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Grant Title: Implication of Microbia polysaccharides in intestinal inflammatory diseases

The overall objective of this project is to investigate the structure to function relationships of intestinal microbiota polysaccharides in the outcome of a number of intestinal chronic inflammatory bowel diseases. Digestive pathologies are invalidating diseases with a very high prevalence among populations with western lifestyle. Most of them cannot be cured at the present time. There is now a clear consensus that (1) gut dysbiosis, including higher prevalence of pathogenic strains, is intimately linked to the onset and perpetuation of inflammatory bowel diseases and (2) complex bacterial polysaccharides exhibit strong modulation of inflammatory processes *in vivo* and appear as key effectors in the immunomodulation of intestinal epithelium. However, we are faced with a complete lack of knowledge concerning the actual polysaccharide and oligosaccharide content of intestinal lumen, although these are quantitatively and biologically extremely relevant. Thus, the appraisal of the role of microbial polysaccharides appears as a new frontier into the comprehension of the molecular mechanisms that control intestinal homeostasis.

The most important objective that was pursued during this work was to provide to the scientific community interested in gut pathophysiology a detailed assessment of the bacterial polysaccharides content of the human gut, including bacterial-associated lipopolysaccharides (LPS) and capsular polysaccharides (CPS). One of the key points was to develop specific methods for the isolation of polysaccharide associated microbiota that are compatible with structural analysis and biological assessment of complex carbohydrates. The main results obtained during this project are:

- The purification and structural analysis of polysaccharide fractions from total intestinal human microbiota. To accomplish that, we assessed the efficiency of current methodologies of microbiota extraction from human stools and adapted them to increase the purification yield of specific polysaccharides, the LPS and CPS.
- The identification and structural analysis of LPS isolated from an enteropathogenic bacterial strain, *E. coli* LF82, that is involved in the onset of IBD in a number of patients. The LPS isolated from *E. coli* LF82, shows unique features compared to other strains. The delineation of its synthetic route and its potential role in infection is under study.
- The observation of a yet untapped physiological processes involving intestinal microbiota. The application of purification methodology to zebrafish demonstrated that intestinal epithelium could scavenge and metabolically incorporate into its own glycome some monosaccharides originating from intestinal microbiota. This result opens new perspectives for the comprehension of host-microbiota relationships.