

## Doctoral position: Biotechnology – Natural products

### Production of *tert*-butyl compounds by lichen-associated bacteria

Application: Doctoral position, 36 months from October 2018

Grant: Bourse ministérielle MNRET

Localisation: Equipe CORInt UMR CNRS 6226 ICR, Rennes – France

<https://iscr.univ-rennes1.fr/corint/>

Application deadline: 30th may of 2018



### Contexte

Natural products having a *tert*-butyl group are poorly represented (about 200 compounds described) and in particular those having a *tert*-butyl substituting an aromatic ring. They generally have an interesting bioactivity. These compounds can be produced by various organisms but they are mostly produced by bacteria.

Previous work has allowed the isolation of *tert*-butyl phenols from a lichen-associated bacterium belonging to Firmicutes. One of the produced compound, never previously identified as a natural metabolite, exhibited remarkable cytotoxic activities against cancer cell lines, with IC<sub>50</sub> around 2 μM. The toxicity could come from a mechanism of DNA damage recently highlighted (R. Pédeux, COSS, Rennes 1).

In this context, a multidisciplinary project describing the production of *tert*-butyl phenolic derivatives by lichen-associated bacteria will be conducted by the CORINT team. This research will provide a better understanding of the biosynthesis of these molecules and the structural diversity that may result. Our research team is one of the few groups in the world to have a library of lichen bacteria, which will also screen homologous bacteria to further expand this diversity.

### Mission

Our project will have a multidisciplinary approach including innovative strategies to produce these molecules using fermentation process, to carry out enzymatic studies, and to optimize culture media. Once the chemical structures will be characterized, their biosynthetic pathways but also their therapeutic potentials will be studied.

The first part of the project will concern the study of the production by fermentation of these *tert*-butyl phenols by the preselected bacterium. The idea is to control this production, to optimize it by varying the culture conditions, to determine the key precursors of the biosynthesis and to identify the enzymes responsible for this production. A complete sequencing of the genome of the bacterial strain will be considered in collaboration with the team of Pr B. Felden (Inserm, UR1) to better know the enzymatic machinery of this strain.

The second part will involve the obtention of a series of structurally close compounds by modifying the biosynthetic precursors (by supplementation in the culture media) and the culture media. We will also be able to use other bacteria from the CORINT team (about sixty lichen-associated bacteria available) to increase structural diversity. After carrying out various purification steps by chromatographic methods (flash chromatography, HPLC, CPC, etc.), a structural analysis of the compounds obtained will be made by various spectroscopic methods (IR, NMR, MS, etc.).

The third part will correspond to the submission of this library of compounds to the screening to determine their activities including cytotoxic against various mouse and human cancer lines (including lung cancer A549) and their putative ability to produce DNA damages. This part will be done in collaboration with the team of Dr. R. Pédeux (COSS, UR1).

### **Required skills for the pHD student**

The student must be coming from a Master 2 oriented towards the study of Natural Products or Biochemistry. Expertise in the use of analytical tools and structural identification will be required (NMR, HPLC, LC-MS, GC-MS, ...). Skills in molecular biology, enzymatic study, bio-informatics would be also appreciated.

### **Contact:**

Candidates must send their CV, a letter of motivation and two contacts of reference persons by e-mail.

Mails: [sylvain.transchimand@ensc-rennes.fr](mailto:sylvain.transchimand@ensc-rennes.fr) ; [sophie.tomasi@univ-rennes1.fr](mailto:sophie.tomasi@univ-rennes1.fr)

Application on [theses.u-bretagne-ouest.fr](http://theses.u-bretagne-ouest.fr) 3m before April.