PhD grant ANR CarboCHIPS

Design of biochips to study carbohydrate sequences within supramolecular assemblies by mass spectrometry

Keywords: Mass spectrometry, Glycosaminoglycans, Biochips, Ion mobility, Protein-carbohydrate interactions, Cellular extracts.

Laboratory: Laboratoire Analyse et Modélisation pour la Biologie et l'Environnement (LAMBE), CNRS UMR 8587. Université d'Evry-Paris Saclay
Building Maupertuis, 1er étage, Bd François Mitterrand 91025 EVRY CEDEX
http://www.lambe.univ-evry.fr
X: @LAMBE_UMR8587

Scientific context and objectives

This thesis proposal is part of the ANR CarboCHIPS project, which aims to design a direct coupling involving oligo-/polysaccharide- or peptide/protein-based biochips with mass spectrometry (MS)-based approaches. Glycosaminoglycans (GAGs) are anionic polysaccharides distributed ubiquitously in living organisms. Because of their wide variety of structures, GAGs have the ability to bind to numerous proteins (cytokines, growth factors, coagulation proteins, antibodies, etc.), modulating their activities. A number of data show that the disaccharide sequence and sulfation pattern of GAGs govern the specificity of their binding to proteins, fuelling the question of the existence of specific GAG sequences that govern their interactions and biological actions. Establishing structure/activity relationships therefore requires very detailed structural data. Unfortunately, since GAGs are not directly encoded by the genome, it remains difficult to obtain sequences that are well defined in size and motif, either by extraction from biological samples or by chemical synthesis. These limitations mean that we need to find alternative ways of deciphering these sequences.

Proposed approach and available resources

The introduction of a biochip-MS coupling aims to be able to selectively capture ligands in a complex mixture. This approach would therefore enable the enrichment with sequences of interest. These will then be released and analysed by MS. Initially, the grafting chemistry will be optimized according to the type of solid support, the immobilised biomolecules and the MS technique used for the analysis. Next, the different configurations will be evaluated on GAG-protein interaction models that have already been well described. Finally, the best conditions will be tested for establishing structure/activity relationships with a peptide library and, complex mixtures such as cell extracts or biological fluids. The laboratory has 7 mass spectrometers on site, 2 of which will be particularly used: a MALDI-TOF/TOF and a SELECT SERIES Cyclic IMS ion mobility instrument coupled with a DESI-XS source. The ANR CarboCHIPS project also includes two other partners: Dr Romain Vivès, SAGAG team (IBS, Institut de biologie Structurale, UMR UMR5075, CEA, CNRS, Université Grenoble Alpes, Grenoble) and Dr Sandrine Sagan, Biomolecules: analyses, molecular and cellular interactions team (LBM, Laboratoire des Biomolécules, UMR7203 CNRS/ENS – PSL/Sorbonne Université, Paris).

Applicant profile

The applicant should have a background in analytical chemistry or biochemistry and more particularly in mass spectrometry, and in biomolecules chemistry. Prior experience in MALDI mass spectrometry will be highly appreciated, and skills in glycochemistry and/or glycobiology would be an asset. The candidate should have a 5-year degree (Master 2 or engineering school) and evidences of scientific English skills (writing and oral communication). The candidate is expected to have good writing and

communication skills and an ability to work in a multidisciplinary team. Thoroughness, curiosity and autonomy are essential for this project.

Full description of the project can be accessed on adum.fr.

Expected starting date: 1st october 2024.
PhD supervisor: Cédric Przybylski (cedric.przybylski@univ-evry.fr).
PhD Co-supervisor: Régis Daniel (regis.daniel@univ-evry.fr).
Application process: Applications must be deposited on ADUM: https://adum.fr/candidature/
They must include a detailed CV, Master's grades (M1 and M2), one or two recommendation letters from direct supervisors (M1 and M2 internships) and a cover letter describing your motivations for the project.