

Clostridium immunis: A human gut commensal with therapeutic immunomodulatory effects

Chin Yee Tan ^{2, 4, 10}
chin.yee.tan@duke.edu

Neil Surana ^{1, 2, 3, 10}
neil.surana@duke.edu

¹ Department of Pediatrics, Duke University

² Department of Molecular Genetics and Microbiology, Duke University

³ Department of Immunology, Duke University

⁴ Duke-NUS Medical School

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*.

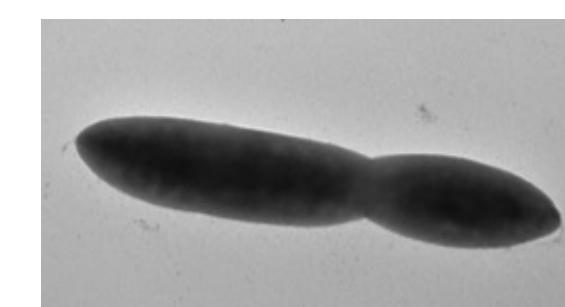


Figure 1: The first image of *C. immunis* captured by Transmission Electron Microscopy.

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

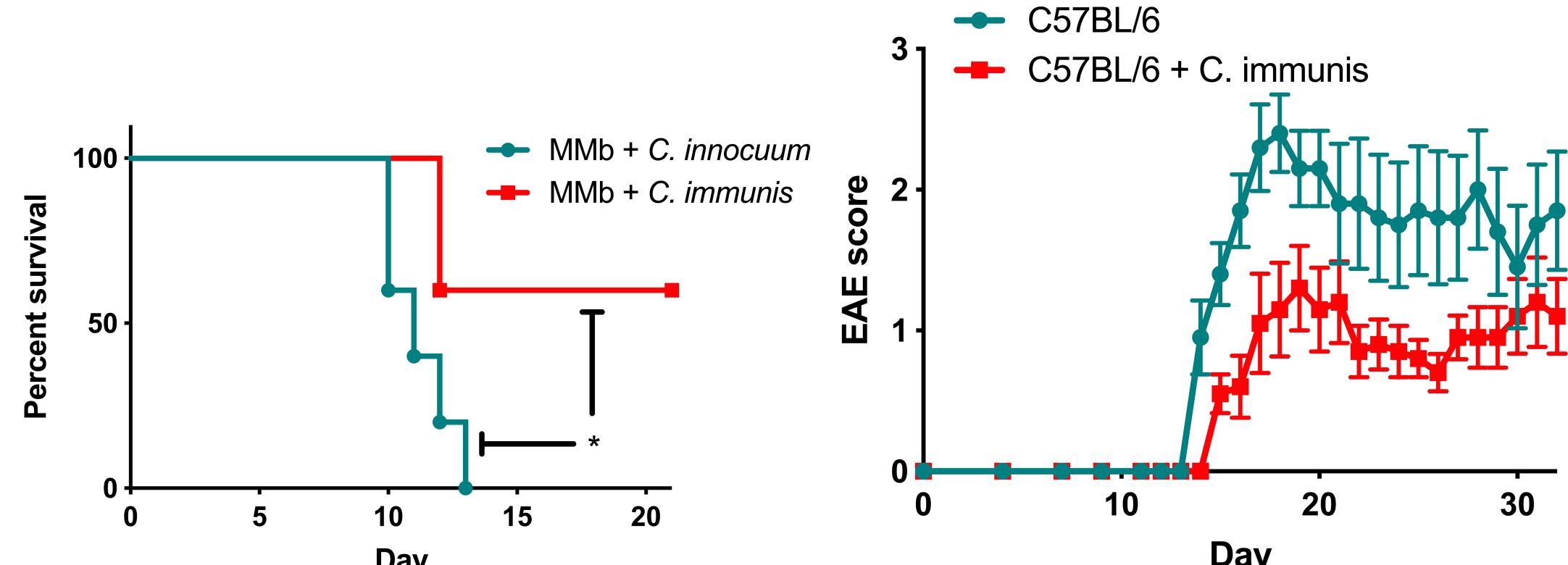


Figure 2: (Left) Oral gavage of *C. immunis* ameliorates lethality in DSS colitis and (Right) clinical severity in experimental autoimmune encephalitis. n=5 mice per group (DSS colitis); n=10 mice per group (EAE); Single dose of *C. immunis* preadministered before disease induction. *p<0.05

Impact:
Oral administration of *Clostridium immunis* to mice ameliorates inflammatory disease

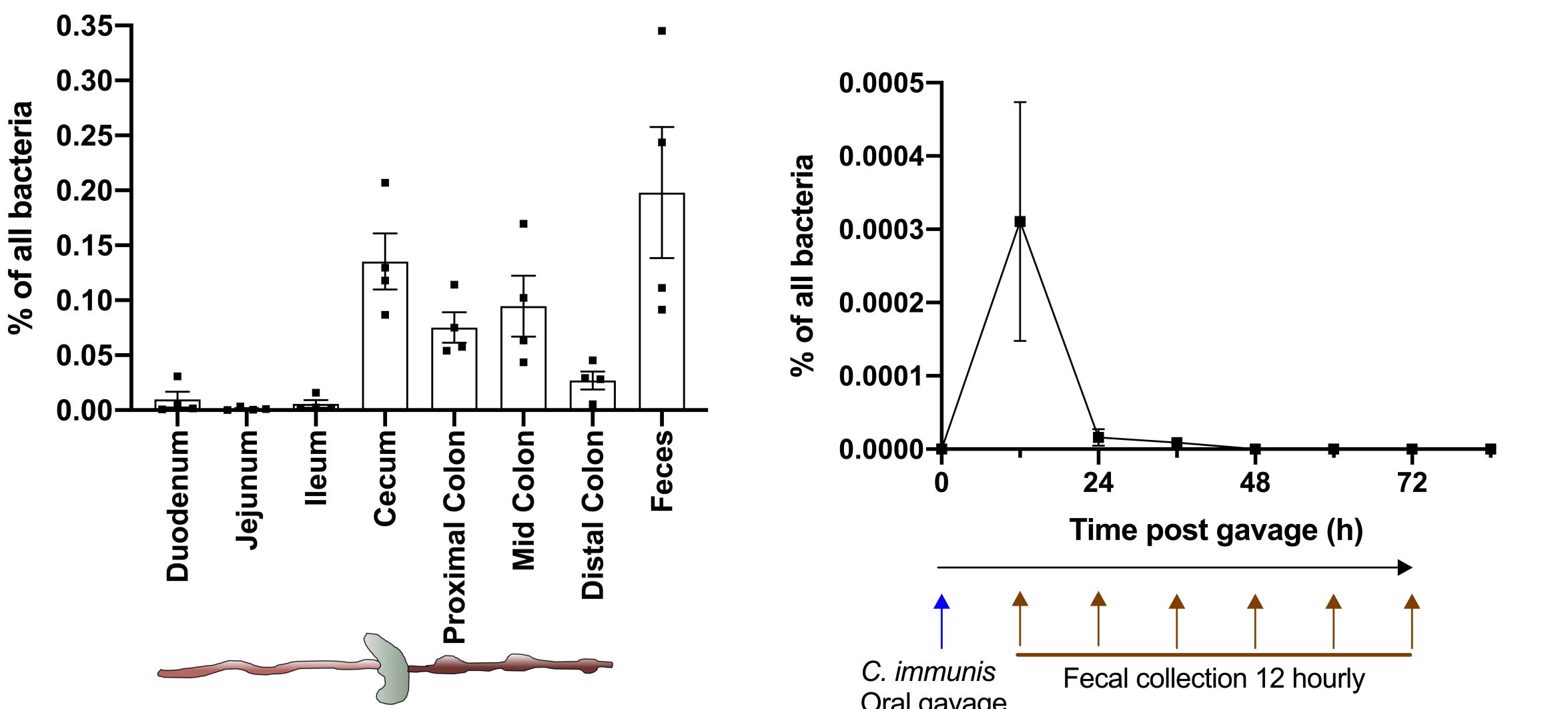
Mechanism:
Clostridium immunis downregulates the intestinal type 3 innate lymphoid cell (ILC3) population

Ongoing work:
a) Reverse genetics to identify bioactive products of *C. immunis*
b) ILC3 knockout mouse model and immune profiling to identify and illuminate host responses to *C. immunis*

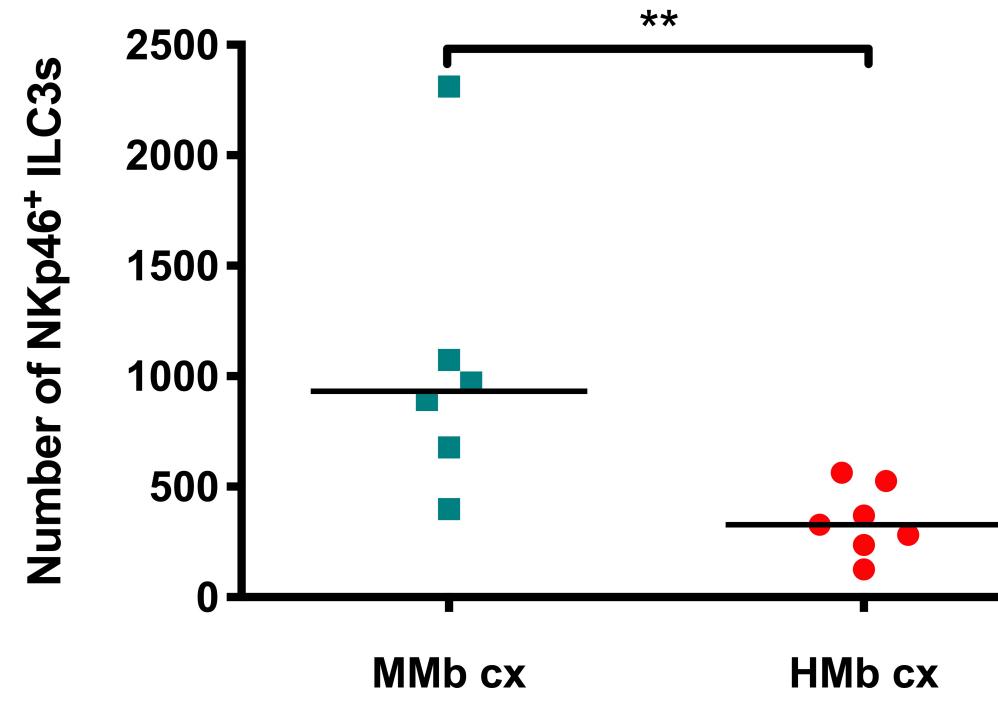


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C. immunis is localized to the cecum and proximal-middle colon; Presence of the *C. immunis* in the naïve mouse gut after a single oral gavage is short-lived



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



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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