Functional and structural mechanisms underlying host/intestinal microbiota interactions

Nikos Nikolopoulos, MMSB - Laboratory of Molecular Microbiology & Structural Biochemistry, Lyon, Stéphanie Ravaud, MMSB - Laboratory of Molecular Microbiology & Structural Biochemistry, Lyon, Renata Matos, IGFL - Institut de Génomique Fonctionnelle de Lyon, Lyon, Marie-Pierre Chapot-Chartier, Institut Micalis, Jouy en Josas, François Leulier, IGFL - Institut de Génomique Fonctionnelle de Lyon, Lyon, Christophe Grangeasse, MMSB - Laboratory of Molecular Microbiology & Structural Biochemistry, Lyon
nikos.nikolopoulos@ibcp.fr

The mutualistic interaction between host and commensal bacteria has an important beneficial effect on normal host physiology. Despite the renewed interest and recent progresses in understanding the impact of this symbiosis, the molecular mechanisms through which the microbiota exerts its beneficial influence remain largely unknown, which limits the efficient use and development of probiotics. In order to characterize these processes, a simple animal model (Drosophila) with a prevalent member of its microbial community (*Lactobacillus plantarum*) have been studied during chronic undernutrition. An operon called pbpX2-dlt has been identified as a key player in promoting host juvenile growth and maturation during these conditions (Matos et al., Nature Microbiology, 2017). The pbpX2-dlt operon encodes for 6 proteins involved in D-alanyl substitutions of teichoic acids, and pbpX2, a putative D,D-carboxypeptidase. However, the precise roles of the 6 proteins encoded by this *L. plantarum* operon and their structure-function relationships are largely unknown. My objective is to reveal the structure-function relationship of these 6 proteins and to understand the roles of all 4 predicted carboxypeptidases found in *L. plantarum* ‘s genome. Having already determined crystallographic structures of individual proteins, I will present the strategy and efforts for the determination of the whole PBPX2-Dlt complex organization and the characterization of novel players in cell envelope synthesis and remodeling of lactobacilli and gram-positive bacteria in general. Furthermore, I will discuss methods for fully integrating my structural data in the cellular context in order to better understand the molecular mechanisms underlying the beneficial symbiosis between host and commensal bacteria.