

**Master 2 internship project
Year 2021-2022**

Laboratory/Institute: IBS

Team: SAGAG group

Director: Winfried Weissenhorn

Head of the team: Hugues Iortat-Jacob

Name and status of the scientist in charge of the project: Rabia Sadir **HDR:** yes no

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Program of the Master's degree in Biology:

- Immunology, Microbiology, Infectious Diseases Structural Biology of Pathogens
 Physiology, Epigenetics, Differentiation, Cancer Neurosciences and Neurobiology

Title of the project:

Protein-induced cross-link of heparan sulfate : structural remodelling of glycocalyx and functional effects

Objectives (up to 3 lines):

The goal of this M2 proposal is to study the structural change of cellular HS induced by protein-ligands and its functional role by using fluorescence nanoscopy approach and biological assays

Abstract (up to 10 lines):

The glycosaminoglycan, heparan sulfate (HS), present in extracellular matrix and at the surface of most cells, is an important component of glycocalyx (or cell-coat). HS binds many soluble extracellular signaling proteins such as chemokines and growth factors, and regulates their biological functions. Previously, we showed by a combination of biophysical analysis techniques in a well-defined biomimetic surfaces that signaling proteins (chemokine CXCL12, growth factor FGF-2) cross-link HS chains and change their mobility and dynamics. This aspect represents a new paradigm of the protein/HS interactions.

The aim of our study is to determine the ability of these signaling proteins to induce cross-linking of cellular HS chains in the cell context by using Stochastic Optical Reconstruction Microscopy (STORM) and to investigate the functional effects of this structural remodelling. The M2 student will prepare samples for single molecule super-resolution imaging (cell culture and immunolabelling assay), and will perform different functional assays (cell adhesion and migration).

Methods (up to 3 lines):

Cell culture, confocal microscopy, super-resolution microscopy (STORM), adhesion assays, western-blot, flow cytometry

Up to 3 relevant publications of the team:

1. Connell B, Sadir R, Baleux F, Laguri C, Kleman JP, Luo L, Arenzana-Seisdedos F, and Iortat-Jacob H. Heparan sulfate differentially controls CXCL12 α - and CXCL12 γ -mediated cell migration through differential presentation to their receptor CXCR4. *Sci. Signal.* (2016): Vol. 9, Issue 452, pp. ra107
2. Liu XQ, Fourel L, Dalonneau F, Sadir R, Leal S, Iortat-Jacob H, Weidenhaupt M, Albiges-Rizo C, Picart C. Biomaterial-enabled delivery of SDF-1 α at the ventral side of breast cancer cells reveals a crosstalk between cell receptors to promote the invasive phenotype. *Biomaterials* : 127 : 61-74 (2017)
3. Annava T, Wild R, Créton Y, Sadir R, Vivès RR, Iortat-Jacob H. Heparan Sulfate Proteoglycans Biosynthesis and Post Synthesis Mechanisms Combine Few Enzymes and Few Core Proteins to Generate Extensive Structural and Functional Diversity. (2020) *Molecules*. 25(18):4215

Requested domains of expertise (up to 5 keywords):

Cell biology & Biochemistry