



Post-doctoral position in organic chemistry

Key-words: quinazoline ; SAR Studies ; antibioresistance ; medicinal chemistry

Project: Fighting Antibiotic Resistance: Dual-target drug for new therapeutic strategies

Duration: 12 months, ideal starting date: January 2025

Funding: LabEx SynOrg project FARD

Salary: 3020 euros /month **before tax**

Location: COBRA, UMR CNRS 6014, Mont-Saint-Aignan, France. Rouen Normandy University

Context: The emergence of antimicrobial resistance (AMR) is a major threat to global health. A recent report indicates that there may have been 4.95 million deaths worldwide due to AMR in 2019 [1] and this figure is expected to increase to 10 million annually by 2050. Given that all species of bacteria are continuously mutating in response to the selective pressure of antibiotics leading to multidrug resistance and potentially untreatable disease, sustained research efforts are needed to develop novel ways of delivering effective treatments [2].

Project: Our collaborative project (France/Japan) aims to design new compounds as selective bacterial MATE-type transporter inhibitor and able to combine the biofilm destruction targeting drug-resistant bacteria [3]. From a synthetic point of view, we will synthesize new heterocyclic scaffolds derived from the hit compounds developed by our research group and our Japanese partners. The capacity of these new scaffolds to inhibit selectively MATE-type transporter and then tackle antibioresistance will be evaluated by dedicated platforms. Full SAR studies will be conducted by chemical transformations at all parts of the targeted molecular structure, with a constant emphasis on the application of efficient and sustainable processes.

Candidate profile: We are looking for a dedicated, experienced and highly motivated candidate with excellent communication skills as well as an open mind towards biological applications. Depending on the progress of the project, the student may have the opportunity to spend 1 month in Japan.

The candidate should have :

- ✓ A Ph.D. in organic or medicinal chemistry with high motivation to work in an interdisciplinary project at the interface of chemistry and biology
- ✓ Strong skills in multi-step synthesis, purification techniques and product characterization.
- ✓ Ability to conduct independent research and demonstrate open-mindedness, curiosity and organization
- ✓ English written and oral communication skills

Application: Application review will begin immediately and will continue until the position is filled. Applications should be sent by e-mail and should include a cover letter and a detailed CV (Master grades, summary of the project results PhD/Post-doc, publications). At least one letter of recommendation is required, sent from the referees to Prof. Fruit and Prof. Besson or contact details of two referees.

Contact: Pr Corinne FRUIT (corinne.fruit@univ-rouen.fr) ; Pr Thierry BESSON (thierry.besson@univ-rouen.fr). Our research group (<https://www.lab-cobra.fr/equipes/heterocycles/>) has extensive experience in the synthesis and functionalization of fused quinazoline derivatives as bioactive compounds. (see : *Synthesis* **2023**, *55*, 3670. *Catalysts* **2021**, *11*, 28. *Catalysts* **2020**, *10*, 483. *Molecules* **2018**, *23*, 2181. *Org. Lett.* **2016**, *18*, 3282. *Org. Lett.* **2015**, *17*, 1700.)

[1] Murray, C. J. L. *et al.*, *Lancet* **2022**, *399*, 629.

[2] (a) Weingarth, M. *et al.*, *Nature* **2022**, *608*, 390. (b) Masič, P. *et al.*, *PLOS Biol.* **2020**, *18*, e3000819. (c) Gitai, Z. *et al.*, *Cell* **2020**, *181*, 1518; (d) Lewis, K. *et al.*, *Nature* **2015**, *517*, 455.

[3] (a) Otsuka, M.; Omote, M. *et al. Bioorg. Med. Chem.*, **2022**, *74*, 117042. (b) Otsuka, M.; Omote, M. *et al. Bioorg. Med. Chem.* **2024**, *99*, 117606.