PhD offer in Analytical Sciences applied to cyclopeptides for therapeutic purposes

Keywords: analytical sciences; cyclopeptides; liquid chromatography; capillary electrophoresis; ion mobility, mass spectrometry; isomers, peptide synthesis.

Project context:

The PhD thesis will be carried out within the framework of the ANR Dynamic Combinatorial Libraries of Cyclopeptides (DynaCycloP) involving 4 research institutes (Physical Chemistry and Chemistry of Life (CPCV) - Sorbonne University ; Laboratoire de Photophysique et Photochimie Supramoléculaires et Macromoléculaires (PPSM) - ENS Paris Saclay; Institut de Chimie Organique et Analytique (ICOA) - Université d'Orléans; Institut des Biomolécules Max Mousseron (IBMM) - Université de Montpellier).
The DynaCycloP project aims to develop an innovative, cost-effective strategy for rapid access to large libraries of cyclic peptides with defined, biologically stable conformations. Dynamic combinatorial chemistry will be used as a tool to graft amino acid side chains onto a peptide backbone of defined 3D structure, enabling the synthesis and screening of numerous structured peptides in a single step. New analytical and synthetic methods for deconvolving mixtures of multivalent compounds in a dynamic library (or DCL) will be developed. This original method should provide easy access to large libraries of structurally sophisticated peptides that are not genetically encodable and drive the discovery of new peptide leads to target processes that are currently little exploited. The method will be applied to the screening of glycosaminoglycan ligands for the development of new cell targeting and vectorization strategies.

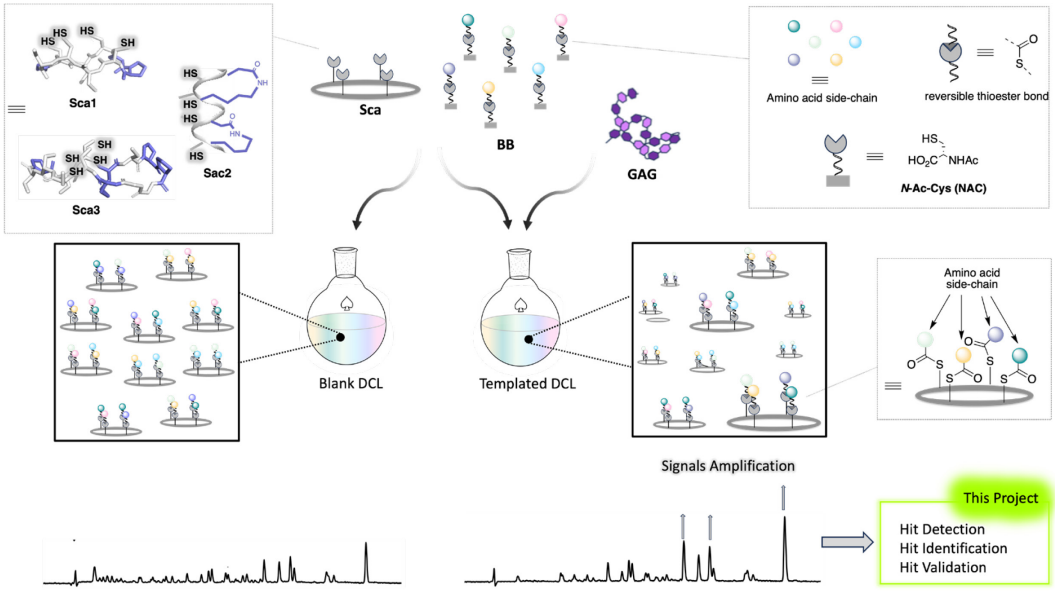

Figure 1. Principle of the DynaCycloP project: dynamic exchange of side chains between cyclopeptides folded into a 3D functional structure (Sca) and a thioester building block (BB). Amplification by glycosaminoglycans (GAGs), targets of biological interest for targeted cellular therapies. Illustration of amplification by HPLC signal monitoring.

Thesis topic:

By joining the DynaCyloP project, you will develop original and innovative analytical approaches using ultra-high performance liquid chromatography, capillary electrophoresis, ion mobility hyphenated with mass spectrometry (MS, MS/MS) to separate and characterize highly complex DCL mixtures. In particular, the separation of different isomers will be a real analytical challenge.
The work will be structured around 4 experimental development tasks, including 3 complementary analytical tasks designed to resolve the complexity of the peptide mixtures obtained:

Task 1: Peptide synthesis
A model peptide library (DCL) will be synthesized (on which analytical developments will be carried out). The library will comprise 81 compounds, with up to 12 isomers among them.

Task 2: Development of LC-MS/MS methods
Development of innovative analytical methodologies for the resolution of complex isomeric mixtures of cyclic peptides, including innovative HPLC approaches such as the HILIC mode, with a view to their characterization by MS/MS.

Task 3: Development of capillary electrophoresis (CE) and CE-MS/MS methods
Development of innovative electrophoretic (CE) analytical methodologies complementary and orthogonal to HPLC for the resolution of complex isomeric mixtures of cyclic peptides with a view to their characterization by MS/MS.

Task 4: Development of ion mobility (IM) and IM-MS methods
Development of ion mobility (IM)/MS analytical methodologies. Ion mobility is a complementary approach to previous techniques (HPLC, CE), enabling isomers to be discriminated in the gas phase.

In view of the large number of analytical results generated, considerable data processing work will also be required.

Profile required:

We're looking for a student with a passion for analytical sciences and a Master degree (or future Master degree) in the field. The candidate must have significant experience in analytical development in separative techniques (liquid chromatography, capillary electrophoresis) and/or mass spectrometry. Knowledge/experience and an interest in organic synthesis is also a prerequisite for this thesis project. If you have skills in hyphenation of separative techniques (chromatography and/or capillary electrophoresis) with mass spectrometry and/or peptide synthesis chemistry, this will be a valuable asset. Your ability to work independently, your creativity and your motivation to take on complex scientific challenges will be highly appreciated.

Start and duration of thesis:
October 1, 2025 - September 30, 2028.

Organizational particularities:
As part of the DynaCycloP project, a 6-month mobility to Paris (Laboratoire Chimie Physique et Chimie du Vivant - CPCV, Sorbonne Université) is required during the first year of the thesis for the synthesis of cyclopeptides.

Scientific, material & financial conditions of the research project:
ANR funding (ANR-24-CE44-1605, DynaCycloP project "Bibliothèques Combinatoires Dynamiques de Cyclopeptides, Scientific leader: Mrs Roba Moumné).
The candidate will participate in the various progress meetings of the ANR project. He/she will be required to present his/her results to the various members of the ANR consortium.
The candidate will benefit from the team's own separative analytical facilities (5 EC, 2 UPLC) and will have full access to the analytical facilities of the Balard Institute's Plateforme d'Analyses et Caractérisations research support unit (Synapt G2-S ion mobility coupled to mass spectrometry, Orbitrap high-resolution mass spectrometer).
The candidate will have the opportunity to present his/her research work as oral communications at recognized international conferences in particular dedicated to analytical sciences (HPLC, MSB ...).

How to apply :
If this thesis opportunity inspires you and you aspire to contribute to cutting-edge research in the field of analytical sciences and peptides of therapeutic interest, we invite you to send your application including your CV, a cover letter describing your interest in the project, as well as your transcripts and the contact details of a referee, to the following e-mail addresses before April 30, 2025.

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