

## Organoid models demonstrate therapeutic potential of MB310, a consortium of gut commensal bacteria linked to clinical benefit in Ulcerative Colitis

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### Introduction

Precision microbiome profiling of a human fecal microbiota transplantation (FMT) study identified 8 bacteria associated with clinical response when engrafted in mild-to-moderate Ulcerative Colitis (UC) patients. These 8 strains form **MB310**, a Live Biotherapeutic Product (LBP) for the treatment of UC.

**Aim of study:** explore MB310 species impact on barrier function and mechanisms of action behind their protective effect

### Methods

**Barrier assays:** barrier function was assessed by measuring transepithelial electrical resistance in Caco-2 cells following treatment with MB310

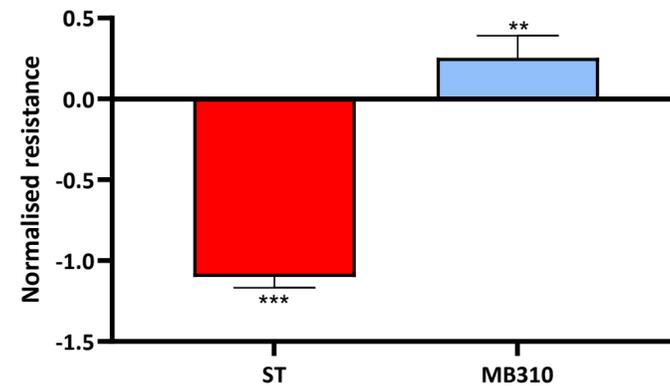
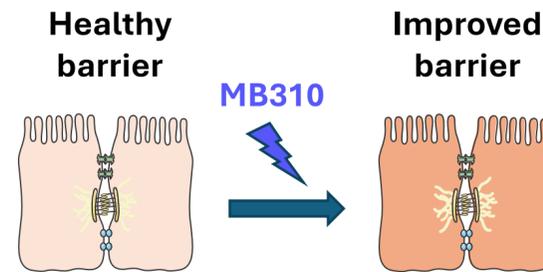
**Permeability assay:** 2-dimensional human colonic organoid-derived monolayer were treated with the barrier disruptor dextran sodium sulfate (DSS). Permeability was assessed by measuring the translocation of fluorescein isothiocyanate (FITC)-labelled dextran

**Transcriptomics analysis:** 3D human colonic organoids were stimulated with inflammatory cytokines (Tumor Necrosis Factor [TNF] and Interferon [IFN $\gamma$ ]), to mimic the conditions in UC. MB310 consortium was micro-injected into the lumen of some organoids. After 24hrs, mRNA was extracted for transcriptomics analysis.

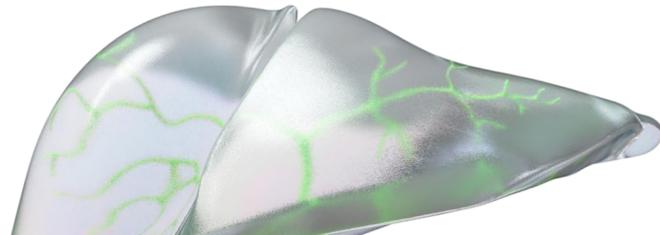
### Summary

- MB310 increases the integrity of Caco-2 epithelial monolayer and 2D-organoid disrupted by DSS.
- MB310 opposes the effects of inflammatory cytokines on epithelial organoids
- These epithelial protective effects of MB310 combined with its immune tolerogenic potential (data not shown) make this consortium an exciting and novel approach for treating UC patients

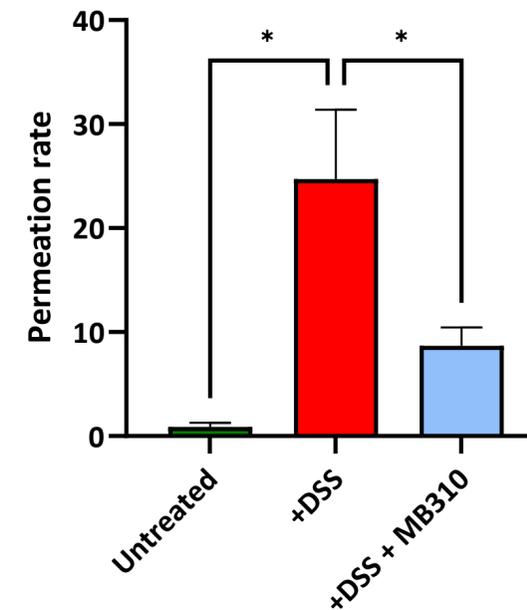
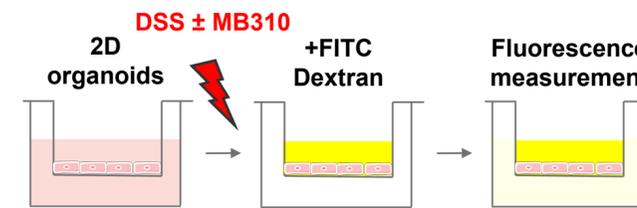
### MB310 improves barrier function



**MB310 increase electric resistance of Caco-2 cells.** Resistance was measured 24 hours post-infection, normalised against time of addition of MB310 and corrected against untreated Caco-2 cells. ST: *Salmonella typhimurium*. Data are shown as mean  $\pm$  SEM for 4 independent experiments (\*\*: FDR  $q < 0.05$ ; \*\*\*: FDR  $q < 0.01$ ).

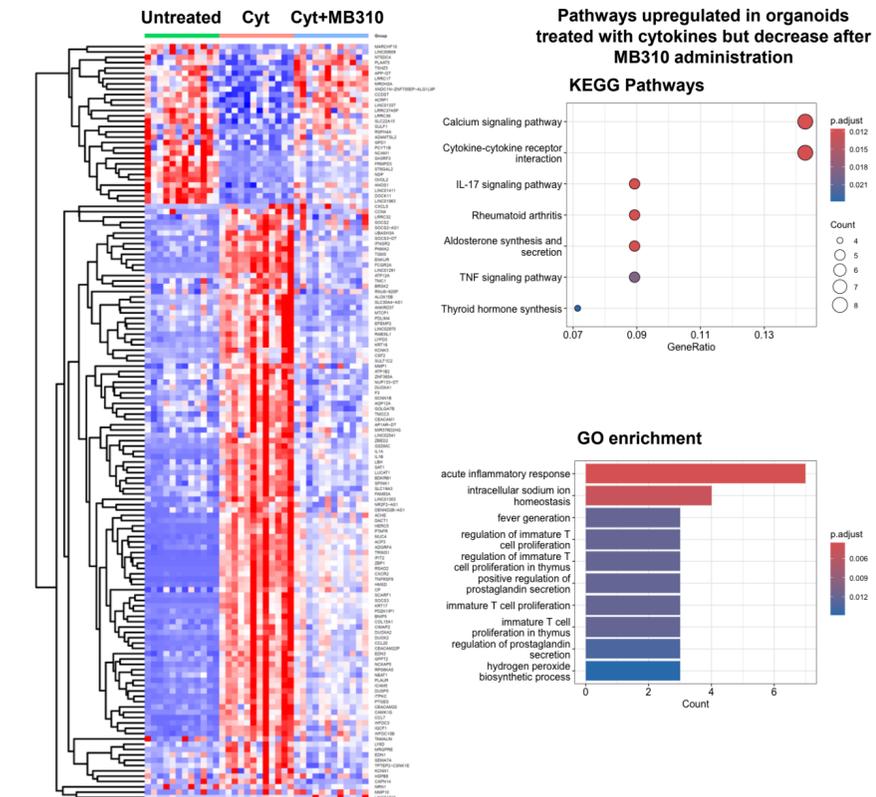


### MB310 improves barrier permeability



MB310 reduces DSS-induced epithelial permeability in 2D organoids. DSS: dextran sodium sulfate. Data are 3 organoid lines (\*: FDR  $q < 0.1$ ). shown as mean  $\pm$  SEM for 3 independent experiments and

### MB310 reprogrammes gut epithelial cells following inflammatory conditions



MB310 reverses the activation of many of the inflammatory genes (left panel) and pathways (right panels), induced by cytokines treatment. The depicted results are from 4 different human colonic organoids.