**Master 2 internship project**

**Year 2024-2025**

**Laboratory/Institute:** IBS **Director:** Winfried WeissenHorn

**Team:** SAGAG-VIVES **Head of the team:** R. VIVES

**Name and status of the scientist in charge of the project:** R. VIVES

**HDR: yes ☑ no ☐**

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**Program of the Master’s degree in Biology:**

**☑** Microbiology, Infectious Diseases and Immunology **☑** Structural Biology of Pathogens

**☐** Physiology, Epigenetics, Differentiation, Cancer **☐** Neurosciences and Neurobiology

**Title of the project:**

**Post-synthesis mechanisms regulating the structure and activity of Cell-surface heparan sulfate**

Objectives (up to 3 lines):

The project aims at studying the activity of 2 extracellular enzymes targeting heparan sulfate (HS) polysaccharides and their role during tumor development and pathogen infection.

Abstract (up to 10 lines):

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 activity of 2 extracellular HS-targeting enzymes and their possible synergetic action in disease, such as tumor progression and pathogen infection. This study should provide significant insights into these major regulation systems of HS activities, and for the design of new HS-based inhibitors for therapeutical approaches.

Methods (up to 3 lines):

The project will include recombinant expression of proteins (eukaryotic cell culture, transfection, chromatography), enzymology, HS analysis, structural and biophysical characterization (MP, MALLS, SPR, BLI…), and functional studies (in vitro and cellular assays).

Up to 3 relevant publications of the team:

N. Veraldi, R.R. Vivès, G. Blanchard-Rohner, A.G. L’Huillier, N. Wagner, M. Rohr, M. Beghetti, A. de Agostini and S. Grazioli. “Endothelial glycocalyx degradation in multisystem inflammatory syndrome in children related to COVID-19” J Mol Med, 100, 735-746 (2022).

R. El Masri\*, A. Seffouh\*, C. Roelants, I. Seffouh, E. Gout, J. Pérard, F. Dalonneau, K. Nishitsuji, F. Noborn, M. Nikpour, G. Larson, Y. Crétinon, M. Friedel-Arboleas, K. Uchimura, R. Daniel, H. Lortat-Jacob, O. Filhol and R.R. Vivès. “Extracellular endosulfatase Sulf-2 harbours a chondroitin/dermatan sulfate chain that modulates its enzyme activity” Cell reports, 38, 110516 (2022).

C. Marques, J. Poças, C. Gomes, I. Faria-Ramos, C.A. Reis, R.R. Vivès and A. Magalhães . “Exostosin-like 2 and Exostosin-like 3 cellular balance dictates Heparan Sulfate biosynthesis and shapes cancer cell motility and invasion” J. Biol. Chem. 298, 102546 (2022).

Requested domains of expertise (up to 5 keywords):

Cell culture, protein purification, western-blot, ELISA