Stage in Organic Chemistry- Level Master 2 or equivalent-

Pin1 Degradation as Therapeutic Approach to Multiple Myeloma

Institution: CY Cergy Paris Université
Research Unit: BioCIS, *Equipe de Chimie Biologie* – UMR 8076
M2 Supervisor: Dr. Chiara ZANATO
Period: January 2027 – July 2027 (6 months)
Application Deadline: Open until filled

Context and Project Objectives: Multiple Myeloma (MM),[1] a haematological malignancy of plasma cells, remains largely incurable due to persistent drug resistance and disease relapse, highlighting the urgent need for innovative therapeutic targets and strategies. Pin1, a small protein belonging to the Peptidyl-Prolyl *cis-trans* Isomerase family, has emerged as a pivotal oncoprotein implicated in the pathogenesis of various tumours.[2] Recent studies emphasise Pin1's critical role in driving resistant MM progression.[3] Despite its compelling oncogenic role, Pin1's small and shallow enzymatic pocket pose significant challenges for conventional drug design, limiting the development of effective inhibitors. To address these obstacles, we propose leveraging Targeted Protein Degradation (TPD).[4] This innovative approach, which has revolutionised chemical biology and drug discovery in recent years, offers a promising strategy to therapeutically target previously "undruggable" proteins such as Pin1. This project aims to develop Pin1 degraders to selectively eliminate this protein, addressing both drug resistance and disease relapse in MM. In addition, Pin1 degraders will serve as valuable tools to further investigate the role of Pin1 in MM progression and the emergence of drug resistance.

Job Description: during this interdisciplinary stage the M2 student will work on the development of Pin1-degraders. This will include the organic synthesis and the biological evaluation of the synthesised molecules. It represents an excellent opportunity for the successful candidate to build a solid foundation in organic chemistry while also acquiring critical interdisciplinary skills in cell biology. The student will benefit from a stimulating research environment within a young and dynamic Team with diverse international backgrounds and strong expertise in the design and development of bioactive molecules and chemical biology.

Candidate's Requirements*:* The candidate must have a very good theoretical knowledge of organic chemistry as well as of the methods of analysis and characterisation of organic compounds. We are looking for a student interested in a multidisciplinary project, at the interface between chemistry and biology, who is passionate for organic synthesis. A good level of English is envisaged.

To apply: send CV and Master degree marks/evaluation to chiara.zanato@cyu.fr

References:

[1] M. Mohty, *et al. Nat Rev Dis Primers* **2024**, *10*, 45.
[2] A. Matena, *et al. Biol. Chem.* **2018**, *399*, 101 .
[3] a) Y. Meng *et al. Cancer Gene Ther* **2025**, *32*, 22; b) C. Zanato *et al., Chem. Commun.*, **2025**, *61*, 5774.
[4] B. L. Ebert *et al. Nat Rev Mol Cell Biol* **2024**, *25*, 740.