Spread of antibiotic resistance. Transfer at the health-environment interface.

We try to develop effective strategies for reducing the burden of antibiotic resistance in pathogenic bacteria.

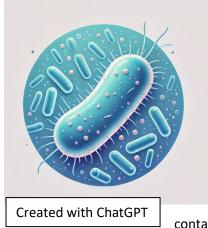
How do antibiotic resistance genes spread in these environments and how can they be combated? What are the genetic carriers of this resistance? Are biofilms more conducive to these transfers between bacteria?

To answer these questions, we are focusing our research on the plasmidome.

The plasmidome corresponds to the plasmid fraction of bacteria, constituting the DNA molecules present in the cytoplasm and which can circulate from one bacterium to another, outside traditional cell division. By looking at the plasmid DNA of a community without culture, *i.e.* the potentially mobile DNA molecules, we are able to obtain a more exhaustive and dynamic picture of the populations, and to develop correlations with the environmental conditions and stresses encountered by the microorganisms concerned.

Sources of bacterial contamination carrying beta-lactam resistance.

As part of our ongoing search for resistance transfer in the environment, we extended our research to include the study of antibiotic-resistant bacteria that are able to survive in clouds. To this end, we carried out selective media plating of various samples following cloudy episodes. The strains



were isolated, purified, identified and analyzed to determine whether they possessed one or more plasmids and we used long fragment NGS sequencing using the Oxford Nanopore technique. Then we will be able to assess the transfer potential of the mobile elements found in these strains.

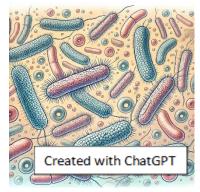
In parallel, we have compiled all the metagenomes available in the databases to extract the plasmidome fraction. A global representation analysis is underway to produce a publication showing the distribution of bacterial resistance genes according to location (city or nature) and degree of pollution. Air is a vector for the spread of antibiotic resistance. It seems that fine particles

contain a variety of resistant bacteria and antibiotic resistance genes, which are transferred from one environment to another.

Specific elimination of plasmids carrying carbapenem resistance genes from bacterial communities.

Complex microbial communities such as hospital effluents and intestinal microbiomes are extremely favorable environments for the selection and propagation of antibiotic-resistant strains. The development of methods to selectively reduce their load of antibiotic-resistant bacteria is necessary.

A few rare studies have provided proof of concept that CRISPR-Cas9 tools can be used to selectively reverse or eliminate antibiotic-resistant bacteria, but none of these studies have focused on complex multi-species communities. The ANR GENDARM project aims to fill this important gap by

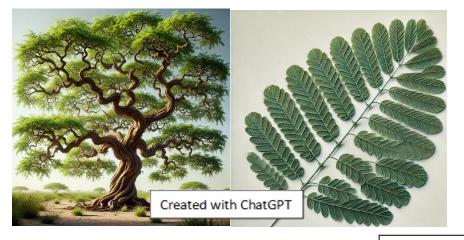


developing genome-targeting approaches that put pressure on carbapenemase-encoding genes and testing them in complex bacterial communities.

Looking for new antibacterial and antifungal compounds from plants.

Collaboration with the University of Yaoundé (Cameroon, Prof. M. NOLA), and the ICCF (Prof. Pierre CHALARD and Dr. Isabelle RIPOCHE of the CESMA "Conception Extraction Synthèse de Molécules Antalgiques" team at the ICCF) will continue.

Some plants are used in traditional medicine, which is a practice or method of using plants for medical purposes that dates back to ancient times. Among these plants, those of the genus Moringa and in particular Moringa oleifera contain compounds with potential antimicrobial effects such as glucosinolates. It was in this context that this research project was launched, with the aim of purifying and characterizing the secondary metabolites produced by this plant, which is found in Central Africa and has a multitude of uses, in order to determine whether the purified molecules would have an antibacterial and/or antifungal effect. The plant organs were supplied by the Institut de Recherches Médicales et d'Etudes des Plantes Médicinales, also in Yaoundé. Several papers were written following this work. Other *Terminalia glaucescens* and *Acacia sieberiana* plants have been collected and will be tested during exchanges with a Cameroonian doctoral student.



Acacia siberiana