

Title: Mapping Host–Microbiome Crosstalk in Crohn’s Disease Using Systems Immunology and Mucosal Microbial Ecology

Crohn’s disease (CD) is a chronic inflammatory bowel disorder characterized by relapsing intestinal inflammation that frequently requires surgery. Despite major advances in immunology and microbiome research, the mechanisms linking mucosal microbial imbalance to local immune activation remain incompletely understood. Most studies rely on fecal microbiota profiling or isolated transcriptomic analyses, limiting the investigation of tissue-level host–microbiome interactions.

This doctoral project aims to decipher mucosal host–microbiome crosstalk in CD by integrating microbiology, immunology, and computational systems biology. Building on the French POP STUDY cohort (>1,000 operated patients), which provides paired mucosal biopsies with matched 16S microbiome sequencing and transcriptomic profiling (microarray and RNA-seq), the project will analyze approximately 400–500 patients with matched multi-omic data.

The interdisciplinary approach combines microbial ecology, mucosal immunology, and advanced multivariate modeling. First, mucosa-associated bacterial communities will be characterized to define dysbiosis patterns associated with distinct clinical phenotypes and post-operative trajectories. Second, transcriptomic data will be structured and analyzed at the pathway and module level to identify immune endotypes linked to microbial configurations. Finally, integrative systems biology methods will model microbe-to-pathway interaction networks using sparse multivariate approaches and machine learning.

By focusing on paired tissue-level data, this project moves beyond descriptive signatures to uncover mechanistic interaction axes between bacteria and host immunity. The work lies at the interface between life sciences and computational modeling, aligning with the InLife/IPV objective of applying theoretical and systems approaches to biological questions. Ultimately, this research will provide a systems-level understanding of host–microbiome interactions in CD and generate mechanistic hypotheses and inform predictive frameworks for patient stratification.