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

Title: Biomimetic platforms to study corticogenesis

Summary: Embryonic differentiation 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. In this project we will mimic the natural presentation of a growth factor, bone morphogenetic protein 2 (BMP2), fundamental during the development of several tissues, among them skeleton and brain [1]. BMP2 will be presented to neuronal precursors together with other ECM adhesion proteins and glycosaminoglycans, in particular heparan sulfate (HS), as it is *in vivo* in the pial basal membrane [2]. **BMP2 and HS have been independently shown to be fundamental for neuronal** [3] **development. However, the role of their mutual interaction has not been considered, so far.** The project aims to (i) engineer a biomimetic platform able to present BMP2 together with HS and adhesion ligands adapted for neuronal culture, and (ii) to study neuronal responses to BMP2 presented *via* the biomimetic platforms in terms of adhesion, dendritogenesis, axonal growth and differentiation.

Detailed subject: We will design surfaces — biomimetic platforms — that present some selected components of the ECM bound to them. On the biomimetic platforms we will graft HS, BMP2 and also adhesion ligands (here called RGD peptides), which permit cells spreading *via* cellular adhesion receptors: integrins (Fig 1).

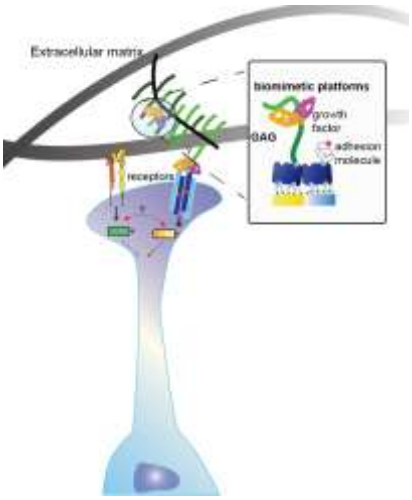

Figure 1: schematic representation of a radial glial cells and of the ECM surrounding the cell that we aim to mimic with the biomimetic platforms that will be developed in this project.

We have previously shown that the presentation of BMP2 *via* HS promotes the osteogenic differentiation of progenitor cells[4]. Being HS proteoglycans specifically present in the pial basement membrane [2], the anchoring ECM for cortical progenitors we expect that extracellular-HS plays a key role on BMP2 regulation during the development of brain cortex (corticogenesis). In this project early cortical neurons will be dissected from embryonic mice and plated on biomimetic platforms on which we will 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 biotinylated molecules on SAv. The effect of BMP2 and HS on **neuronal adhesion, dendritogenesis, axonal outgrowth, SMAD 1/5 phosphorylation** will be addressed.

Location

The candidate will be working between LMGP (for the platforms characterization) and GIN laboratory (for neuronal studies) both located in Grenoble

Profile & requested skills

5th year engineering school with an interest for biomedical engineering, neurobiology, biophysics. Aptitude for teamwork, good spoken and written English are requested.

Stipend: this project is going to be submitted to the NeuroCog AAPG conjoint 2020 to obtain financial funding for the “gratification” and for consumables

Continuation of the project : the project may be continued as a PhD contract (if funding will be allocated)

Related Publications:

1. Obradovic Wagner, D., et al., Science Signaling, 2010. **3**(107): p. mr1-mr1.
2. Dwyer, C.A. and J.D. Esko, Mol Aspects Med, 2016. **51**: p. 104-14.
3. Mabie, P.C., M.F. Mehler, and J.A. Kessler, The Journal of Neuroscience, 1999. **19**(16): p. 7077-7088.
4. Migliorini, E., et al., Advanced Biosystems, 2017. **1**(4): p. 1600041.

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