

# Multifunctional membrane vesicles produced by *L. reuteri* DSM 17938 and their potential link to relief of infantile colic

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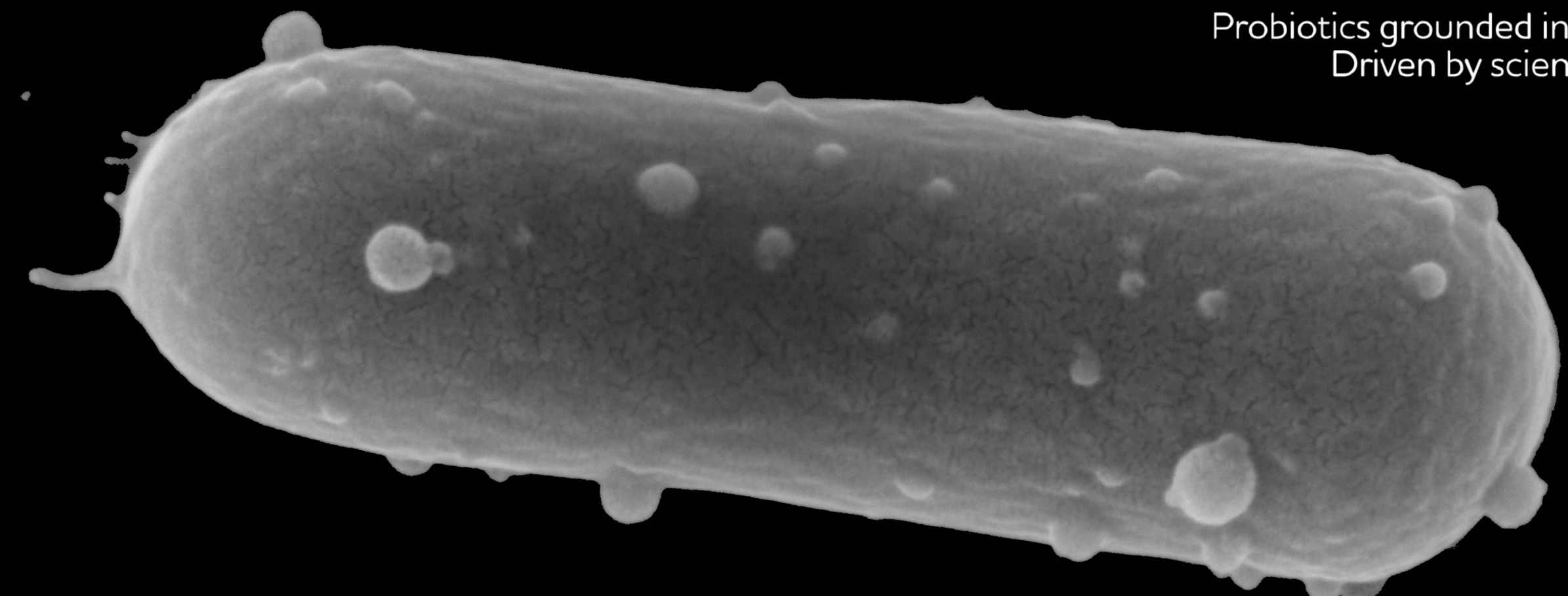
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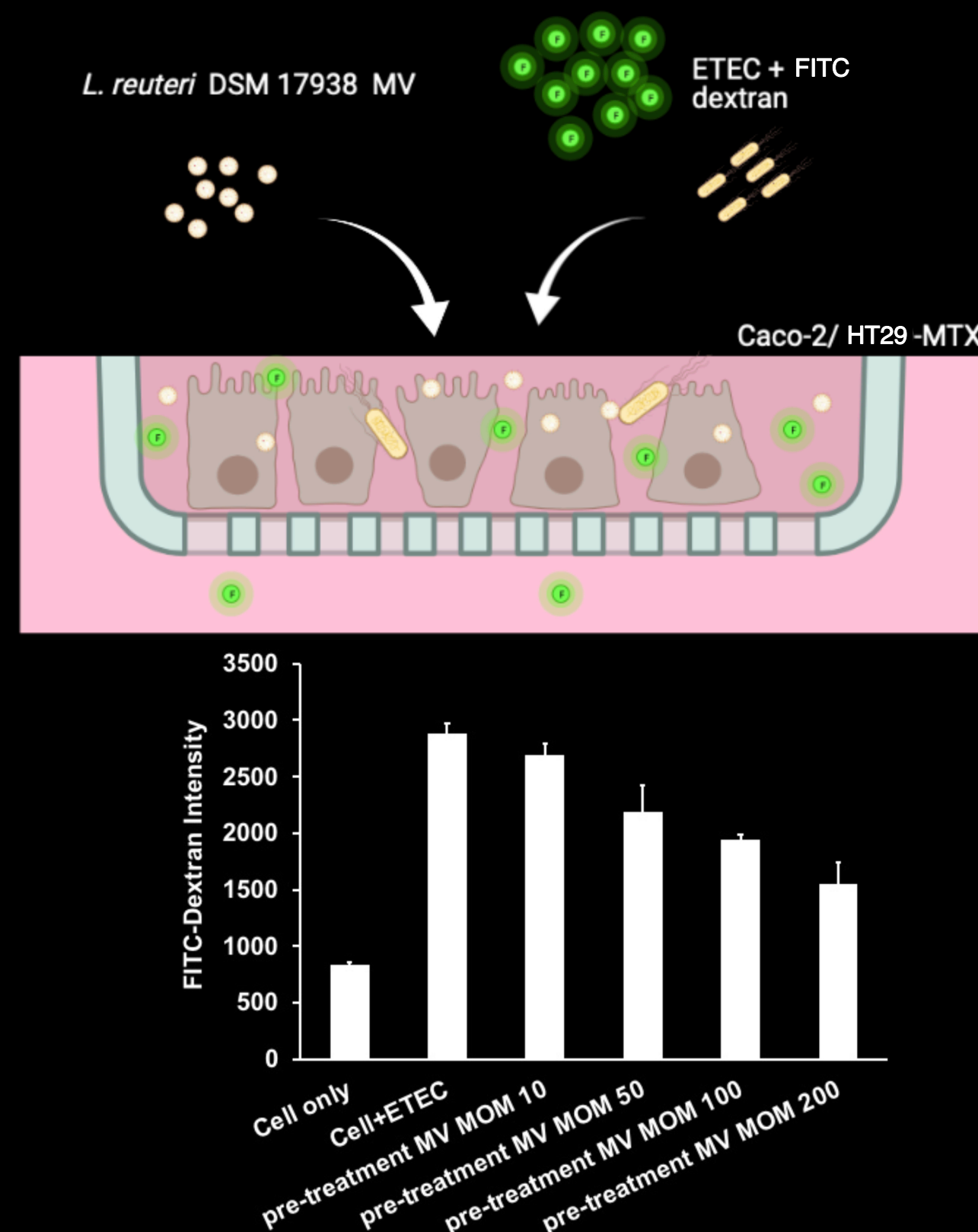
## Introduction

Bacterial extracellular membrane vesicles (MV) are potent mediators of microbe-host interactions, and not only important in host-pathogen interactions but also for the interactions between mutualistic bacteria and their hosts. *Limosilactobacillus reuteri* DSM 17938 is a well-studied probiotic bacterium and have among other been proven to ameliorate infantile colic. MV from DSM 17938 have recently been shown to modulate gut motility in an *ex vivo* mouse model (1) and dampen pro-inflammatory cytokine responses in stimulated PBMC (2). Here we wanted to investigate the mode of action of DSM 17938 derived MV.

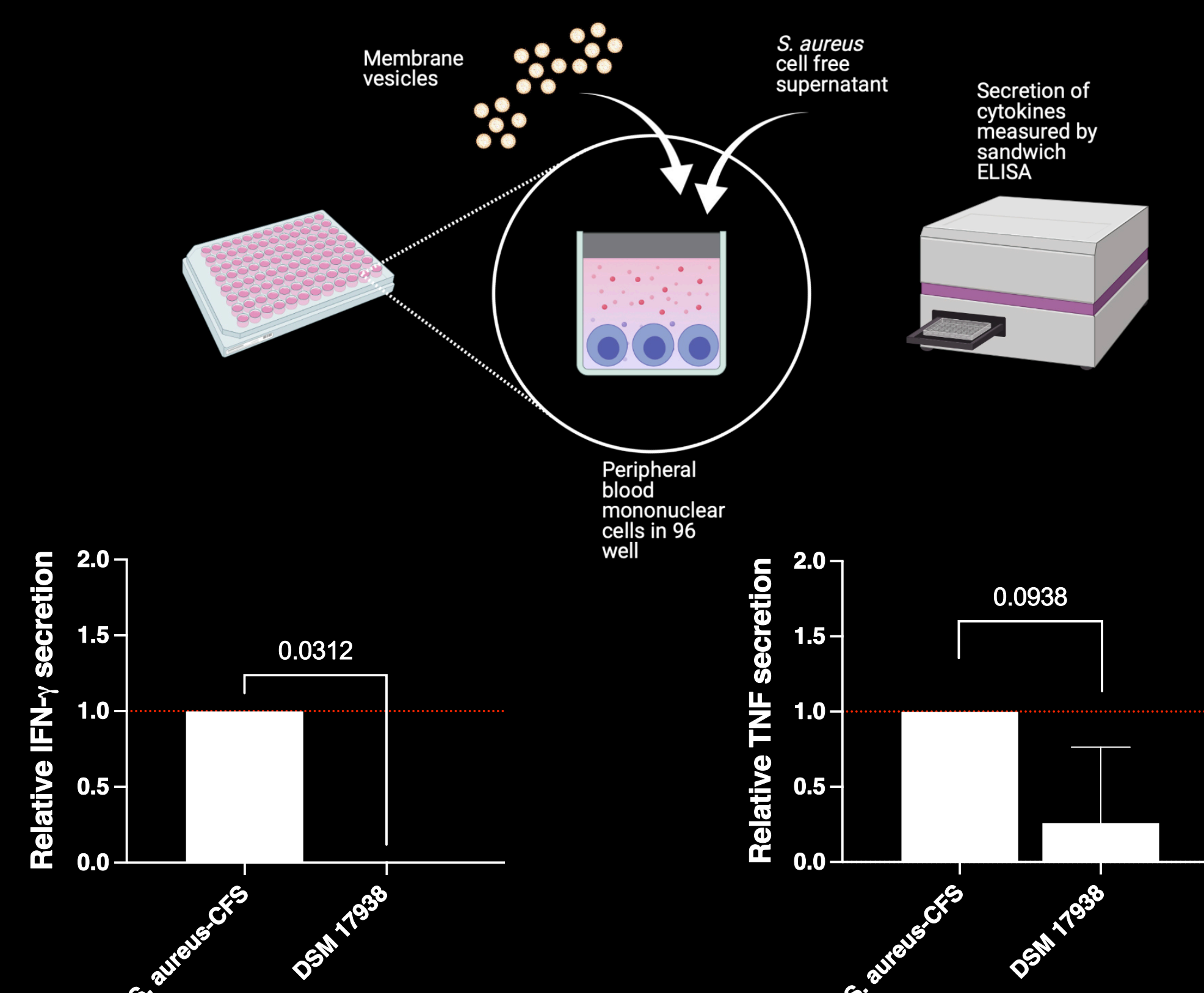


## Host interactions

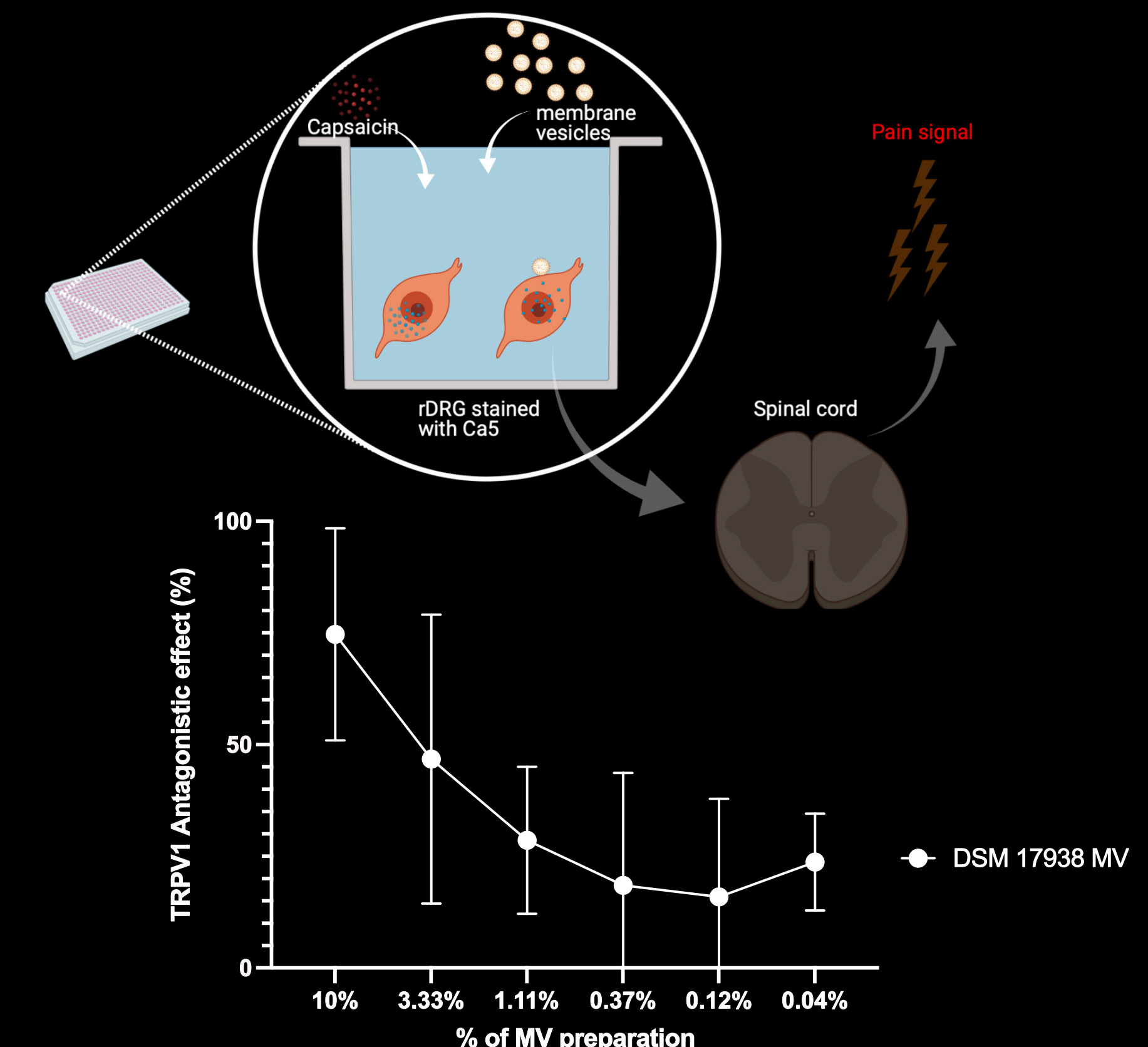
MV dose-dependently reduce leakage induced by ETEC in a Caco-2/HT29-MTX model.



MV dampen IFN- $\gamma$  and TNF- $\alpha$  secretion induced by *S. aureus* cell free supernatant in a peripheral blood mononuclear cells model.



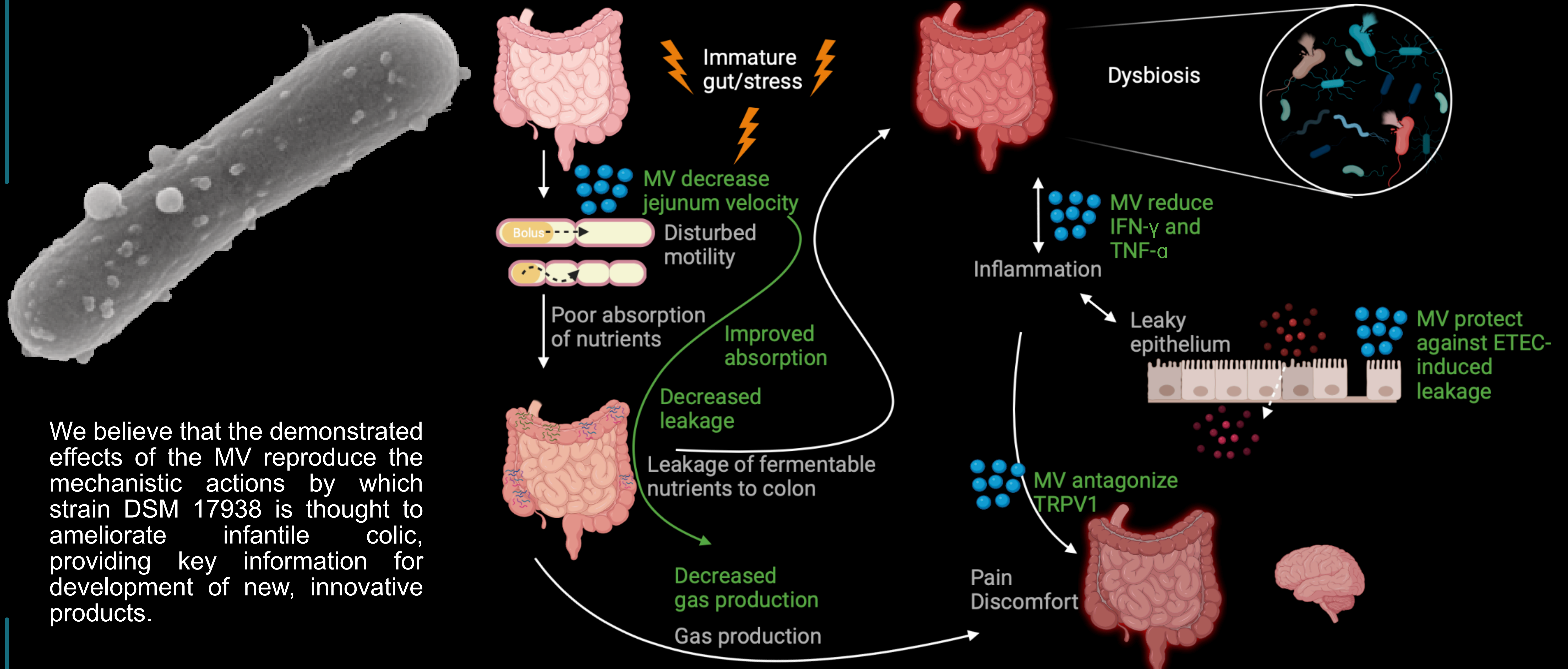
MV antagonize the pain receptor TRPV1 in a dose-dependent manner in rDRGs.



## Summary

Here we describe further multifunctionality of *L. reuteri* DSM 17938 derived MV:

- MV Contain DNA, RNA and carry both lipoteichoic acid and a 5'-nucleotidase. This enzyme is an analogue to CD73 present on e.g. Treg cells, and catalyze the production of the potent signal molecule adenosine (data not shown).
- MV display additional effects in host interaction models:
- Dampen capsaicin activation of the pain receptor TRPV1 in a model with primary dorsal root ganglion cells from rat.
- Decrease epithelial cell leakage caused by enterotoxigenic *E. coli* (ETEC) in Caco-2/HT29-MTX monolayers.
- Induce upregulation of IL-1 $\beta$  and IL-6 in naïve PBMC, and dampened IFN- $\gamma$  and TNF- $\alpha$  responses in *Staphylococcus aureus* challenged PBMC.



We believe that the demonstrated effects of the MV reproduce the mechanistic actions by which strain DSM 17938 is thought to ameliorate infantile colic, providing key information for development of new, innovative products.

## Conclusion

The demonstrated effects of the *L. reuteri* derived MV reproduce the mechanistic actions by which strain DSM 17938 is thought to ameliorate infantile colic. MV from *L. reuteri* are potent, bioactive nanoparticles that demonstrate a novel type of multifunctionality of MV from a mutualistic bacterium.

## References

- (1) West, C.L. et al., 2020. *PloS one*, 15(1), p.e0225481.
- (2) Forsberg, M.M. et al., 2019. *Scientific Reports*, 9(1), pp.1–13.

## Acknowledgements



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