# Gut commensal bacteria, associated with clinical remission in ulcerative colitis, induce anti-inflammatory and tolerogenic pathways

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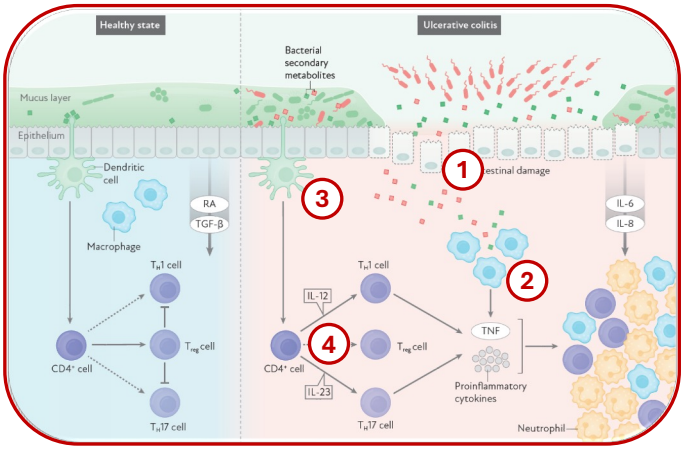
## Background

- Precision microbiome profiling of a human FMT study identified 8 bacteria associated with clinical response when engrafted in mild-to-moderate Ulcerative Colitis (UC) patients
- MB310 is an 8-strain Live Biotherapeutic Product for the treatment of UC covering all major beneficial fila, tested in a Phase 1b clinical study in Europe (COMPOSER-1)
- **Aim of study:** In this work we describe how both bacteria and their metabolites were tested to understand the mechanistic drivers of clinical benefit, targeting key aspects of UC pathology

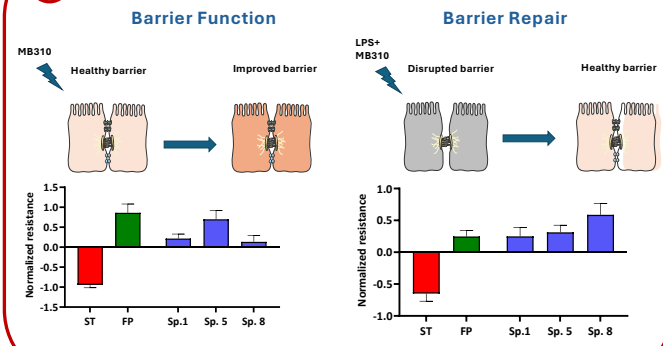
## Methods

To understand how MB310 drives beneficial effects we tested the effect of individual strains or their metabolites on:

- **Barrier function**: measuring effect of bacteria on transepithelial electrical resistance on healthy or damaged Caco-2 monolayers
- **Macrophage and dendritic cell activation**: measuring effect of bacteria on pro- (TNF) and anti-inflammatory (IL-10) cytokine secretion by ELISA
- **Regulatory T cell (Treg) induction**: measuring effect of bacterial metabolites present in bacterial cultures supernatants on FoxP3 expression (Flow Cytometry) and IL-10 production (ELISA)
- **Treg suppressive function**: measuring functionality of Tregs by bystander T cell proliferation suppression (Flow Cytometry)

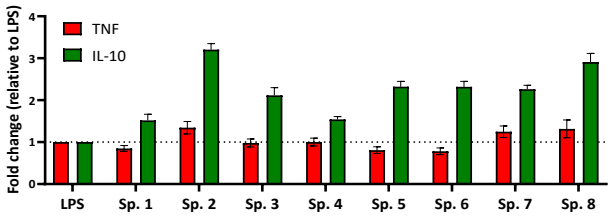



## 1 ↑ Barrier Function



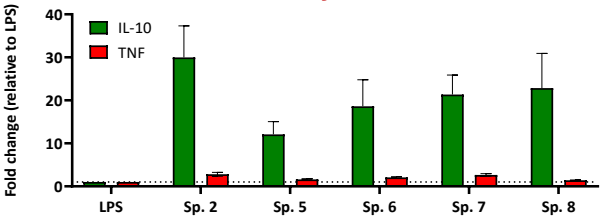

3 of the strains enhance epithelial barrier function and repair

## 2 ↓ Inflammatory M1 Macrophages



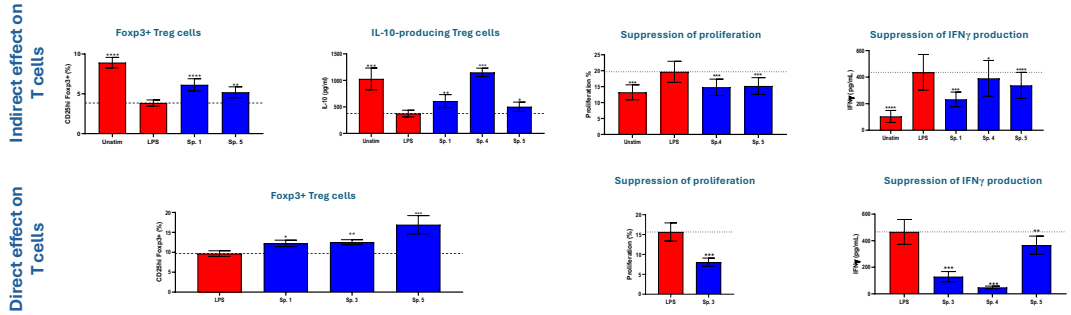

All 8 strains enhance IL-10 release but not TNF skewing the macrophage response to an anti-inflammatory cytokine profile

## 3 ↑ IL-10 Production by Mature Dendritic Cells




5 strains enhance IL-10 production but not TNF skewing the DC response to an immunomodulatory cytokine profile

## 4 ↑ Regulatory T Cells induction ↑ Suppressive T Cells induction




Metabolites from 3 strains alter DC maturation and subsequently modulate CD4+ T polarisation, inducing Foxp3+ and IL-10 producing Tregs with suppressive activity

Metabolites from 3 induce polarisation of CD4+ T cells to increased FoxP3+ expression and suppressive activity

## Conclusions

- The 8 MB310 strains, identified as being associated with clinical benefit, interact with the host in different ways to oppose key UC disease pathologies by:
  - improving gut epithelial barrier integrity
  - promoting an anti-inflammatory profile of innate immune cells
  - metabolites of some MB310 strains lead to induction of different types of functionally suppressive Treg cells
- COMPOSER-1 is a Phase 1b trial testing MB310 in UC patients (concluded)

## Contact

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