

Master 2 internship in Grenoble

Design of peptide nanoparticle conjugates for targeted therapy

The objective of this internship is to synthesize peptide compounds for their grafting onto nanoparticles, which can be used to detect or treat tumors with high degree of accuracy, whose applications could be surgical assistance or targeted therapy. This work will benefit from a collaboration with the *Département de Chimie Moléculaire* (DCM, UMR 5250, Grenoble) and *NH TherAguix* company (Grenoble), focusing on a potential CIFRE Ph D project.

Educational interest: The internship will allow the discovery of peptide synthesis, assembly by «click» chemistry (CuAAC, oxime ligation) to access polyfunctional macromolecules. The master student will develop skills in bioorganic synthesis, bioconjugation chemistry and characterization methods such as liquid chromatography and mass spectrometry. He will also explore biological applications for instance the targeted therapy increasingly used to treat cancer.

Abstract: Chemistry has been largely and successfully used in the last 20 years to design biomolecular compounds for numerous applications such as diagnostics and targeted therapies. In our research group, we develop peptide-based compounds and we have shown that some are very effective and selective for tumor targeting. These compounds, comprising a multimeric system with four copies of the cyclopentapeptide c(RGDfK), are a promising synthetic vehicle for optical-guided surgery¹ and drug delivery.² In parallel, we recently discovered new cyclopeptides that are able to target specifically lymphomas. Based on these results, we propose to develop peptide derivatives that contain chemoselective functions for functionalization of nanoparticles such as AGuix. The latter was developed by NH TherAguix company and are currently in clinical trials for cancer. RGD peptide grafting onto AGuix nanoparticles and its derivatives has already shown a great potential in improving targeting specificity and efficiency. Herein, we propose to graft tetrameric RGD compounds onto nanoparticles to enhance the tumor targeting. Comparison of the different constructs (mono RGD vs tetrameric RGD) will help determining their potential for clinical applications in targeted therapy and tumor imaging.^{3,4}

Approaches & equipment used: This master's internship will allow you to develop expertise in peptide synthesis and nanoparticle biofunctionalization. You will learn solid-phase peptide synthesis (SPPS), peptide modifications in solution (cyclization, fluorescent labeling), and their assembly using "click" chemistry. You will also gain proficiency in their characterization through UPLC-MS, as well as in nanoparticle biofunctionalization and characterization techniques such as DLS, Zeta potential, ICP-MS, and Biacore.

Period of the internship: 6 months starting in January 2025

The candidate must have a good knowledge in organic chemistry, previous experience in synthesis and an interest in Chemistry for Health.

To apply for this internship, you must send your CV and a cover letter to:

Dr Didier Boturyn : didier.boturyn@univ-grenoble-alpes.fr

Dr Léna Carmes : carmes@nhtheraguix.com

1. C. H. F. Wenk, F. Ponce, S. Guillermet, C. Tenaud, D. Boturyn, P. Dumy, D. Watrelot-Virieux, C. Carozzo, V. Jossierand, J.-L. Coll. Near-infrared optical guided surgery of highly infiltrative fibrosarcomas in cats using an anti- α v β 3 integrin molecular probe. *Cancer Lett.* **2013**, *334*, 188-195. DOI: 10.1016/j.canlet.2012.10.041
2. A. Borbély, F. Thoreau, E. Figueras, M. Kadri, J.-L. Coll, D. Boturyn, N. Sewald. Synthesis and Biological Characterization of Monomeric and Tetrameric RGD-Cryptophycin Conjugates. *Chem. Eur. J.* **2020**, *26*, 2602–2605. DOI: 10.1002/chem.201905437
3. J. Morlieras, S. Dufort, L. Sancey, C. Truillet, A. Mignot, F. Rossetti, M. Dentamaro, S. Laurent, L. Vander Elst, R. N. Muller, R. Antoine, P. Dugourd, S. Roux, P. Perriat, F. Lux, J.-L. Coll, O. Tillement. Functionalization of Small Rigid Platforms with Cyclic RGD Peptides for Targeting Tumors Overexpressing α v β 3-Integrins. *Bioconjugate Chem.* **2013**, *24*, 1584-1597. DOI: 10.1021/bc4002097
4. L. Carmès, phdthesis, Université Claude Bernard- Lyon I, 2024 (patent in progress).