

## **Title: Impact of an antibiotic treatment on the intestinal microbiota**

### **Abstract**

The development of next generation sequencing broadened our knowledge on the role of commensal bacterial communities on their host's health, and the negative impact of their disruption. Antibiotics are the main disrupting factor, but their impact has not been precisely quantified.

We quantified the relationship between antibiotic fecal concentrations and the loss of bacterial diversity in the intestinal microbiota, and modelled the link between the loss of diversity and mortality in a hamster model of antibiotic-induced *Clostridium difficile* infection. We showed that the Shannon diversity index and the unweighted UniFrac distance are the 2 indices that best predict mortality in this model.

In healthy volunteers, we developed a semi-mechanistic model of the evolution over time of bacterial diversity – measured by two indices – after an antibiotic perturbation, and quantified the relationship between antibiotic concentrations in plasma and feces and the loss of bacterial diversity in the intestinal microbiota. We also analyzed the role of the antibiotic elimination pathway in the reduction of their impact on the microbiota. In this work, we showed that the intestinal microbiota is highly susceptible to antibiotics, and that the elimination route doesn't have a major role, in the perspective of limiting antibiotics' impact on the intestinal microbiota.

**Keywords:** antibiotics ; intestinal microbiota ; dysbiosis ; metagenomics ; bacterial resistance ; *Clostridium difficile* ; pharmacokinetics ; pharmacodynamics ; moxifloxacin ; cefotaxime ; ceftriaxone ; nonlinear mixed effects modelling