UFR de Chimie et de Biologie
UNIVERSITÉ Grenoble Alpes

Master's degree in Biology – Chemistry-Biology Department

Internship project Master 2
Year 2017-2018

Laboratory/Institute: IBS
Team: SAGAG

Director: W. Weissenhorn
Head of the team: H. Lortat-Jacob

Name and status of the scientist in charge of the project: VIVES Romain **HDR: yes** ☑ **no** ☐
Address: IBS, 71 Avenue des Martyrs, CS 10090, 38044 Grenoble Cedex 9, France
Phone: 0457428508 **e-mail:** romain.vives@ibs.fr

Program the Master's degree in Biology:

☐ Neurosciences and Neurobiology ☐ Immunology, Microbiology, Infectious Diseases
☑ Integrative Structural Biology ☐ Physiology, Epigenetics, Development, Differentiation

Title of the project:

Structural and functional specificities of HSulf isoforms

Objectives (up to 3 lines):

HSulf1 and HSulf2 are two sulfatases, which display the same enzyme activity in vitro, but antagonist functions in vivo during tumor progression. The aim of the project is to study and compare the structural and enzymatic features of these tow isoforms.

Abstract (up to 10 lines):

Heparan sulfate (HS) are complex polysaccharides of the Glycosaminoglycan (GAG) family, that bind through specific saccharide motifs to a wide array of proteins. Assembly of such functional motifs is tightly controlled during biosynthesis of the polysaccharide, and by the post-synthesis action of extracellular sulfatases termed Sulfs. These enzymes are therefore implicated in many physiopathological processes, including cancer. Surprisingly, the 2 human isoforms HSulf-1 and Hsulf-2 display antagonist activities in the control of tumor growth. Clarifying the underlying mechanisms is thus crucial for better understanding this major regulation system of HS activities, and for the design of new anti-tumoral strategies targeting the Sulfs. In this context, this project aims at studying the dynamic, structural and functional features of Sulf isoform to identify isoform specificities.

Methods (up to 3 lines):

Enzymes will be expressed recombinantly in mammalian cells, and purified by chromatography techniques. Characterization will involve biochemical enzyme assays, binding experiments (SPR, FACS..) and biophysical approaches (SEC-MALS, crystallogenesis asssays…).

Up to 3 relevant publications of the team:

- R. El Masri, A. Seffouh, H. Lortat-Jacob, **R.R.Vivès**. "The "in and out" of glucosamine 6-O-sulfation: the 6th sense of Heparan sulfate". Glycoconj. J. In press.

- G. Heidari-Hamedani, **R.R. Vivès**, A. Seffouh, N.A. Afratis, A. Oosterhof, T.H. van Kuppevelt, N.K. Karamanos, M. Metintas, A. Hjerpe, K. Dobra, T. Szatmári. "Syndecan-1 alters heparan sulfate composition and signaling pathways in malignant mesothelioma". Cell Signal. 27, 2054-67 (2015).

- A. Seffouh, F. Milz, C. Przybylski, C. Laguri, A. Oosterhof, S. Bourcier, R. Sadir, E. Dutkowski, R. Daniel, T. H. van Kuppevelt, T. Dierks, H. Lortat-Jacob and **R. R. Vivès** : "HSulf sulfatases catalyses processive and orientated 6-O-desulfation of heparan sulfate that differentially regulates FGF activity". FASEB J. 27, 2431-9 (2013).

Requested domains of expertise (up to 5 keywords):

Protein expression – site directed mutagenesis – protein purification – enzyme assay