Internship proposal (Master or final project engineering school) at the LMGP

Title: Biomimetic platforms for molecular and cellular studies

Summary: Embryo differentiation but also cancer and tissue homeostasis are supported by the extracellular matrix (ECM) which has not only a structural but also a functional role: the presentation of bioactive molecules. The first aim of this project is to mimic the natural presentation of a potent osteoinductive growth factor, bone morphogenetic protein 2 (BMP-2), by immobilizing it on biomimetic platforms, together with other ECM adhesion proteins and glycosaminoglycans, in particular heparan sulfate (HS), as it is *in vivo*. The second aim is to study cellular responses to BMP-2 presented *via* the biomimetic platforms.

Detailed subject: 15 years after FDA approved the clinical use of BMP-2 for spinal cord injuries, raises an unmet industrial need of optimizing biomaterials for BMP-2 presentation and dose-control. For that is important to totally understand which are the "molecular regulators" of BMP-2 activity *in vivo.* Fundamental studies are therefore needed. We adopt a biomimetic approach to study at the molecular level BMP-2 binding to the natural ligand HS and the cellular responses to this type of presentation.

We design surfaces — biomimetic platforms — that present some selected components of the ECM bound to them. On the biomimetic platforms we will graft HS, BMP-2 and also adhesion ligands (here called RGD peptides), which permit cells spreading *via* cellular adhesion receptors: integrins (Fig 1).

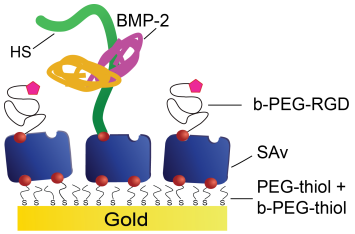

Figure 1: schematic representation of the biomimetic platforms that will be developed in this project.

We have shown that the presentation of BMP-2 *via* HS promotes the osteogenic differentiation of progenitor cells (Migliorini et al. 2017). To understand the molecular mechanism behind the *role of HS on BMP-2 bioactivity* we immobilize biotinylated HS with different chemical composition on SAv monolayer. With quartz crystal microbalance with dissipation monitoring (QCM-D) we will characterize the binding of biotiylated molecules on the top of SAv and calculate the average nanometrical distances between ligands. After the characterization of the molecular assembling, we will use the well-defined biomimetic platforms for studying cellular adhesion and differentiation with molecular biology methods.

Related Publication: Migliorini, E., P. Horn, T. Haraszti, SV Wegner, C. Hiepen, P. Knaus, PR. Richter, and EA. Cavalcanti-Adam. 2017. 'Enhanced biological activity of BMP-2 bound to surface-grafted heparan sulfate', *Advanced Biosystems*, 1: 1600041.

Background and skills: master student from last year university or engineering school interested in glycobiology and/or physical chemistry. Aptitude for teamwork, good spoken and written English are required. A "gratification" will be provided following the French law.

Supervisor : Migliorini Elisa
Laboratory : LMGP – CNRS-UMR 5628
Team/Group : IMBM
Contacts - E-mail : elisa.migliorini@grenoble-inp.fr Tel : +33 4 56529324 Web-page : http://www.lmgp.grenoble-inp.fr/annuaire-/migliorini-elisa--869551.kjsp?RH=LMGP_ANNUAIRE

This project is part of the core interest of the main investigator, therefore a PhD thesis might follow the master thesis. Please send a CV + a cover letter (including names/contact email of 2 referees) + the record of your grades of the 2 past academic years to: elisa.migliorini@grenoble-inp.fr