

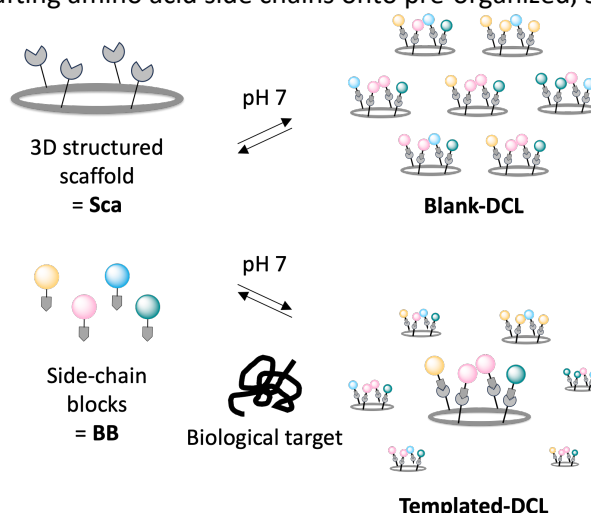
Master 2 Internship in Chemical Biology CPCV- Sorbonne Université - Paris

Dynamic Combinatorial Chemistry for the Discovery of Bioactive Cyclopeptide

Position Details: 6-month internship in Chemical Biology in the CPCV research unit (UMR CNRS 8228) at Sorbonne Université, under the supervision of Dr. Roba Mourné, January–July 2027. The CPCV laboratory (<https://cpcv.chimie.ens.fr/>) is a joint research unit of Sorbonne Université, École Normale Supérieure de Paris, and CNRS. It is located on the Jussieu Campus, in the heart of Paris's Latin Quarter. This internship is part of the ANR-funded DynaCycloP research project (ANR-24-CE44-1605; 2025–2028).

Keywords: Peptide Chemistry, Dynamic Combinatorial Chemistry, Protein-Protein Interactions.

Research Program: Cyclic peptides are promising candidates for targeting challenging molecular interfaces,¹ yet their identification is still limited by screening constraints.² In our group, we address this challenge using target-directed dynamic combinatorial chemistry.³ By dynamically grafting amino acid side chains onto pre-organized, 3D cyclic scaffolds^{4,5} or stapling linear peptides⁶, we generate adaptive libraries of cyclic candidates. In the presence of a biological target, these libraries self-select: the best binders are amplified and directly identified. (Figure 1) We demonstrate the potential of these approaches using the p53–hDM2 interaction, thereby highlighting their relevance in the discovery of modulators of therapeutically relevant protein-protein interactions. In this project we wish to extend these approaches to glycosaminoglycans (GAG), biologically relevant target in the field of cell-targeting therapies. These highly charged polysaccharides involved in cell adhesion, signaling and molecular recognition are attractive targets for the development of cell-targeting strategies, but their structural complexity and repetitive nature make the discovery of selective ligands challenging.



The intern will contribute to the synthesis and characterization of amino acid building blocks and cyclic peptide, the generation and characterization of dynamic combinatorial libraries as well as their target-directed selection, and the identification and study of amplified binders. The work will combine **peptide chemistry, dynamic combinatorial chemistry, analytical characterization**, biophysical and cellular studies.

Highly motivated candidates with a strong background in organic chemistry and a keen interest in working at the interface between chemistry and biology should send their **CV, cover letter, and undergraduate (L3) and first-year Master's (M1) transcripts** to roba.mourné@sorbonne-universite.fr. Applications from candidates interested in pursuing a PhD after the internship, and in particular in applying for PhD funding, are particularly welcome.

References:

¹ Zorzi, A. et al [Cyclic Peptide Therapeutics: Past, Present and Future](#). *Curr. Op. Chem. Biol.* **2017**, 38, 24. ² Zhang et al [High-Throughput Screening of Stapled Helical Peptides in Drug Discovery](#). *J. Med. Chem.* **2023**, 66, 95.; ³ Rodrigues, A.; Rocard, L.; Mourné, R. [Peptide and Peptidomimetic Assemblies in Dynamic Combinatorial Chemistry](#). *ChemSystemsChem* **2023**, e202300011; ⁴ Zagiél, B.; Peker, T.; Marquant, R.; Cazals, G.; Webb, G.; Miclet, E.; Bich, C.; Sachon, E.; Mourné, R. [Dynamic Amino Acid Side-Chains Grafting on Folded Peptide Backbone](#). *Chem. Eur. J.* **2022**, e202200454; ⁵ Peker, T.; Zagiél, B.; Rocard, L.; Bich, C.; Sachon, E.; Mourné, R. [Analytical Tools for Dynamic Combinatorial Libraries of Cyclic Peptides](#). *ChemBioChem* **2023**, e202300688; ⁶ Rodrigues, A.; Coll, J. G.; Ravault, D.; Zagiél, B.; Carlier, L.; Rocard, L.; Mourné, R. [Target-Directed Stapled Peptides through Dynamic Combinatorial Chemistry](#). *under review*, preprint on ChemRxiv.