INTERNSHIP PROPOSAL

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Research project title: enzymatic regulation of cell-surface glycanic landscape in human disease

5 Keywords to describe the project: heparan sulfate, interactions, enzymes, structure/function relationships, disease

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

Many pathological conditions have been associated with an alteration of cell-surface glycan structure and function. This is particularly relevant for Heparan sulfate (HS), a complex polysaccharide that play key regulatory roles in most biological processes, including cell proliferation and development, inflammation and immune response, angiogenesis, tissue repair or host-pathogen interaction and cancer. HS elicits these activities through the binding and modulation of a wide array of proteins. These interactions depends on specific sulfations of the polysaccharide, which are tightly controlled during both its biosynthesis and post-synthetically, through the action of extracellular enzymes. The objective of the project is to study the patterning of HS for one type of sulfation (6-sulfation), which is critical in many pathologies. For this, we will carry out the structural and functional characterization of the enzymes involved in the addition and removal of HS 6-sulfates. The project will thus include recombinant expression of proteins, enzymology, structural biology approaches (NMR, X-ray crystallography, SAXS), and functional assays (in vitro, in cellulo). This study should provide significant insights into this major regulation system of HS activities, and for the design of new HS-based inhibitors and therapeutical approaches.

Justification that the internship’s subject fits with the general theme of GRAL:

HS is a major cell-surface receptor for many pathogens, including a wide variety of viruses (HIV, HSV, dengue, Ebola...). Understanding the mechanisms regulating HS structure and binding properties is thus fully in the frame of GRAL Axe 1: Host-pathogen interactions.

Relevant publications of the team:

