

Titre du projet : Dynamics of REsistance to Antibiotics within the human gut Microbiota: combining diet informed population cohort and quantitative *in vitro* and *in vivo* gut studies

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PROJET/RESEARCH PROJECT

Upon Antibiotic Treatment (AT), the densely populated gut microbiota is almost systematically impacted whether or not gut microbes were the cause of antibiotic prescription. Consequently, the gut is a major environment for the emergence and spread of Antibiotic Resistance (AR). Surprisingly, the response to AT in terms of AR genes (ARG) selection appears to be highly variable both quantitatively and qualitatively. Even negative selection on ARG upon treatment has been observed. One likely explanation for these diverse responses is that the microbiota itself influences this impact of AT. Species from the microbiota may consume the antibiotic, release some stress factors when affected or deprive AR strains from resources upon perturbation.

For an in depth investigation of the role of microbiota composition on AR, we have built a solid consortium of teams with complementary expertise capable of analyzing AR *in vitro* (minigut) and *in vivo* (mice) gut systems combined to a large-scale diet informed cohort.

Miniguts, despite limitations like the absence of interactions with an immune system, allow us to deploy diverse molecular and synthetic biology tools to study AR in a complex and near to natural environment in which hundreds of species coexist. Miniguts allow the sampling of the microcosm at will and have a mid-throughput (96 replicates). This sustained replication is needed to explore the diversity of microbiota that is shaped by host diet. As input, we will use the NutriNet- Santé cohort that offers a precise characterization of the food habit of its 170,000 participants or Nutrinauts. Finally, *Escherichia coli*, the workhorse of molecular biology, and now a major public health concern due to its high AR will be used as sentinel species. We have selected 100 Nutrinauts according to their usual dietary fiber intakes in order to generate a fresh collection of feces and characterize their intrinsic microbiota diversity with metagenomics. A panel of these feces will be fed in the miniguts and analyzed for AT impact with 16S-sequencing and selective plating.

To contribute actively to this project, we are looking for a post-doctoral fellow with strong expertise in some of the following fields:

- basic microbiology and molecular genetics (from manipulation to design)
- microbiota (from production to data analysis)
- animal models of gut colonization.

STRUCTURE D'ACCUEIL/LOCATION

Team « Robustness and evolvability of life » is part of the Department of Infection, Immunity and Inflammation of the Institut Cochin located in the center of Paris, 22 rue Méchain – 75014 Paris, France.

Institut Cochin is one of the biggest biomedical French Research Center located in the center of Paris that provides a multidisciplinary scientific environment and very efficient core-facilities.

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CONTRAT/FINANCIAL SUPPORT

Type: CDD

Funding:

Début/Beginning: 01/04/2023

Durée du contrat/Length of contract: 48 months

Structure employeur/organization

INSERM

CNRS

UNIVERSITE

Applicants should send their CV, letter of motivation and name of 2 references.

Envoyez votre CV, lettre de motivation et deux contacts de recommandations à :

- Olivier Tenaillon
- Email : olvier.tenaillon@inserm.fr