

Mechanistic understanding of MB310: a consortium of gut commensal bacteria for the treatment of Ulcerative Colitis

F. Schreiber, C. Villemain, T. Sharpington, T.D. Lawley, M.J. Robinson, G. Bakdash
Microbiotica Ltd, Cambridge, UK

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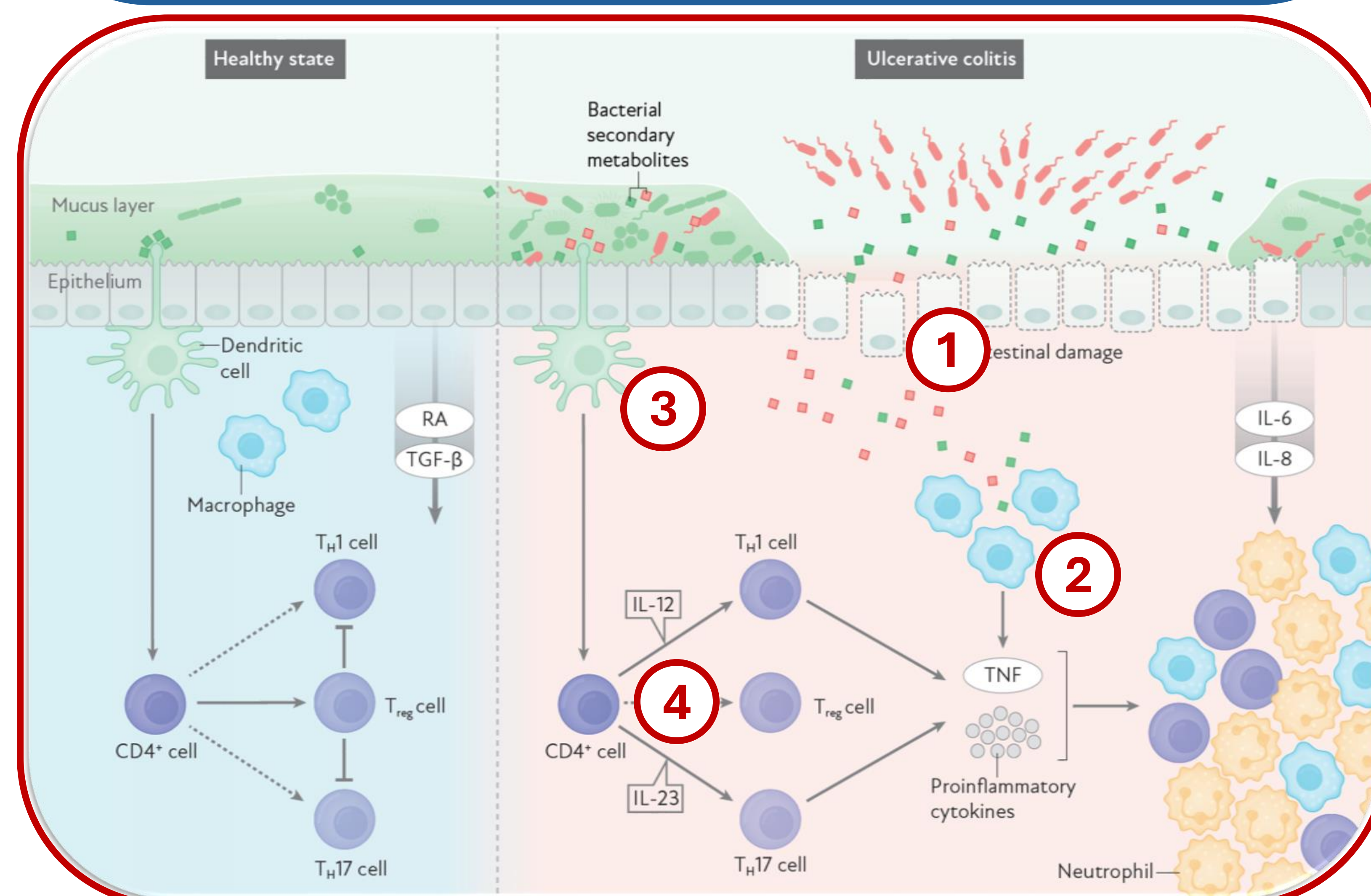
Background

- 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 a Live Biotherapeutic Product for the treatment of UC comprising a strain of each of the beneficial gut commensal bacteria currently in a Phase 1b clinical study ongoing in Europe (COMPOSER-1)
- In this work we describe how both bacteria and their metabolites were tested to understand the mechanistic drivers of clinical benefit

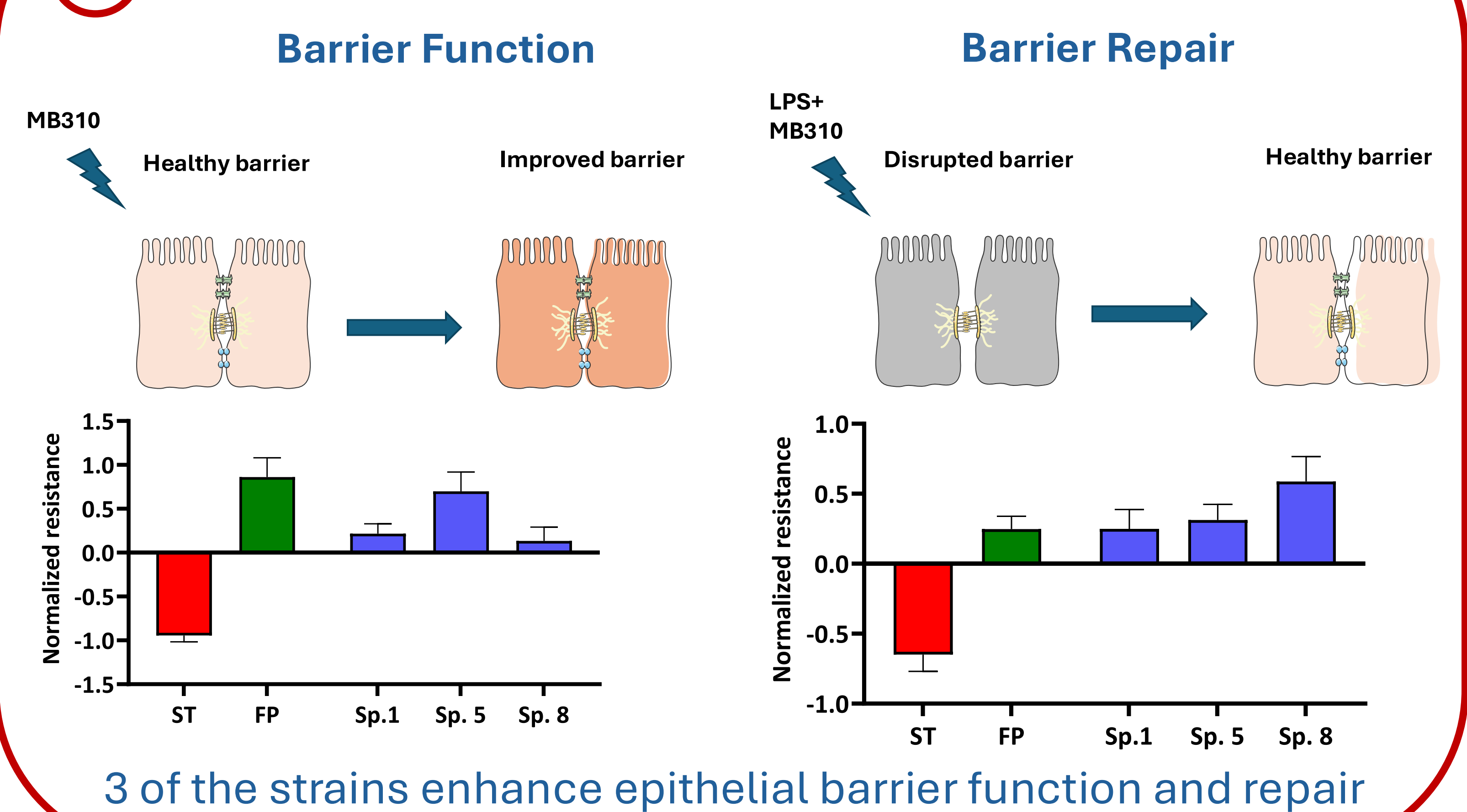
Methods

To understand how MB310 drives clinical benefit we tested how the individual strains impacted:

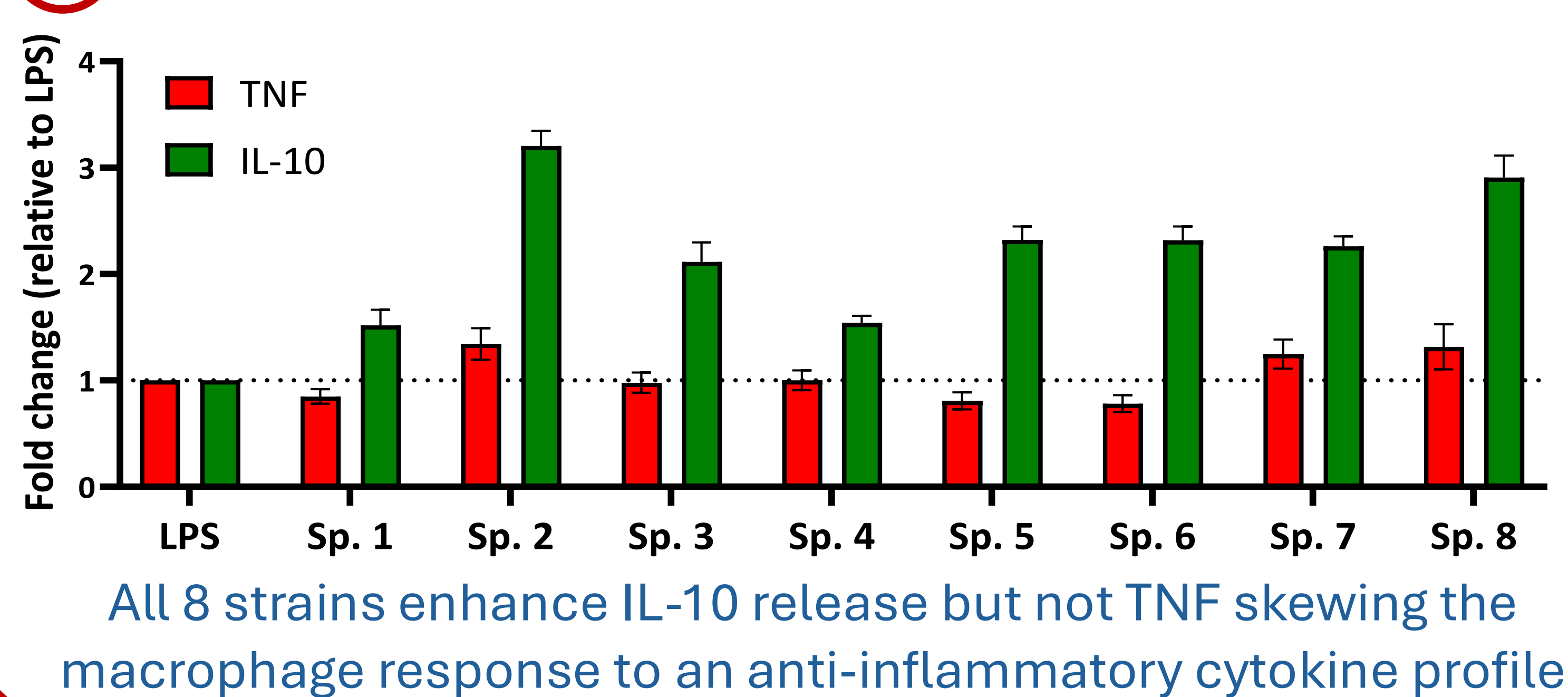
- **Barrier function:** transepithelial electrical resistance
- **Macrophage and dendritic cell activation:** cytokine secretion by ELISA
- **Treg induction:** FoxP3 expression (Flow Cytometry) and IL-10 production (ELISA)
- **Treg suppressive function:** Bystander T cell proliferation suppression (Flow Cytometry)



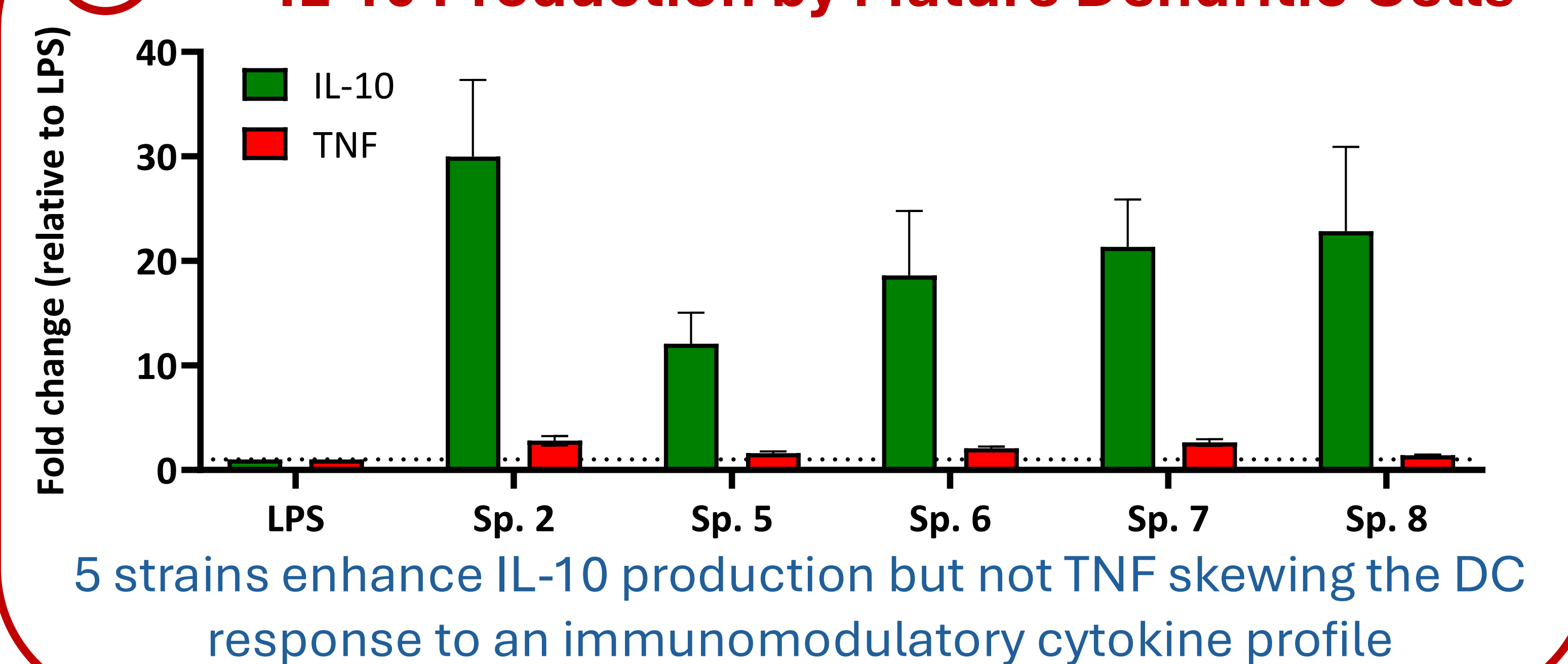
1 ↑ Barrier Function



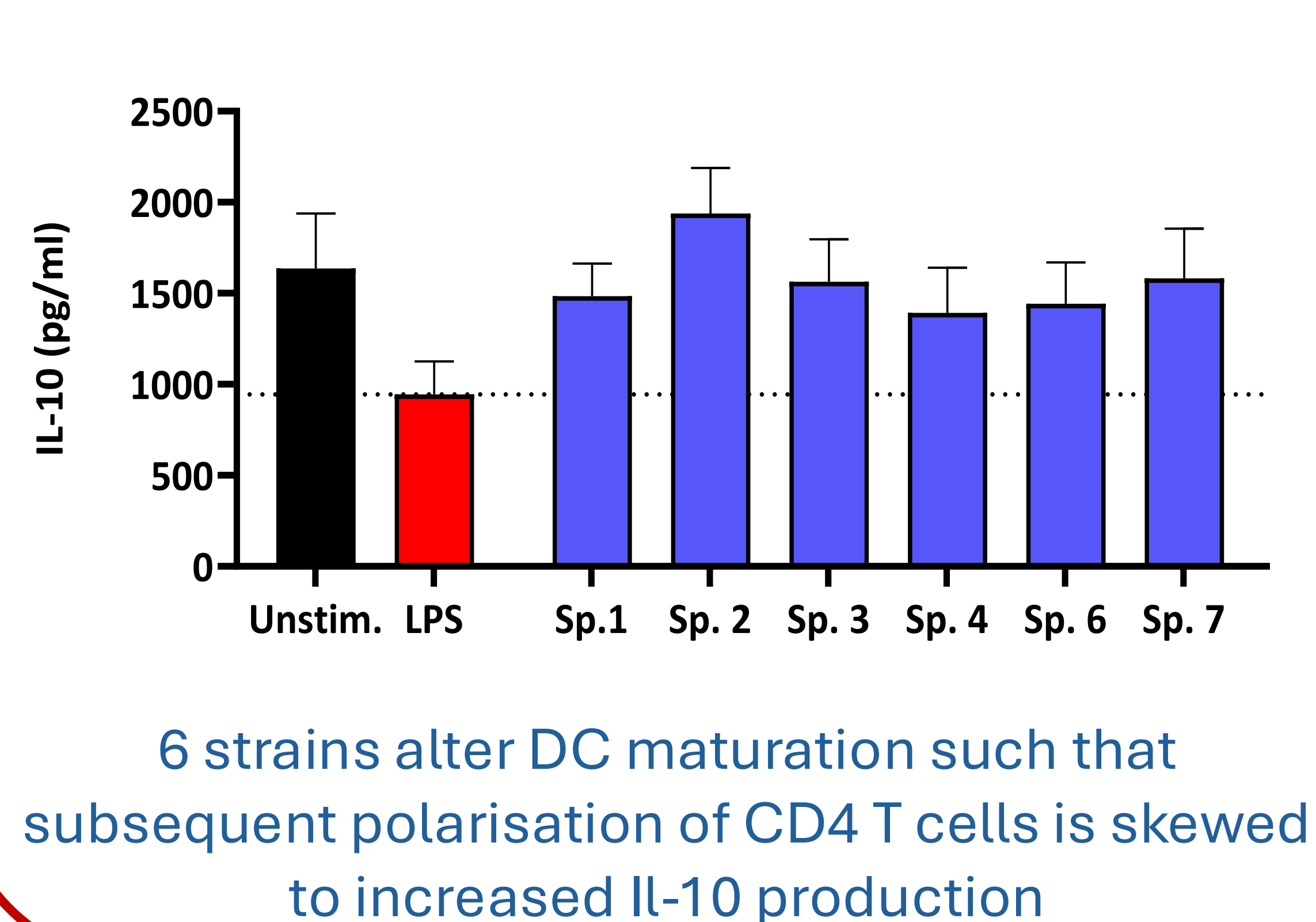
2 ↓ Inflammatory M1 Macrophages



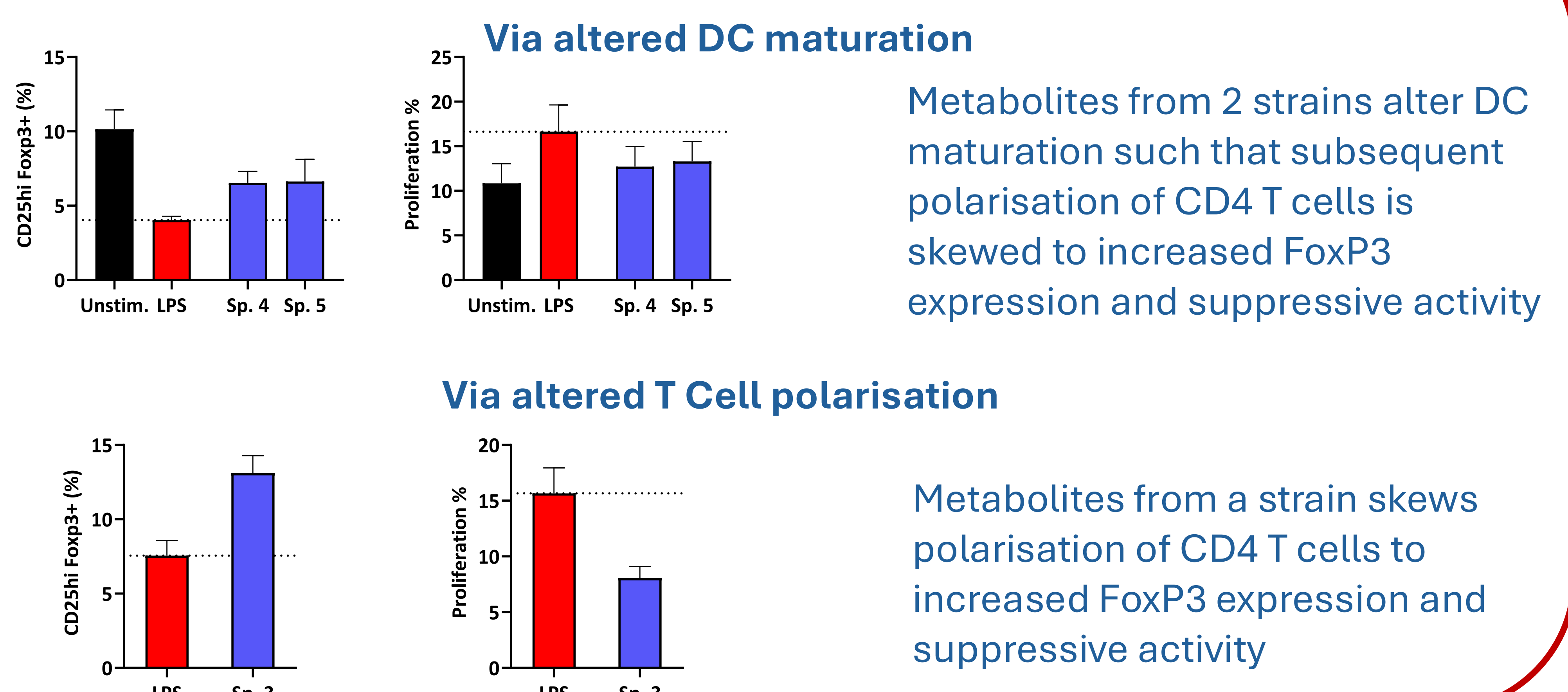
3 ↑ IL-10 Production by Mature Dendritic Cells



4 ↑ Regulatory T Cells induction by bacteria



↑ Suppressive T Cells induction by bacterial metabolites



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
 - inducing Treg cells
 - metabolites of some MB310 strains lead to induction of different types of functionally suppressive Treg cells
- COMPOSER-1 is an ongoing Phase 1b trial testing MB310 in UC patients

Contact

Fernanda Schreiber, PhD.
Associate Director, Translational
Biology; fschreiber@microbiotica.com

