Immune Mechanisms of protection from hypervirulent *C. difficile* infection

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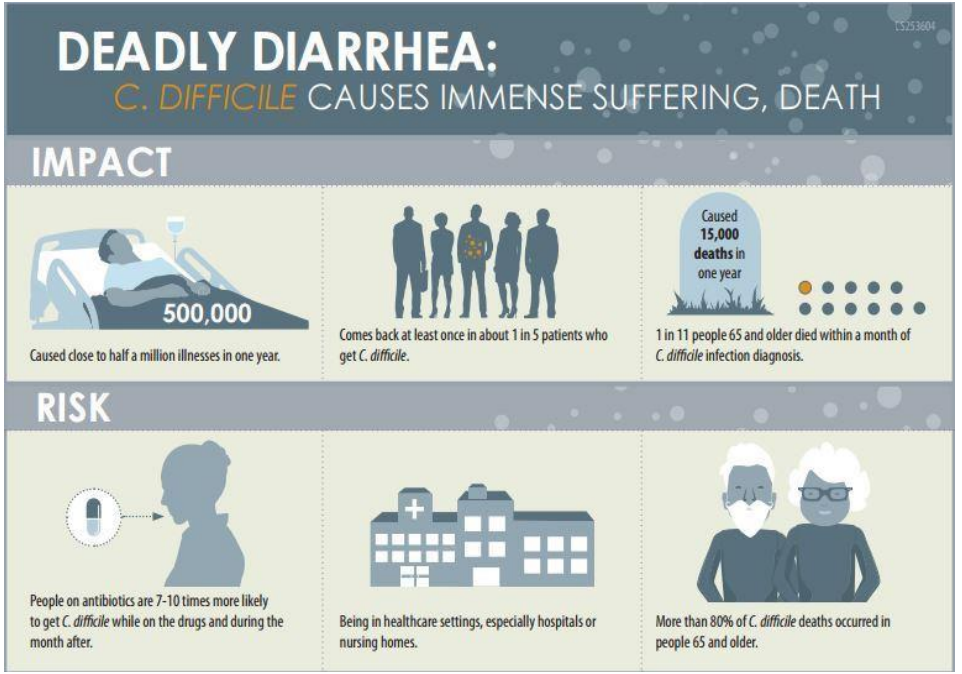
Clostridium difficile

- ***C. difficile* infection (CDI) is the leading cause of hospital acquired antibiotic-associated diarrhea in the US**
- **Causes inflammation of the colon and severe diarrhea**
  - **15,000 deaths/year**
  - **1/5 patients relapse**

- **<u>Clinical Problem</u>:**
  - ***C. difficile* is spread easily in healthcare facilities and impacts both patients and providers**
  - **Can live for long periods on surfaces**



CDC

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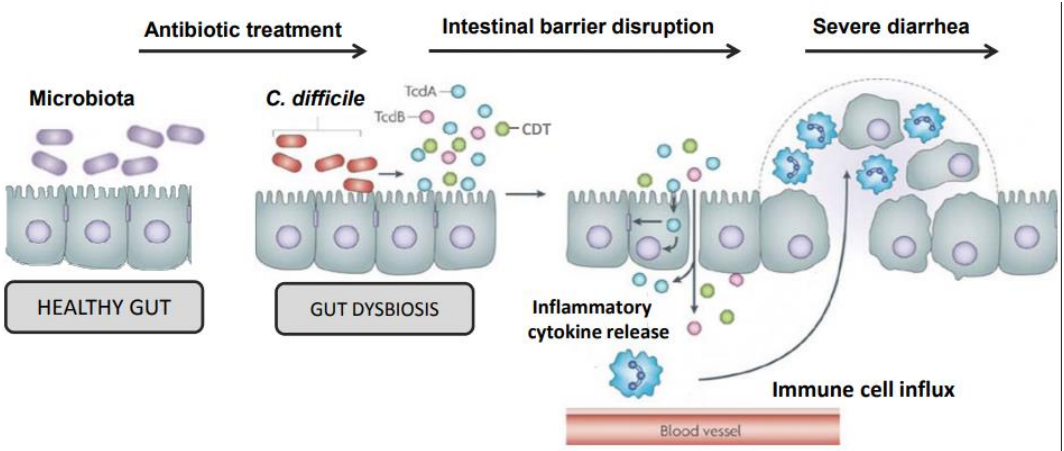
Virulence Mechanisms of *C. difficile*

<u>Solution:</u> Researchers at the University of Virginia have determined virulence mechanisms utilized by *C. difficile*

- **Highlight the importance of *C. difficile* toxin (CDT), which induces pathogenic host inflammation via a TLR2-dependent pathway**
- **IL-33 signaling plays a protective role for the immune system in CDI**



Rupnik et al, Nat Rev Micro 2009

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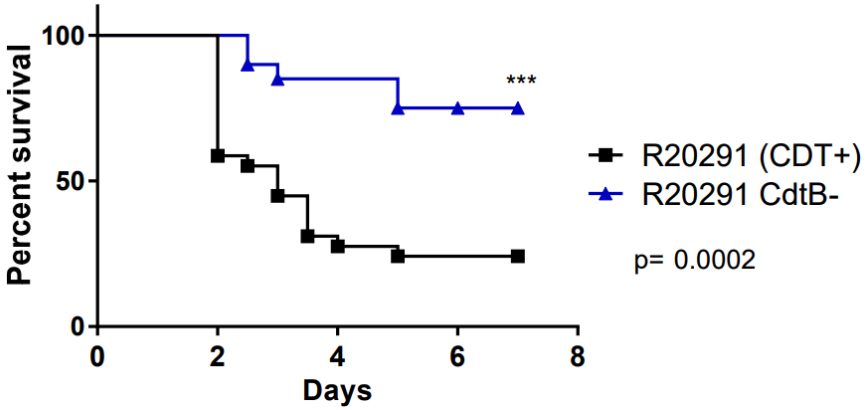
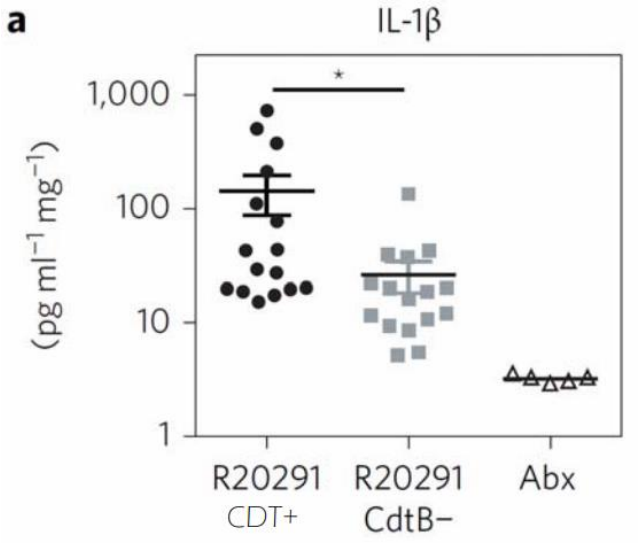
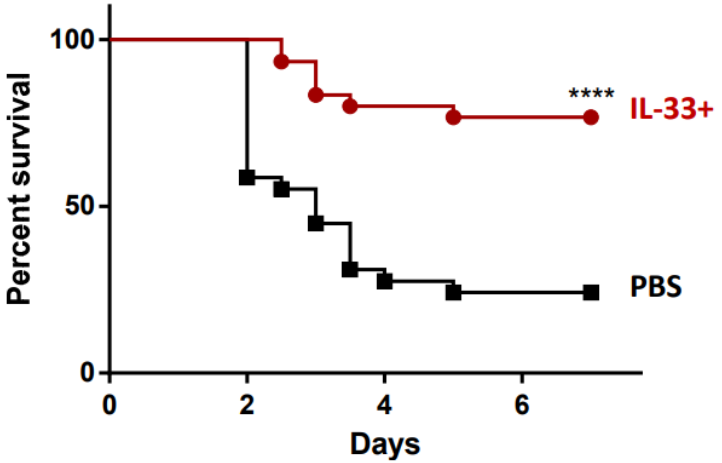
CDT expression enhances virulence and inflammation during CDI

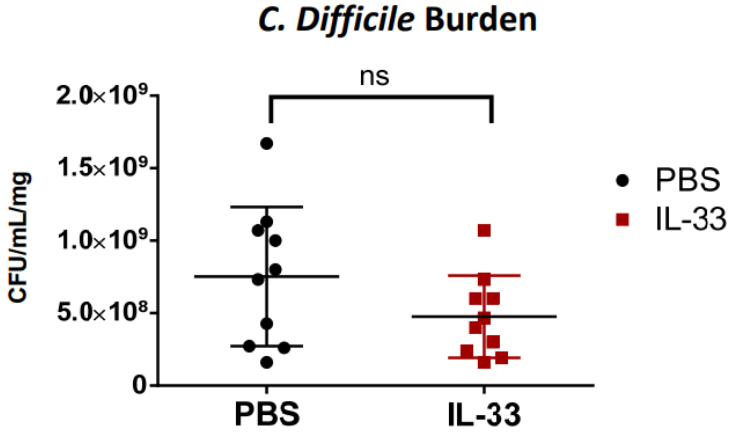




Expression of CDT leads to a significant decrease in survival of mice infected with CDI. Additionally levels of secreted IL-1β (marker of inflammation) are significantly higher when infected with CDT+ *C. difficile*.

IL-33 plays a protective role during CDI





Mice given IL-33 have a significant increase in survivability following CDI. This is not due to the reduction in *C. difficile* burden, as demonstrated by CFU counts.

Relevant Publications

- Nat Microbiol. 2016 Jul 11;1(8):16108. **Petri WA**, et. al.

Intellectual Property

- UVA Tech ID: PETRI-IL33
  - Title: Compositions and methods for treating Clostridium difficile infection
  - PCT Application PCT/US2017/043651 filed Jul. 25, 2017

- UVA Tech ID: PETRI-CDT
  - Title: Compositions and methods for treating Clostridium difficile infection
  - U.S. Patent Application 15/597,384 filed May 17, 2017