

**Master 2 internship project
Year 2020-2021**

Laboratory/Institute: IBS
Team: SAGAG/VIVES

Director: W. Weissenhorn
Head of the team: Romain Vivès

Name and status of the scientist in charge of the project: Romain Vivès **HDR:** yes no
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Program of the Master's degree in Biology:

- Immunology, Microbiology, Infectious Diseases Integrative Structural Biology
 Physiology, Epigenetics, Differentiation, Cancer Neurosciences and Neurobiology
 Planta International

Title of the project:

Structural 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 two 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 structural features of the Sulfs that determine the substrate specificities of each isoform.

Methods (up to 3 lines):

Enzyme and enzyme domains will be expressed recombinantly in mammalian cells or bacteria, and purified by chromatography techniques. Characterization will involve biochemical enzyme assays, binding experiments (SPR, ELISA..) and biophysical approaches (NMR, crystallogenesiss assays...).

Up to 3 relevant publications of the team:

- R. El Masri, Y. Créton, E. Gout and **R.R. Vivès**. "The Sulfs in inflammation: first steps in uncharted territories". Front. Immunol. 3:570 (2020).

- A. Seffouh, R. El Masri, O. Makshakova, E. Gout, Z.el Oula Hassoun J.P. Andrieu, H. Lortat-Jacob and **R.R. Vivès**. "Expression and purification of recombinant extracellular sulfatase HSulf-2 allows deciphering of enzyme sub-domain coordinated role for the binding and 6-O-desulfation of heparan sulfate". Cellular and Molecular Life Sciences, 76, 1807-1819 (2019).

- 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 – protein purification – enzyme assay – NMR – crystallogenesiss