

INTERNSHIP PROPOSAL

Institute and Group : IBS – SAGAG group

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Research project title:

Identification of enzyme complexes involved in Heparan sulfate biosynthesis

5 Keywords to describe the project:

Proteomic, protein complex, immunopurification, cell culture, Golgi extraction

Description of the project (aims, experimental techniques, recommended background):

Heparan sulfate (HS) is a complex polysaccharide of the glycosaminoglycan (GAG) family, ubiquitously present on cell surfaces and within extracellular matrices. HS influences, through interactions with various proteins, embryonic development as well as adult physiology and pathological conditions (cancer, viral infections, Alzheimer disease,...). These interactions depend on HS structure, which is largely determined during biosynthesis by Golgi enzymes. HS is synthesized in the Golgi network through complex, concerted action of several distinct enzymes, and how these enzymes organize this machinery is far from fully understood.

Our goal is to characterize the nature and the organization of these enzyme complexes by the combination of affinity purification and mass spectrometry (MS), a powerful tool for studying protein-protein interaction. It will be necessary to determine the best strategies to prepare enzymes or enzymes complex samples for MS analysis. This work, which is challenging, could decipher, in the cellular context, the supramolecular organization of enzyme complexes involved in biosynthesis of HS.

Justification that the internship's subject fits with the general theme of GRAL:

This project strengthens and broadens the study supported by Labex Gral. Here, we propose to identify the Golgi enzymes complex involved in HS biosynthesis, in collaboration with Yohann Couté from Edyp (CEA-BGE) for MS.

Relevant publications of the team:

Connell B, Sadir R, Baleux F and Lortat-Jacob H. Heparan sulphate differently regulates CXCL12 α and γ mediated chemotaxis through differential presentation to CXCR4. *Science Signaling* (2016) 9 : ra107

Pegeot M, Sadir R, Eriksson I, Kjellen L, Simorre JP, Gans P, Lortat-Jacob H. Profiling sulfation/epimerization pattern of full-length heparan sulfate by NMR following cell culture ¹³C-glucose metabolic labeling. *Glycobiology*. 25:151-156 (2015)

Saesen E, Sarrazin S, Laguri C, Sadir R, Maurin D, Thomas A, Imberty A, Lortat-Jacob H. Insights into the mechanism by which interferon- γ basic amino acid clusters mediate protein binding to heparan sulfate. *J Am Chem Soc*. 135 :9384-90 (2013)