

Ph.D. position (2024-2027)
Therapeutic peptides:
effectors, vectors, targets, and nanoparticles.
PhyMedExp Laboratories, Montpellier, France

Context. The **SMaRT** project (“**S**mart nanoparticles delivering siRNA to treat gastrointestinal stromal **T**umors) is funded by the **Inter-Disciplinary & In-Lab Graduate Program** of **Université de Montpellier** with 2 mirror PhD positions starting in 2024: one in Biology @PhyMedExp (UMR9214, P.I.: **Prisca BOISGUERIN**) and one in Chemistry @IBMM (UMR5247, P.I.: **Sébastien ULRICH**).

Overview of the project. Gastrointestinal stromal tumors (GIST) are the most common mesenchymal neoplasms of the gastrointestinal tract, showing increased resistance to conventional chemotherapy and radiotherapy. In this context, the design of **smart vectors of nucleic acids** that degrade in cells at the appropriate place and within the appropriate time scale is a major current challenge to develop novel potent therapeutics.

This Ph.D. project rests on our recent achievements in making smart pH-sensitive peptide conjugates as vectors of siRNA (ANR-funded project NanoCard, 2022-2025, manuscript in preparation). In this new project, we will tackle the engineering of **multi-dynamic peptide-based conjugates with improved sensitivity and controlled degradation**. The candidate will focus on establishing the in vitro and in vivo proof-of-concept for multiple siRNA-based protein silencing using smart nanoparticles to tackle GIST proliferation and apoptosis.

The work will involve the **evaluation of smart vector efficiency in GIST cells** (cell culture, Western blot, viability assay), the **mechanism** of cellular internalization and targeting (flow cytometry, confocal microscopy, endocytosis inhibition) and validation of the novel **GIST treatment in vivo** (chicken embryo and mouse models). A close collaboration with the mirror PhD in chemistry will contribute to this interdisciplinary project.

Host laboratory. The **PhyMedExp** Laboratories are devoted to research in muscle-based pathophysiology. In this context, we develop peptide-based nanoparticles for nucleic acid delivery to evaluate digest development and associated pathologies (see for instance: [Int J Mol Sci, \(2023\) 24\(8\):7138](#), [Biomedicines, \(2021\) 9\(5\):583](#), [J Nanobiotechnology \(2021\) 19\(1\):236](#), [Bioconjug Chem \(2019\) 30\(3\):592-603](#)).

Ph.D. candidate. You have recently graduated (M.Sc., Ecole d’Ingénieur) with excellent theoretical and practical knowledge in biochemistry or biology. You have a strong interest in the interface with chemistry, with a desire to learn and practice. You are a self-starter, working autonomously, willing to take initiative, and eager to work on a multidisciplinary project. You show a clear enthusiasm for research. You are a team player with very good communication skills. Knowledge of French would be useful but is not essential. Starting date: October 2024 (flexible), salary: ca. 2,100 €/month.

Interested? Applications to the **SMaRT** project must contain: 1) a cover letter, signed and dated, 2) a CV/resume, and 3) the transcripts of L3, M1, M2 with rankings should be emailed to idil-team@umontpellier.fr.

APPLICATION DEADLINE: 15 APRIL 2024, 2:00 pm. For more information, contact Dr. Prisca Boisguérin (prisca.boisguerin@inserm.fr).