to tissue engineering. *Chemistry of Materials*, 2012. 24(5): p. 854-869.

Gilde, F., et al., Cellular internalization of matrix-bound BMP-2 and associated endocytosis pathways. *Acta Biomaterialia*, 2016. 46: p. 55-67.

Machillot, P., et al., Automated buildup of biomimetic films in cell culture microplates for high-throughput screening of cellular behaviors. *Adv Mater*, 2018. 30(27): p. e1801097.

Sales Ramos, R et al. Differential bioactivity of four BMP members as function of biomaterial stiffness. *Biomaterials* 2022 Feb;281:121363. doi: 10.1016/j.biomaterials.2022.121363.

Valat A, Fourel L, ... Bruckert F, Albigès-Rizo C, Picart C. Front Cell Dev Biol. 2023 Jan 4;10:1027334. Interplay between integrins and cadherins to control bone differentiation upon BMP-2 stimulation. doi: 10.3389/fcell.2022.1027334. eCollection 2022