

Regulation of Heparan sulfate cellular functions by Sulf extracellular sulfatases



Laboratory/Institute : IBS, Grenoble, France / Industrial partner

Project supervisor: Romain Vivès

Scientific Context and objectives

Heparan Sulfate (HS) polysaccharides bind a very large array of signaling proteins, thereby modulating their availability, stability, structure and reactivity. These interactions occur through saccharide domains (termed S-domains) of specific sulfation pattern, present within the polysaccharide. Assembly of such functional domains is orchestrated by a complex biosynthesis machinery and their structure is further regulated at the cell surface by post-synthetic modifying enzymes, including extracellular sulfatases of the Sulf family. Sulfs catalyze the selective removal of 6-*O*-sulfate groups, which are required for the recognition of many proteins, and specifically target HS S-domains. Although structurally subtle, these modifications have great functional consequences, and Sulfs have emerged as critical regulators of HS activity, in physiological processes such as embryogenesis and tissue regeneration, and in diseases such as cancer. However, despite increasing interest, these enzyme mechanisms remain poorly characterized. In this context, we propose to investigate Sulf substrate specificities and to study the regulation of HS binding growth factors by these enzymes.

The recruited engineer will be in charge of this multidisciplinary project, which involves the production of recombinant proteins (in eukaryotic and prokaryotic expression systems), the preparation and screening of oligosaccharide substrate libraries using functional assay (SPR, enzyme assays...) and the functional analysis of Sulf activity using cellular assays (proliferation, migration...).

Location

The project will take place in the SAGAG group at the Institute for Structural Biology (IBS, <http://www.ibs.fr/research/research-groups/structure-and-activity-of-glycosaminoglycans-group/>), within Grenoble EPN campus, which offers a stimulating and international scientific environment,

Grenoble is a highly dynamic city located in the heart of the French Alps, ranked as the 5th most innovative city in the world (FORBES 2013). It is very easily accessible (3h from Paris by train, 1h from Lyon international airport).

Candidate profile

The PhD candidate should hold a Master's degree (or equivalent) with honor (top rank > 25%), in biochemistry and/or cell biology and show high interest in working at the interface between these two

disciplines. Previous successful laboratory internship experience, notably in cell culture, functional assays (proliferation, migration, signaling cascades...) and FACS analysis will be an indisputable advantage for the candidate selection. Experience in recombinant protein production will be a plus. A demonstrated ability to perform independent work and communication/writing skills are also considered as important criteria.

Position

18-24 month CDD contract funded by an ANR program.

Application

Please send a CV (including reference for possible recommendation), to romain.vives@ibs.fr

Deadline: 30th of September 2019