

EX-VIVO EXPERIMENTAL APPROACHES TO EXPLORE THE IMMUNOMODULATORY AND HOMEOSTATIC POTENTIAL OF PRE- AND PROBIOTICS

Authors: Ilia Belotserkovsky, Benoit Beitz, Ana Delgado

Affiliation: BIOASTER Technological Research Institute, Paris, France.

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Abstract:

Introduction:

Intestinal microbiota plays a key role in human health, while the epithelium maintains the necessary barrier between the microbes and the internal organs. Disruption of this barrier provokes activation of local and systemic immune system, leading to a variety of inflammatory, metabolic and neurodegenerative pathologies.

Probiotics and prebiotics are extensively developed to aid maintaining and repairing the impaired balance between intestinal microbiota and host immune response. Their selection and validation is a complex process involving *in-vitro* and *in-vivo* models, while the former is lacking the complexity of the physiological system, the latter often fails reflecting the effect in humans. The development of new pertinent and easy-to-access models is therefore needed.

Objectives:

Set up of *ex-vivo* experimental systems to assess:

1. the homeostatic potential of prebiotics using human fecal microbiota
2. the immunomodulatory potential of oral probiotics in the context of SARS-CoV-2 lung infection (gut – lung axis)

Methods:

1. Synthetic polysaccharide prebiotics were fermented *ex-vivo* by fecal microbiota from healthy donors and the resulting supernatants were tested for their impact on barrier function, homeostatic gene expression and cytokine secretion of epithelial cell *in vitro*.
2. Probiotic *Lactobacillus rhamnosus* LA801 was applied on the apical side of the intestinal epithelial cell line (Caco-2) grown on filters of transwells, while the human peripheral blood leukocytes were co-cultured below the filters and exposed to epithelial lung cell line (Calu-3) infected by SARS-CoV-2. Activation of immune cells and secreted cytokines analysis was then performed.

Results:

1. Some of the tested prebiotics improved epithelial barrier function *via* modification of tight junctions and chemokine secretion in a (fecal) microbiota dependent manner.
2. *Lactobacillus rhamnosus* LA801 enhanced the secretion of pro-inflammatory cytokines by immune cells upon contact with SARS-CoV-2 infected lung cells across the intestinal epithelial barrier.

Conclusion:

Ex-vivo experimental systems are useful for the evaluation of pre- and probiotic immunomodulatory and homeostatic potential, including complex settings such as gut–lung axis.