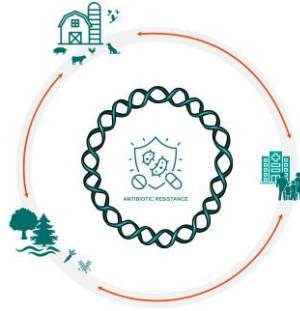


# MASTER BIOINFORMATIQUE

## Master Internship offer M2



### **Internship supervisors and host laboratory**

**Supervisor:** Coluzzi Charles (Professeur Junior, Université de Lyon, charles.coluzzi@univ-lyon1.fr)

**Host laboratory:** Laboratoire de Biométrie et Biologie Evolutive (LBBE), 43 boulevard du 11 Novembre 1918, Villeurbanne <https://lbbe.univ-lyon1.fr>

### **Research project title:**

***Detection of antibiotic resistance plasmids in environmental metagenomes.***

### **Project description:**

Antimicrobial resistance (AMR) has emerged as one of the leading public health threats around the world. The spread of antimicrobial resistance can be largely attributed to the dissemination of antibiotic resistance genes (ARGs) through horizontal gene transfer, primarily mediated by plasmids. However, ARG-plasmids are not exclusive to pathogenic species. Non-pathogenic microbial communities serve as significant reservoirs for plasmids carrying ARGs, where they can persist even without antibiotic pressure [1]. In fact, many plasmid-mediated resistance genes in pathogens may originate from environmental, animal, or non-clinical human sources [2]. Therefore, the AMR crisis can only be tackled with a One Health approach [3].

Yet, despite evidence of plasmids mobilizing ARGs between these habitats, our understanding of the evolutionary mechanisms driving this process remains limited. Previous studies on the spread of ARG-plasmids have focused mainly on clinically relevant pathogenic bacteria in single isolate cultures [4]. However, tackling antibiotic resistance demands a global perspective. Therefore, it is essential to investigate the presence and evolution of these plasmids within metagenomes of various habitats.

Recent advancements in metagenomic approaches offer solutions to this challenge by providing a substantial number of metagenomes from various environments. However,

existing methods still struggle to detect novel plasmids in metagenomes as they rely heavily on reference genome sequences. Put simply, the absence of universal genetic markers for plasmids limits current approaches from a complete understanding of plasmid diversity across different habitats.

The internship project will investigate the presence and distribution of antibiotic resistance-associated plasmids across different habitats. To achieve this, we will develop a computational pipeline tailored for the detection and analysis of plasmids within metagenomic datasets. It will rely on the plasmid marker database we have recently established in the laboratory [5]. This pipeline will then be applied to screen metagenomic samples from various environments, including soil, water, and human-associated microbiomes. The findings from this study will offer valuable insights into how different environments contribute to the spread of antibiotic resistance genes. Ultimately, the project can be continued as a PhD project and focus on the investigation of the role of different habitats as potential reservoirs for antibiotic resistance plasmids, contributing to our understanding of environmental AMR dynamics.

### **Specific tasks**

- **Develop a Comprehensive Metagenome Database:** Download, organize, and index metagenomic sequences, categorizing them based on their environmental habitats to create a robust and accessible database.
- **Establish Detection Thresholds for Plasmids in Metagenomes:** Determine and validate optimal thresholds for the accurate identification of plasmids within metagenomic datasets.
- **Identify Antibiotic Resistance Plasmids Across Diverse Habitats:** Detect and analyze plasmids linked to antibiotic resistance within metagenomes from various environments, utilizing the database.

As part of this project, the student will develop valuable skills in processing high-throughput genomic data and in designing bioinformatics workflows. They will become proficient in handling common genomic data formats and gain hands-on experience with a wide range of clustering and comparative genomics techniques. Additionally, the student will deepen their understanding of microbiology and antibiotic resistance.

### **Expected profile and skills of the candidate**

The ideal candidate should have a strong interest in microbiology and be willing to acquire extensive training in bioinformatics and big data analysis. They should possess strong communication skills in English and have a genuine enthusiasm for science.

## Laboratory publications or recommended review on the subject:

1. Carroll, A.C. and A. Wong, *Plasmid persistence: costs, benefits, and the plasmid paradox*. Can J Microbiol, 2018. **64**(5): p. 293-304.
2. Matlock, W., et al., *Enterobacterales plasmid sharing amongst human bloodstream infections, livestock, wastewater, and waterway niches in Oxfordshire, UK*. Elife, 2023. **12**.
3. McEwen, S.A. and P.J. Collignon, *Antimicrobial Resistance: a One Health Perspective*. Microbiol Spectr, 2018. **6**(2).
4. Mughini-Gras, L., et al., *Attributable sources of community-acquired carriage of Escherichia coli containing beta-lactam antibiotic resistance genes: a population-based modelling study*. Lancet Planet Health, 2019. **3**(8): p. e357-e369.
5. Coluzzi, C. and E.P. Rocha, *The spread of antibiotic resistance is driven by plasmids amongst the fastest evolving and of broadest host range*. bioRxiv, 2024: p. 2024.07.23.604842.