DEVELOPMENT OF A HOST MICROBE INTERACTION *IN VITRO* MODEL OF THE SMALL INTESTINE

Marta Calatayud [a], Olivier Dezutter [a], Emma Hernandez-Sanabria[a], and Tom Van de Wiele [a*]
[a] Laboratory of Microbial Ecology and Technology (LabMET), Ghent University, Coupure Links 653, 9000 Ghent, Belgium

Abstract

The intestinal epithelium is a gatekeeper of the internal milieu. Approximately 70% of all the lymphocytes of the human body are concentrated in the intra-epithelial and sub-epithelial intestinal layers (gut-associated lymphoid tissue, GALT), keeping a delicate balance between tolerance and protective immune response to infectious agents. Current *in vitro* models miss the inclusion of the gut immune-microbiome interface, thus presenting a gap in resembling the physiological aspects of the *in vivo* small intestine.

We developed and characterized an innovative model including a triple co-culture of epithelial cells (Caco-2), goblet cells (HT29-MTX) and immune cells (THP-1), together with a synthetic microbial consortium representative of the small intestine microbiome.

The three cell lines were physically in contact with in a double chamber insert. Cell lines were maintained for 23 days, with tight junction formation and cellular viability above 85%. At day 23, the chemical differentiation of THP-1 cells caused a significant drop in epithelial barrier function (~50%). Furthermore, a synthetic microbial consortium was added into the model to simulate the host microbiome interaction without (healthy model) or with LPS (inflammation model). The simultaneous exposure of the cells to bacteria and LPS induced ~ 2-fold increase on IL-8 (1042 ± 82 pg/mL), compared to both the control (480 ± 45 pg/mL) and the model exposed to the synthetic microbial consortium without LPS challenge (684 ± 44 pg/mL). Additionally, Sanger sequencing of bacteria adhered to the epithelium showed that *Veillonella parvula* could play a key role in the cross-talk between the host and the small intestine microbiome during inflammation events. Our novel model would assist to overcome sampling difficulties and in effectively simulating the small intestine ecosystem for addressing host-microbiome interaction, intestinal absorption, and inflammatory studies. Further research would be required for validating the model with *in vivo* data.