POST-DOC FELLOW PROPOSAL

2025-2026

12 months

DEciphering the molecular COmplexity of DErived-products of bacteria (DECODE)

Laboratories:

Laboratoire LCP-A2MC (Laboratoire de Chimie et Physique – Approche Multi-échelles des Milieux Complexes), Université de Lorraine, Metz, France

Laboratoire DynAMic (Dynamique des Génomes et Adaptation Microbienne) INRAE-Université de Lorraine, Nancy, France

Principal Investigators: Prof. Vincent Carré (LCP-A2MC), Prof. Bertrand Aigle (DynAMic)

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Starting date: between October and December 2025

Salary: 2040 € Net Salary

(LUE grant – B4B program, WP1: Discovering and production of active biomolecules and extracts)

PROJECT DESCRIPTION

Context

Microbial genome sequencing has unveiled numerous cryptic specialized metabolite gene clusters, most of which remain unexpressed under standard cultivation conditions. These clusters are believed to encode a wide variety of biologically active natural products, but their activation often requires specific environmental stimuli. For instance, changes in nutrient availability, co-culturing with competing species, or exposure to signaling molecules can trigger the expression of these latent metabolic pathways.

In addition, the discovery of novel natural products remains challenging due to the chemical and biological diversity of samples. To address this, untargeted metabolomics has emerged as a powerful tool. This approach enables the comprehensive measurement and analysis of all detectable metabolites within a sample, a way for the identification of previously unknown compounds.

Current technologies are in full development to decipher such complex metabolomic samples. Tandem analytical techniques are becoming increasingly common, including hyphenated methods that combine one separation method such as liquid chromatography and a detection system. As a detector, high-resolution mass spectrometry (HRMS) capable of working in tandem mass spectrometry (MS/MS) has emerged as a powerful analytical tool to partly elucidate the structural complexity of bioactive compounds. Indeed, fragmentation data

can be used to annotate features by querying natural product databases and searching MS/MS feature similarities. However, the identification confidence of metabolites such as isomers may remain low or even unsuccessful because of the numerous non-elucidated isomers. Recently, the implementation of ion mobility (IM) system on LC-MS/MS adds an unrivalled potential of separation of such compounds as it discriminates their collision cross section value in a specific gas (CCS_{gaz}), an orthogonal feature to LC and MS. This is a novel indicator, linked to the gas phase structure of the metabolites, that improve the identification level of natural compound.

Objectives & approaches

The aim of the project is to develop a specific workflow on the new LC-IM-MS/MS system of the Université de Lorraine (LC-timsTof Pro 2) to accelerate the discovery of new therapeutic candidates by facilitating comprehensive chemical profiling of microbial strains. As a proof of concept and for methodology development, the project will initially focus on well-characterized compounds produced by *Streptomyces ambofaciens* before being extended to the discovery of novel bioactive compounds from this strain, especially those involved in an antiproliferative activity observed in specific culture conditions.

RESEARCH TEAM & EQUIPMENTS

The post-doctoral fellow will integrate the Sustainable Chemistry and Environment team of the LCP-A2MC lab (UR4632 Université de Lorraine). His/her research will be based at Metz (France) and will regularly exchange with the DynAMic Lab (Nancy) for microbial assay and sample preparation. The post-doctoral fellow will be mentored by Prof. Vincent CARRÉ (LCP-A2MC) who is a specialist in developing new bioanalytical and biochemistry approaches by high resolution mass spectrometry technique and Prof. Bertrand AIGLE (DynAMic) who is a specialist in microbiology, genomics and specialized metabolism of Streptomyces.

Material

The LC-IM-HRMS/MS instrument is installed at the MassLor platform (LCP-A2MC, Metz) – Tims-TOF Pro2 (Bruker) with UPLC Elute
Softwares adapted for data metabolomic monitoring are accessible.
Strepromyces strains and cell culture room equipment's are present in the DynAMic Lab.
Other MS instruments available at the MassLor plateform will also be accessibles such as an FT-ICR MS (Solarix 7T 2xR, Bruker)) and another LC-MS/MS system (Ultimate 3000 Velos Pro, Thermoscientific).

Additional human ressources (technical and scientific support)

LCP-A2MC:
Jasmine HERTZOG et Lionel VERNEX-LOSET (Research Engineers of the MassLor platform) and Prof. Patrick CHAIMBAULT (LC-MS)
DynAMic:
Laurence HOTEL (Assistant Ingineer, genetics and microbiology)

Location of the LCP-A2MC:

Laboratoire de Chimie et de Physique Approche Multi-échelles des Milieux Complexes (LCP-A2MC)
Institut de Chimie Physique et Matériaux (ICPM)
1 Boulevard Arago
57070 METZ
http://lcp-a2mc.univ-lorraine.fr/

EXPECTED PROFILE OF THE CANDIDATES AND HOW TO APPLY

Candidates will have received a PhD in Mass Spectrometry for biology purpose. They will be familiar with the technique of IMS-MS2 and metabolomic workflow. Applied knowledge in microbial ecology or microbial metabolomics will be a plus. The candidate must have good human skills and be able to write reports and publications in English.
To apply: send your Curriculum Vitae (your most recently updated C.V. including list of publications, a Cover Letter, Statement of Research before the 10th of September 2025 at the address: vincent.carre@univ-

lorraine.fr. Selected applicants will be interviewed by an Ad Hoc Commission by the middle of September 2025/beginning of October 2025.