PHD POSITION: *Bioinspired synthesis of C-glycoconjugates by remodeling of the catalytic pocket of glycosidases*

Localisation: Rennes, Brittany, France

Host Institute: Rennes Institute of Chemical Sciences (ISCR), Team: Organic Chemistry & Interfaces (COrInt), UMR CNRS 6226

Supervision: Dr Laurent LEGENTIL (laurent.legentil@ensc-rennes.fr) and Dr Sylvain TRANCHIMAND (sylvain.tranchimand@ensc-rennes.fr)

Starting from: 1st of October 2026

Application deadline: 11th of March 2026

- *Please use the following link to apply: https://emploi.cnrs.fr/Offres/Doctorant/UMR6226-LAULEG-001/Default.aspx?lang=EN*

Description of the project: Galactofuranose (Gal*f*) is one of the most abundant hexofuranoses identified to date and has been found in the glycocalyx of certain microorganisms, often pathogens such as *Leishmania*, *Trypanosoma* or *Mycobacteria*[1,2]. As the Gal*f* scaffold is completely xenobiotic in mammals, it is an attractive target for new pharmacophore. Already, different families of alkyl *O*- and *S*-galactofuranosides have demonstrated growth inhibition against strains of *Mycobacteria* or *Leishmania* with micromolar minimum inhibitory concentration[3,4]. However, their therapeutic use is limited by high sensitivity to enzymatic or acidic hydrolysis. Replacing the *O*-glycosidic bond with a *C*-glycosidic bond not only improves activity but also enhances stability. We have already demonstrated the superior antimycobacterial and antileishmanial activity of a range of alkyl *C*-galactofuranosides.[5] Nevertheless, accessing such molecules requires toxic catalysts, multi-step syntheses or protecting group manipulations. Alternatively, eco-friendly routes have been reported but are limited to pyranosides. Thus, no selective synthesis of bioactive *C*-hexofuranoconjugates exists using eco-friendly procedures.
In this context, the thesis project will focus on developing environmentally friendly alternatives based on enzyme-catalyzed reactions under mild conditions in aqueous media. Already, glycoenzyme engineering has enabled tailoring glycoside hydrolases activity toward *O*- or *S*-glycosylation but not C-glycosylation.[6] The PhD project aims to overcome these limitations by creating a novel enzymatic reactivity: C-glycoligation. Specifically, we will engineer the catalytic pocket of an arabinofuranosidase by incorporating specific amino acids known to selectively activate the phenol ring, enabling C-glycosylation. This innovative approach will generate a diverse library of aryl C-furanosides for further biological evaluation against targeted microorganisms.

Methodology: During the thesis, the PhD student will produce and purify mutated enzymes using well-established molecular biology techniques within the host research team. The student will screen for the best mutants and reaction conditions to perform *C*-glycoligation on a model substrate before extending the strategy to other polyphenols.

Work environnement: The recruited PhD student will join the Organic Chemistry & Interfaces (COrInt) team at Rennes Institute of Chemical Sciences. The team focuses on designing and synthesizing molecules with High Potential for Innovation with applications in health and well-being, prioritizing sustainable chemistry. This thesis aligns with the team's Glycochemistry and Biocatalysis research axis, which combines organic chemistry and biochemical approaches to develop glycoconjugates of interest through biocatalytic synthesis strategies. The PhD student will work under the supervision of Dr Laurent Legentil (full-time CNRS researcher) and the co-supervision of Dr Sylvain Tranchimand (associate professor at the Rennes School of Chemistry). The project is funded by the French National Research Agency (ANR PRC 2025 ProSacc) and involves collaboration with a research group in Nantes (Unit in Biological Sciences and Biotechnology). The successful candidate will benefit from a dynamic and well-equipped research environment, including state-of-the-art analytical and synthesis tools (LC-MS, 600 MHz NMR, parallel synthesis platform). The enzymes will be produced in-house in our dedicated molecular biology laboratory, a unique facility within the Chemistry Institute.

Candidate Profile: The candidate must hold a Master's degree in organic chemistry, organic synthesis, or chemical biology, and demonstrate a strong interest in biotechnology, biochemistry, and/or molecular biology. A solid background in synthetic chemistry (theoretical and practical) and biomolecules chemistry is essential. Additional assets include: experience in multidisciplinary research and teamwork, familiarity with biocatalysis or glycochemistry (a plus), qualities such as the ability to work in a team or for multidisciplinary project would be an asset.

1. P. Peltier, *et al.*, *Carbohydr. Res.*, **2008**, *343*, 1897.
2. L.-P. David, *et al.*, *Org. Biomol. Chem.*, 2024, 22, 2395.
3. R Dureau, *et al.*, *Org. Biomol. Chem.*, **2015**, *13*, 4940.
4. M. Suleman, *et al.*, *Antimicrob. Agents Chemother.*, **2014**, *58*, 2156.
5. M. Kratochvil, Chemo-enzymatic and organic synthesis of C-galactofuranosides with parasitostatic activities, ENSCR, 2024.
6. Q. Pavic, *et al.*, *Chem. Commun.*, **2018**, *54*, 5550.

ENSCR
11, allée de Beaulieu - CS 50837 - 35708 Rennes Cedex 7
Tél. : (33) 02 23 23 80 00 - www.ensc-rennes.fr