

Clostridium immunis: A human gut commensal with therapeutic immunomodulatory effects

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Introduction

- The modulation of our microbiome is an attractive method to promote health and abrogate disease (Mimee, Citorik, and Lu 2016), but this has been an onerous venture given the staggering complexity in pinpointing consortia or individual species that causally impact host health from a laundry list of taxa merely associated with disease states (Fischbach 2018).
- Members of the host microbiota are known to regulate host immunity (Blander et al. 2017), illuminating a potential entry point for microbiome therapy in autoimmune and inflammatory diseases.
- A technique we use in the Surana lab: “Host-microbe triangulation” (Surana and Kasper 2017) had identified a hitherto unknown taxon of bacteria strongly associated with a protective phenotype in mouse colitis; subsequent characterization led to the discovery of a new species, designated *Clostridium immunis*.

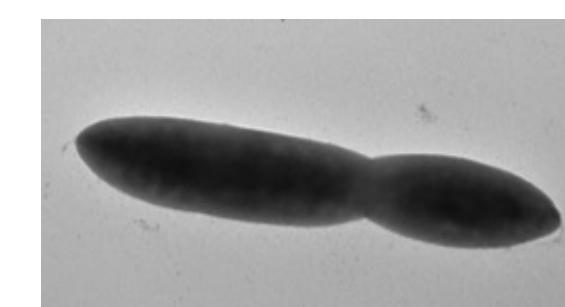


Figure 1: The first image of *C. immunis* captured by Transmission Electron Microscopy.

Approach

- Immunomodulatory effects of *C. immunis* were assessed using classical disease models with robust phenotypic readout.
- Finding out the ‘where’ and ‘when’ of *C. immunis* colonization will educate the search for mechanistic clues.
- Genetic manipulation of *C. immunis* is critical to identify genetically-encoded functions of its effects.

Results

Single oral administration of *C. immunis* mitigates clinical severity in two distinct mouse models of inflammatory disease

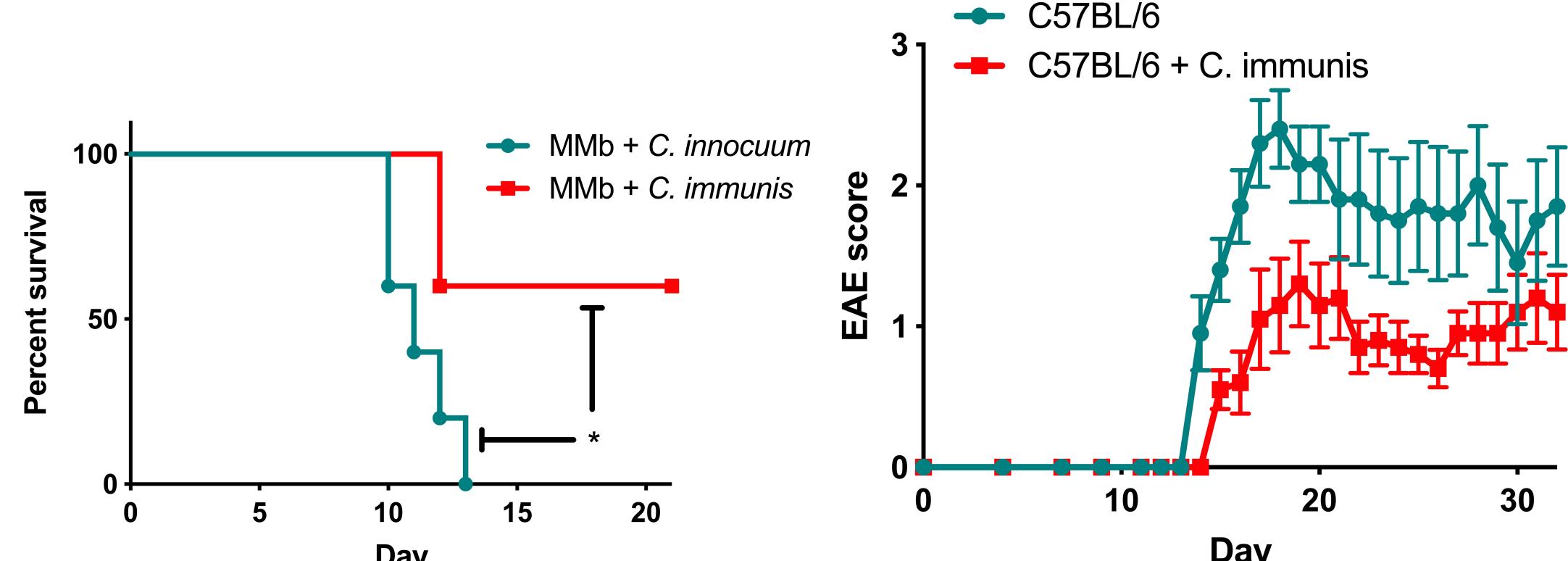
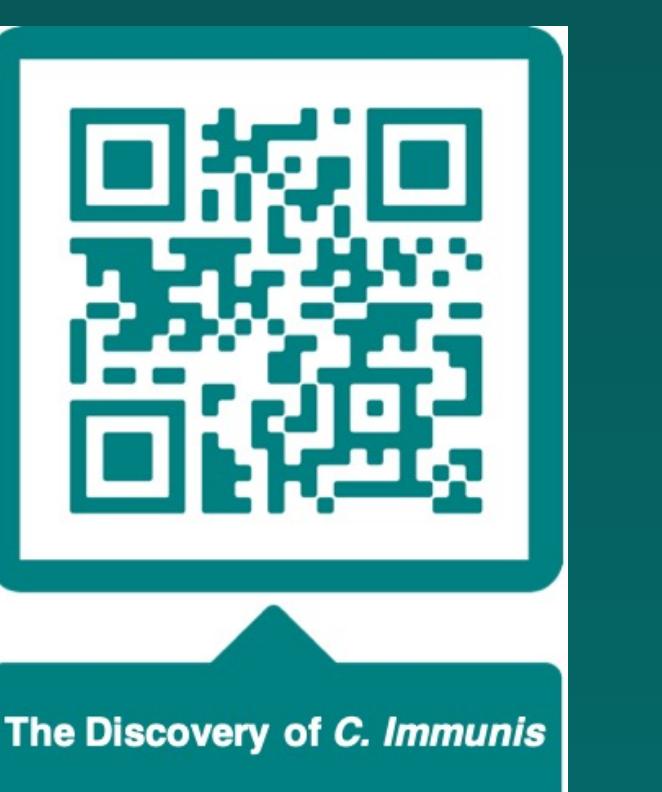


Figure 2: (Left) Oral gavage of *C. immunis* ameliorates lethality in DSS colitis and (Right) clinical severity in experimental autoimmune encephalitis. n=5 mice per group (DSS colitis); n=10 mice per group (EAE); Single dose of *C. immunis* preadministered before disease induction. *p<0.05

Therapeutic Potential: Oral administration of *Clostridium immunis* to mice ameliorates colitis and autoimmune encephalitis severity

Localization and Colonization: *Clostridium immunis* localizes to the mouse cecum and proximal colon and displays short term kinetics upon single gavage

Immunomodulatory Effects: *Clostridium immunis* modulates the intestinal type 3 innate lymphoid cell (ILC3) population



C. immunis is localized to the cecum and proximal-middle colon; Presence of the *C. immunis* in the naïve mouse gut after a single oral gavage is short-lived

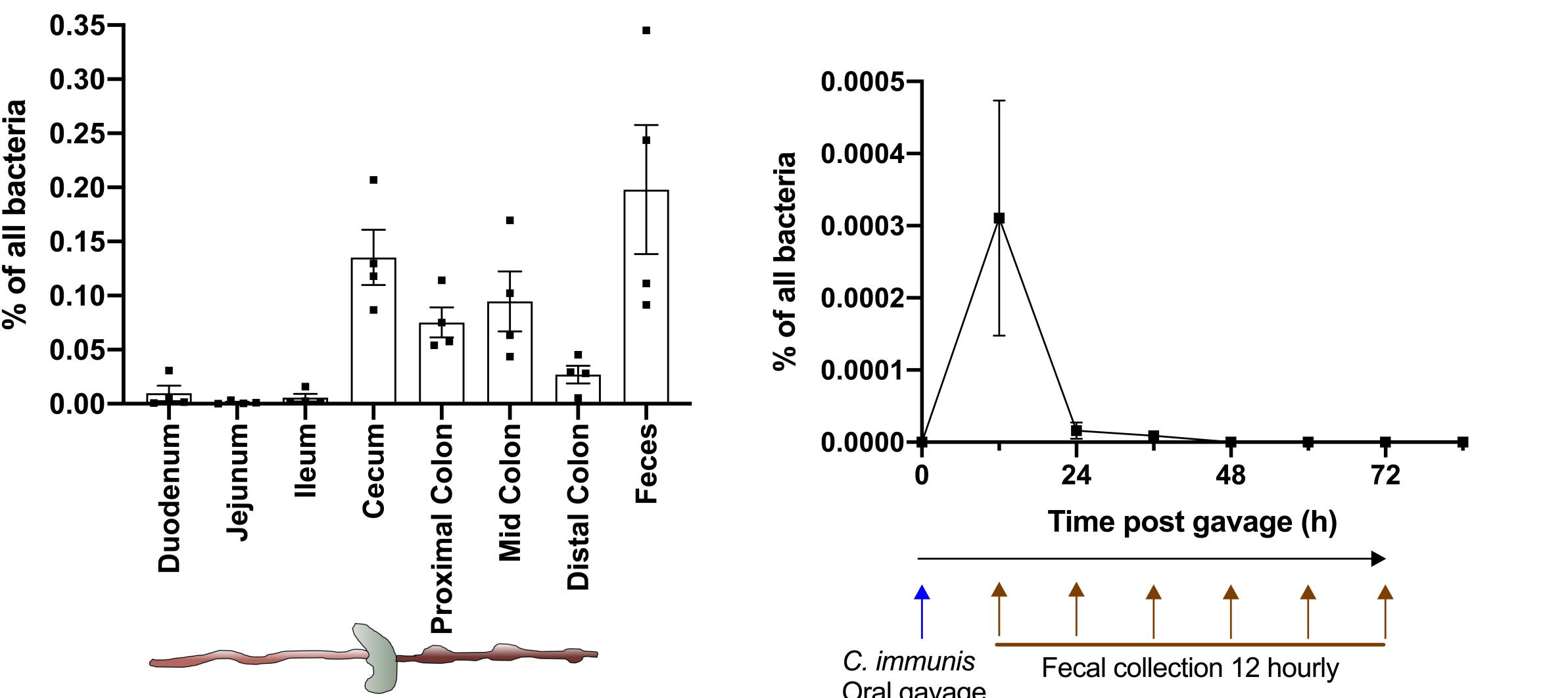


Figure 3: (Left) *C. immunis* is mostly localized to the cecum and proximal-mid colon in colonized mice at steady-state, n=4 mice; (Right) *C. immunis* naïve C57BL/6 MMb do not retain *C. immunis* beyond 24 hours after single oral gavage, n=9 mice; fecal pellets collected 12-hourly

Oral administration of a *C. immunis* enriched culture decreases the abundance of colonic Type 3 innate lymphoid cells (ILC3)

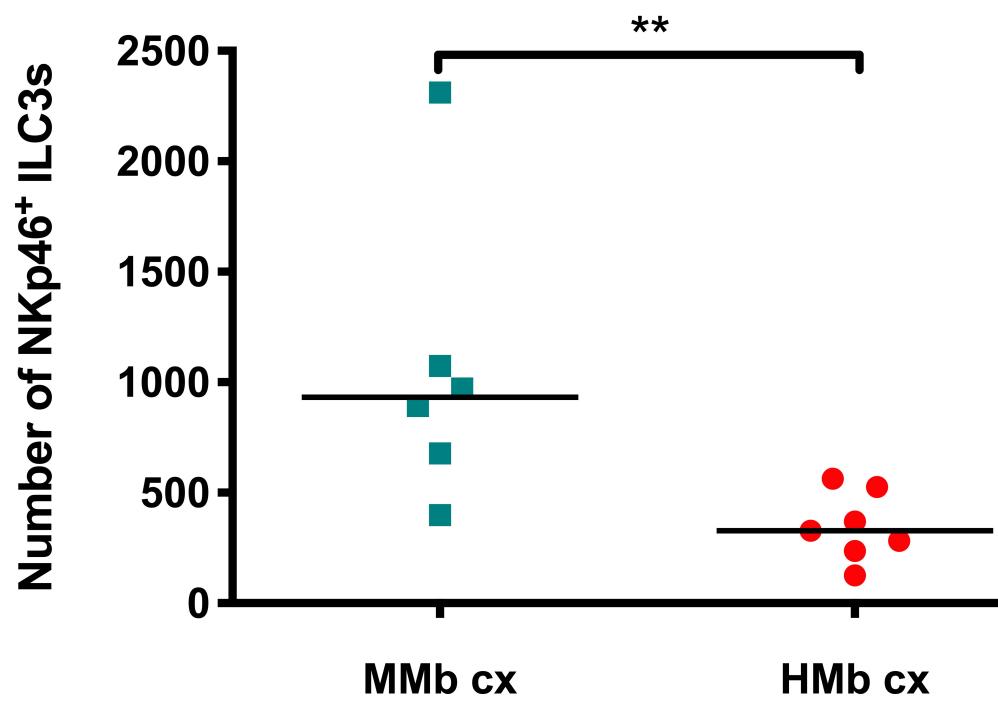


Figure 4: Colonic type 3 innate lymphoid cells were decreased in mice gavaged with a culture enriched for *C. immunis* (HMb cx) compared to a culture low in *C. immunis* (MMb cx). **p<0.005

Ongoing work

Bacterial end: Comparative genomics and genetic manipulation of *C. immunis* to unveil bacterial products that induce protection

- I am performing whole genome comparisons between closely related strains and *C. immunis* to identify candidate genes that confer protection.
- The lab is testing techniques to introduce exogenous genetic material into *C. immunis*, with the aim to performing CRISPR-mediated gene knockouts against candidate genes.

Host end: Unravelling changes to host immunological status mediated by *C. immunis*

- I am currently generating ILC3 knockout mice to confirm and study the mechanism of *C. immunis* modulation of the host colonic ILC3 population.

Acknowledgements and References

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Blander, J. M., R. S. Longman, I. D. Iliev, G. F. Sonnenberg, and D. Artis. 2017. “Regulation of Inflammation by Microbiota Interactions with the Host.” Journal Article. *Nat Immunol* 18 (8): 851–60. doi:10.1038/ni.3780.

Fischbach, M. A. 2018. “Microbiome: Focus on Causation and Mechanism.” Journal Article. *Cell* 174 (4): 785–90. doi:10.1016/j.cell.2018.07.038.

Mimee, M., R. J. Citorik, and T. K. Lu. 2016. “Microbiome Therapeutics - Advances and Challenges.” Journal Article. *Adv Drug Deliv Rev* 105 (Pt A): 44–54. doi:10.1016/j.addr.2016.04.032.

Surana, Neeraj K., and Dennis L. Kasper. 2017. “Moving Beyond Microbiome-Wide Associations to Causal Microbe Identification.” Journal Article. *Nature* 552 (7684): 244–47. doi:10.1038/nature25019.

Thorne, Brent. 2019. Posterdown: Generate Pdf Conference Posters Using R Markdown. <https://github.com/brentthorne/posterdown>