**Master's degree in Biology – Chemistry-Biology Department**

# Master 2 internship project
# Year 2026-2027

**Laboratory/Institute:** IBS
**Director:** Winfried Weissenhorn
**Team:** SAGAG/VIVES
**Head of the team:** Romain Vivès

**Name and status of the scientist in charge of the project:**

Romain Vivès, DR1 CNRS

**HDR: yes** ☒ **no** ☐

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

☐ Microbiology, Infectious Diseases and Immunology ☐ Biochemistry & Structure
☐ Physiology, Epigenetics, Differentiation, Cancer ☒ Neurosciences and Neurobiology

**Title of the project:**

**Deciphering the Role of Heparan Sulfate Remodeling by Sulf Endosulfatases in VEGF-Mediated Endothelial Functions**

Objectives (up to 3 lines):

Objectives of the project are to clarify the role of Sulf in the regulation of VEGF activity and to identify potential specificities of vascular versus brain endothelial cell response to VEGF.

Abstract (up to 10 lines):

Brain function depends on a highly specialized vascular network that ensures oxygen and nutrient delivery, protects against neurotoxic molecules through the blood–brain barrier (BBB), and facilitates waste clearance. Vascular endothelial growth factor (VEGF) is a key regulator of vascular biology and angiogenesis, with important roles in neurobiology. VEGF displays dual and context-dependent effects: it promotes neuroprotection through direct actions on neural cells and progenitors, as well as through improved vascular support. However, excessive VEGF signaling increases vascular permeability, disrupts BBB integrity, thereby contributing to pathological conditions such as demyelinating diseases. The endothelial glycocalyx is a critical regulator of vascular homeostasis and angiogenesis. Heparan sulfates (HS) is major glycocalyx components that regulate cell adhesion, chemokine recruitment, and growth factor signaling. However, the functional specificities of HS in vascular versus brain endothelial cells remain poorly understood. This project aims to investigate how HS-modifying Sulf extracellular endosulfatases specifically regulate HS-dependent VEGF activity in vascular and brain endothelium. This study will provide new insights into HS-dependent regulation of VEGF responses and endothelial specialization.

Methods (up to 3 lines):

Sulf will be produced recombinantly using protocols established in the lab. Effect of Sulf on VEGF/HS interaction will be assessed in vitro using biophysical techniques such as biolayer interferometry. We will

then use HUVEC and hCMEC/D3 as cell models, to assess the impact of Sulf on VEGF signaling, migration, tube formation, and endothelial barrier integrity.

Up to 3 relevant publications of the team:

B.B. Timm, J.L. Follmar, R.N. Porell, S.D. Vallet, K. Glass, B.E. Thacker, C.A. Glass, P. Gordts, R.R. Vivès and K. Godula. "Human Sulfatases Use Dual Mechanisms to Control Growth Factor-Heparan Sulfate Interactions". ACS Chem Biol. 21, 1585-1594. doi: 10.1021/acschembio.6c00368. (2026)

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).

A. Kerever, F. Nagahara, K. Keino-Masu, M. Masu, T.H. van Kuppevelt, R.R. Vivès, and E. Arikawa-Hirasawa. "Regulation of fractone heparan sulfate composition in young and aged subventricular zone neurogenic niches". Glycobiology, 31, 1531-1542 (2021).

Requested domains of expertise (up to 5 keywords):

Glycobiology, cell signaling, enzymology, cell assays