

INTERNSHIP PROPOSAL

Institute and Group: IBS, group GAG

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Research project title: Regulation of heparan sulfate structure by biosynthetic and post-synthetic machineries

5 Keywords to describe the project: Heparan sulfate, protein complex, enzyme, structure/function relationship

Description of the project (aims, experimental techniques, recommended background):

Heparan sulfate (HS) is a complex polysaccharide that emerged as a key regulator of most biological processes, including cell proliferation and development, inflammation and immune response, angiogenesis, tissue repair or host-pathogen interaction and cancer. Consistently with its extensive functional repertoire, HS is characterized by a unique level of structural complexity, which is thought to enable HS to finely modulate the bioactivity of its vast array of ligands (growth factors, cytokines, adhesion molecules, etc.). An emerging paradigm is that unique oligosaccharide motifs are assembled during biosynthesis and through post-synthetic processes, by enzymatic complexes, to display the necessary information for protein ligand recognition. To decipher how cells control the generation of such specific oligosaccharide sequences we will biochemically characterize the HS biosynthetic machineries and post-synthetic enzymes. For that purpose, the successful applicant, who ideally has a biochemistry background, will have in charge the overexpression of recombinant enzymes, using eukaryotic cells, and their subsequent purifications. Various biophysical techniques will be used in order to achieve structure/function studies on either proteins alone or reconstituted poly-enzymatic machineries.

Relevant publications of the team:

1. Monneau Y. *et al.* The sweet spot: how GAGs help chemokines guide migrating cells. *Journal of leukocyte Biology* 99, 935-953 (2016)
2. Préchoux A. *et al.* C5-epimerase and 2-O-sulfotransferase associate in vitro to generate contiguous epimerized and 2-O-sulfated heparan sulfate domains. *ACS ChemBiol* 10, 1064-1071 (2015)
3. Seffouh A. *et al.* HSulf sulfatases catalyse processive and orientated 6-O-desulfation of heparan sulfate that differentially regulate fibroblast growth factor activity. *FASEB J.* 27, 2431-2439 (2013)