

PhD fellowship in “Identification and characterization of the antibacterial activity of new pyrimidine derivatives” at CMD-COAT SA in collaboration with the GIGA Biomedical Research Institute, University of Liège, Liège, Belgium

The PhD is part of the EU funded “Cell Envelope Anti-bacterials” Doctoral Network (CLEAR)

The CLEAR Doctoral Network

The discovery of penicillin initiated the antibiotic era and saved millions from dying of life-threatening bacterial infections such as tuberculosis, and pneumonia. Antibiotics also paved the way for complex medical interventions such as organ transplants or cancer treatments. Today, these progresses are challenged by the world-wide spread of drug resistant bacteria no longer responding to antibiotic treatment. The effects of antibiotic resistance are already devastating with at least 1.2 million yearly deaths worldwide. The aim of the EU funded Doctoral Network “Cell Envelope Anti-bacterials” (CLEAR) is to train 10 PhD students to become outstanding researchers in the field of antimicrobial resistance (AMR). All projects are embedded in a tight and synergistic academic-industrial collaboration focusing on developing novel leads or alternative strategies to combat drug resistant bacterial pathogens.

The project

Cécile Oury research team discovered that the antiplatelet drug ticagrelor possesses bactericidal and anti-biofilm activity against a broad range of Gram-positive bacteria including major challenging antibiotic resistant pathogens such resistant Gram-positive bacteria such as methicillin-resistant *S. aureus* (MRSA). Ticagrelor is an orally active cyclopentyl-triazolopyrimidine antiplatelet drug acting by reversibly inhibiting the platelet P2Y₁₂ receptor. It has been approved for the prevention of myocardial infarction and stroke in patients with coronary artery disease. Since this discovery, clinical observations in large patient populations have demonstrated that patients on ticagrelor therapy have significantly reduced risk of bacterial infections as compared to patients taking similar antiplatelet drugs (clopidogrel or prasugrel). Due to its antiplatelet activity and related risk of bleeding, the administration of ticagrelor as antibiotherapy will hardly be possible in patients who do not need this treatment. The team therefore set out to find a way of exploiting the antibacterial properties of ticagrelor while ensuring the absence of its potentially harmful antiplatelet activity. They proceeded iteratively by synthesizing a series of pyrimidine derivatives, comprising ticagrelor metabolites, purines and pyrazolo-pyrimidines. Some of them possessed antibacterial properties without inhibiting platelets. The present project aims at selecting and characterizing the antibacterial activity of these compounds (patented by ULiège) as compared to ticagrelor using a broad panel of strains, and relevant murine infections models (bacteremia, implant infection, endocarditis). The mechanisms of action of selected compounds will be determined thanks to a collaboration with the University of Tuebingen (Germany).

CMD-COAT’s team

Cécile Oury, PhD, Research Director at the University of Liège and CEO of CMD-COAT SA has extensive expertise in platelet biology, infection, immunology and thrombosis, including the interactions between these processes. She has strong experience in mouse models of *S.*

aureus infection. The CMD-COAT's team also comprises experts in polymer chemistry and coating technologies. The company develops drug-releasing coatings to prevent infection and thrombosis of blood-contacting medical devices, such as catheters, pacemaker leads or prosthetic heart valves. The use of innovative antimicrobial agents causing no or limited resistance is being evaluated. www.cmd-coat.com

The institution

CMD-COAT SA is hosted in the GIGA Biomedical Research Institute of the University of Liège www.giga.uliege.be. GIGA is an interdisciplinary research center aiming at providing advanced medical solutions from cutting-edge academic research with a real impact on health. The PhD candidate will be registered at the Doctoral School of Pharmaceutical and Biomedical Sciences, Faculty of Medicine, University of Liège.

Required qualifications

- Master degree in biomedical, biological or pharmaceutical sciences. Please note that your master's degree must be equivalent to a Belgian master's degree (two years 120 ECTS/2 FTE MSc + 180 ECTS/3 FTE BSc).
- Enthusiasm for research
- Good English skills, written and spoken
- Collaborative, interactive mindset but capable of working independently
- Experience in pharmacology, cellular biology, or medical chemistry is of advantage

In addition, applicants will also be required to meet the MSCA Doctoral Network eligibility criteria, notably:

- You must not have resided or carried out your main activity (work, studies, etc.) in Belgium for more than 12 months in the 36 months immediately before the start of your employment at CMD-COAT. Compulsory national service, short stays such as holidays, and time spent as part of a procedure for obtaining refugee status under the Geneva Convention are not taken into account.
- You must not be in possession of a doctoral degree when starting your employment at CMD-COAT.

Applicants will only be considered for the position if they fulfill both of the above eligibility criteria.

Terms of employment

The position as PhD fellow is full time and lasts 3 years. It is funded by Horizon Europe and will start 1 February 2024 (or 1 April 2024 at the latest).

The employment is conditioned upon the applicant's successful enrolment as a PhD student at the Doctoral School at the Faculty of Medicine, University of Liège. This requires submission and acceptance of an application for the specific project to the Doctoral School. The PhD study must be completed in accordance with the Faculty's rules on achieving the degree.

Salary, pension and terms of employment are in accordance with the requirements from the European Commission related to the MSCA programme. The monthly salary is around 3,100 EUR (taxable) plus benefits in kind offered by the company. In addition, a mobility allowance (gross amount 600 EUR per month from the EU to CMD-COAT) and (if eligible) also a family allowance (gross amount 660 EUR per month from the EU to CMD-COAT).

Application procedure

Your application, written in English, must be submitted electronically by clicking “Apply now” below and should include the following documents in PDF format:

- Letter of motivation
- CV
- Master of Science diploma and transcript of records in the original language, including an authorized English translation if not in French
- Publication list
- Letters of reference (optional)

The deadline for applications is January 2, 23.59pm CET. Candidates will be assessed and short listed for interviews, which are supposed to take place from mid-January. All candidates will be informed of the outcome of their application.

For specific questions please contact cecile.oury@cmd-coat.com.