M1-Molecular and Cellular Biology (MCB)
Internship Proposal Form
Chemistry-Biology Department

(Deadline Friday 15th December 2023)

Laboratory Address and Affiliation:

IBS, UMR 5075 CEA-CNRS-UGA
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CS 10090
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France

Laboratory/Team Research area (Keyword)

SAGAG-VIVES team : polysaccharides – enzymes – Structural biology – Cancer

Summary of the Proposed Internship Project (10 lines)

Title: Regulation of Glycan structures in tumor progression

DESCRIPTION:

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. In cancer, its structure and binding properties are altered, promoting tumour progression and metastasis. Two major actors of this process are the extracellular pro-oncogenic enzymes Heparanase and Sulf. Although these enzymes have been thoroughly studied individually, potential concerted action or synergetic activities have never been investigated. This project aims at comparing the individual or combined effects of these enzymes on HS structure, first in vitro, using ELISA-base assays, then in functional cell assays. This study should provide significant insights into this major regulation system of HS activities, and its contribution in cancer.

Methodologies and/or Techniques to be used

The project will involve a large array of biochemical techniques (recombinant protein expression, WB, HPLC…), in vitro assays (ELISA, enzyme assays…), cell culture and cell assays (cell migration, cell proliferation, FACS).

Person to contact:

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Proposal Form send as a PDF file to: sabrina.boulet@univ-grenoble-alpes.fr

File has to be named as: name-Internship-M1-MCB-2023-2024.pdf

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Additional information

3 publications related to the project:

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, 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).

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).