Public Abstract

First Name:Jared

Middle Name:Stephen

Last Name:Manse

Adviser's First Name:Michael

Adviser's Last Name:Baldwin

Co-Adviser's First Name:

Co-Adviser's Last Name:

Graduation Term:SP 2016

Department:Microbiology- Medicine

Degree:PhD

Title:STRUCTURAL AND FUNCTIONAL CHARACTERIZATION OF *CLOSTRIDIUM DIFFICILE* TOXIN B BINDING AND ENTRY

Clostridium difficile, or as it is better known, *C. diff*, is bacteria that has recently emerged as a worldwide infection in hospitals and other clinical settings. *C. diff* makes two toxins, TcdA and TcdB, which are the cause of all the associated problems with infection. Recent evidence has highlighted the importance of TcdB specifically, so we set out to investigate the causes underlying its toxicity. We used modern cloning and expression techniques to create modified TcdB proteins for use in experiments, then performed a bunch of biochemical experiments to more fully understand the role of TcdB in disease.

We found that three separate pieces of TcdB are each able to interact with cells, which was novel. For the first time, we showed that huge portions of TcdB can be removed, but TcdB still remains toxic. We found that there is actually a previously unknown independent binding domain; and we identified the specific protein that this region of TcdB binds on cells. Additionally we showed that a new more dangerous form of TcdB has a greater ability to bind cells and also acts more quickly to kill these cells.

We hope that the information we generated in this study can provide new targets for therapies against infection by the *C. diff*. It is only by working across fields and disciplines that we will ever control this new *C. diff* scourge.