PhD in Medicinal Chemistry

Synthesis and biological assessment of new antifungals targeting the Gwt1 enzyme involved in GPI anchor biosynthesis

Duration: 36 months

Start date: October 2025

Qualification: Master's level (M2)

Project description:

Invasive fungal infections (IFIs) pose a serious threat to immunocompromised patients, with mortality rates reaching 70%. The scarcity of effective antifungals and the increasing resistance—particularly to azoles—necessitate the development of new therapeutic strategies. The GPI anchor biosynthesis pathway, essential for fungal membrane integrity and virulence, offers a promising target. Manogepix, a Gwt1 enzyme inhibitor in this pathway, has shown strong antifungal activity and is currently in phase III trials as its prodrug, fosmanogepix. However, emerging resistance to manogepix calls for the discovery of novel Gwt1 inhibitors.

This doctoral project aims to design and synthesize innovative Gwt1-targeting antifungal agents, using manogepix as a structural template and integrating original pharmacochemical modifications. Leveraging the laboratory's expertise in heterocyclic chemistry, the project will focus on optimizing molecular affinity, selectivity, and resistance evasion. Molecular modeling and engineered yeast strains will support the design process, while biological evaluation will be conducted on clinical isolates, including resistant strains. Mechanistic studies and physicochemical profiling will guide preclinical development.

We are looking for a highly motivated Master's (M2) student in medicinal chemistry, organic chemistry, or chemical engineering, with strong theoretical and practical training in organic synthesis (heterocyclic chemistry, organometallic reactions, peptide coupling, purification and characterization techniques). Additional competencies in molecular modeling or basic biology will be considered strong assets. The ideal candidate is rigorous, dynamic, and collaborative, with strong communication abilities in both French and English. A genuine passion for drug discovery and medicinal chemistry is essential to contribute to this innovative antifungal project.

Required skills:

- ✓ Organic synthesis, medicinal chemistry
- ✓ Analytical chemistry (NMR, MS, HPLC, IR),
- ✓ English reading, writing, and speaking

Funding: Contrat Doctoral d'Etablissement (CDE)

Affiliated doctoral school: Ecole Doctorale Biologie Santé-ED 605, Collège doctoral des Pays de la Loire

Host Laboratory: UR 1155 IICiMed Cibles et Médicaments des Infections et de l'Immunité, Nantes Université, Institut de Recherche en Santé 2, 22 Boulevard Bénoni Goullin, 44200 Nantes, France.
Additional information can be found on our website: https://iicimed.univ-nantes.fr/fr/

Supervisors of the PhD project: Dr M-A BAZIN and Pr F. MORIO

Contact: Applications should be submitted as soon as possible to Dr. **Marc-Antoine Bazin** (marc-antoine.bazin@univ-nantes.fr) and must include a detailed CV, a cover letter, one or more references (including that of the M2 internship supervisor), as well as transcripts and class rankings for both M1 and M2.