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

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**DEADLY DIARRHEA:**
*C. DIFFICILE CAUSES IMMENSE SUFFERING, DEATH***

**IMPACT**
- Caused close to half a million illnesses in one year.
- Come back at least once in about 1 in 5 patients who get *C. difficile*.
- 1 in 11 people 65 and older died within a month of *C. difficile* infection diagnosis.

**RISK**
- People on antibiotics are 7-10 times more likely to get *C. difficile* while on the drugs and during the month after.
- Bring in healthcare settings, especially hospitals or nursing homes.
- More than 80% of *C. difficile* deaths occurred in people 65 and older.
Virulence Mechanisms of *C. difficile*

**Solution:** 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
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

Intellectual Property

• UVA Tech ID: PETRI-IL33
  – Title: Compositions and methods for treating Clostridium difficile infection

• UVA Tech ID: PETRI-CDT
  – Title: Compositions and methods for treating Clostridium difficile infection