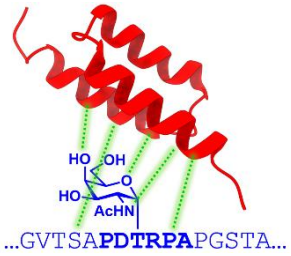
Fully-funded PhD position in Chemical Biology (3 years)

Start date: October 2024

Discovery and total chemical synthesis of D-proteins for the molecular targeting of tumor glyco-epitopes

Laboratory: Center for Molecular Biophysics (CBM) CNRS UPR 4301, Orléans, France https://rb.gy/gzb0s5

Subject description: Synthetic D-proteins (entirely composed of D-amino acids and achiral glycine) hold an enormous potential for molecular targeting strategies thanks to their enhanced resistance towards proteolysis, and extremely low immunogenicity, when administered in living organisms. In addition, synthetic D-proteins of smaller size than monoclonal antibodies would benefit from enhanced *in vivo* biodistribution, while providing complete control over chemical conjugation of diverse moieties, providing next-generation tools for molecular imaging and drug delivery.



This multidisciplinary project involves the discovery and chemical synthesis of small D-proteins (≈ 6-7 kDa) capable of selectively binding glycopeptide epitopes from taMUC1, a clinically-relevant tumor-associated glycoprotein. The candidate will be in charge of the total chemical synthesis and characterization of glycopeptide targets as well as protein ligands, and will be involved in the phage display discovery process and in the structural characterization of the interacting complexes by X-ray crystallography. The project will be carried out in close collaboration with experienced scientists from the host laboratory: biologist and pharmacologist Dr. Séverine Morisset-Lopez, and structural biologist Dr. Franck Coste.

Keywords: Protein Chemical Synthesis; Affibody; Phage Display; Affinity Ligand Discovery; Crystallography

Applicant profile: Synthetic organic chemist interested to work at the interface of chemistry and biology. Experience in peptide synthesis and HPLC/LC-MS will be a plus. We are looking for a curious, self-motivated and goal-oriented researcher, committed to work in a pluri-disciplinary environment as a team player.

The host laboratory: CBM is a hallmark of interdisciplinary research in France. It accounts for ≈ 90 permanent scientists from physics, chemistry and biology disciplines. Broad range of state-of-the-art instrumentation, combined with multidisciplinary technical expertise make CBM a unique breeding ground to address fundamental biological questions and probe the limits of new concepts. Key instrumentation includes: NMR (400, 600 and cryoprobe 700 MHz), mass spectrometers (ion trap, MALDI-TOF, ultra-high-resolution Q-TOF), peptide synthesizers, HPLCs (preparative, semi-preparative, analytical, LC-MS, *etc.*), isothermal titration microcalorimetry, pipetting and crystallization robots, circular dichroism spectrometer, confocal microscopes, and more.

To apply, please send a CV, a cover letter, and the names of two referees to:

Dr. Vincent Aucagne (vincent.aucagne@cnrs-orleans.fr) and Dr. Carlo Pifferi (carlo.pifferi@cnrs-orleans.fr)

Application deadline: 10.04.2024

Applications will be considered upon their reception, do not wait until the last minute to apply!

Representative publications of the host research group:

► "Enzyme-cleavable linkers for protein chemical synthesis through solid-phase ligations" S. A. Abboud, M. Amoura, J.-B. Madinier, B. Renoux, S. Papot, V. Piller and **V. Aucagne***, *Angew. Chem. Int. Ed.* **2021**, *60*, 18612-18618; DOI: 10.1002/anie.202103768

► "A straightforward methodology to overcome solubility challenges for N-terminal cysteinyl segments in native chemical ligation" S. A. Abboud, E. Cisse, M. Doudeau, H. Bénédetti and **V. Aucagne***, *Chem. Sci.*, **2021**, *12*, 3194-3201; DOI: 10.1039/D0SC06001A

►"An efficient site-selective, dual bioconjugation approach exploiting N-terminal cysteines as minimalistic handles to engineer tailored anti-HER2 affibody conjugates" A. Novak, F. Kersaudy, S. Berger, S. Morisset-Lopez,* F. Lefoulon, **C. Pifferi*** and **V. Aucagne***, *Eur. J. Med. Chem.*, **2023**, *260*, 115747; DOI: 10.1016/j.ejmech.2023.115747

►"Development of synthetic, self-adjuvanting, and self-assembling anticancer vaccines based on a minimal saponin adjuvant and the tumor-associated MUC1 antigen" **C. Pifferi**, L. Aguinagalde, A. Ruiz-de-Angulo, N. Sacristán, A. Poveda, J. Jiménez-Barbero, J. Anguita and A. Fernández-Tejada, *Chem. Sci.*, **2023**, 14, 3501-3513; DOI: 10.1039/D2SC05639A