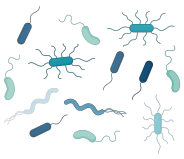
Member: D. Borden Lacy, PhD
Rank: Professor
Department: Pathology, Microbiology and Immunology, and Biochemistry
VDDRC Status: Full Member
Research Group: GII



Rationale for VDDRC Membership

I am an Associate Director of the VDDRC, and my laboratory focuses on understanding the molecular mechanisms by which bacterial protein toxins contribute to human disease. Particular interests include the virulence properties of the *C. difficile* toxins and the development of novel strategies for *C. difficile* infection prevention and therapy. Our most recent VDDRC-supported publication is: Thomas AK, Peritore-Galve FC, Ehni AG, Lança BBC, Coggin J, Brady EJ, Yoder SM, Shrem R, Rodríguez RC, Kroh HK, Gibson-Corley KN, Washington MK, Olivares-Villagómez D, Creech CB, Nicholson MR, Spiller BW, **Lacy DB**. Mucosal vaccination clears *Clostridioides difficile* colonization. *Nature.* 2026; 652,1289–1297. PMID: 41708852.

Digestive Diseases-Related Grants

Grant Number	Title	Project Period	Annual Direct Costs
5R37AI095755-16	Structural mechanisms of *Clostridioides difficile* pathogenesis	05/01/2021-04/30/2026	$360,000

Summary of Digestive Disease Research

The primary focus in my laboratory has been to understand the three toxins produced by *C. difficile* and the roles these toxins play in pathogenesis, and this was initially funded as a VDDRC Pilot Project. Most of this work has been focused on TcdA and TcdB, two homologous glucosyltransferase toxins that are considered the major virulence factors in *C. difficile* infection. We have more recently studied the *C. difficile* transferase (CDT) toxin, a third toxin that can impact disease severity. In addition, we have maintained a 20-year collaboration with Dr. Tim Cover studying the mechanistic basis of virulence in *Helicobacter pylori*. Specifically, we study the vacuolating toxin VacA and the Cag Type Four Secretion System.

VDDRC-Related Training and Activities

Associate Director, VDDRC
Pilot & Feasibility Award Recipient
Retreat Speaker

VDDRC Collaborations

We collaborate with Drs. Algood, Byndloss, Cover, Goldenring, Kaji, Markham, Nicholson, Olivares-Villagomez, Skaar, Tyska, and Washington on projects related to human tissue, cell, and animal models of *C. difficile* toxin function. We also collaborate with Dr. Cover on projects in *H. pylori* pathogenesis. A recently published collaborative paper is: Peritore-Galve FC, Kaji I, Smith A, Walker LM, Shupe JA, Washington MK, Algood HMS, Dudeja PK, Goldenring JR, **Lacy DB**. Increased intestinal permeability and downregulation of absorptive ion transporters Nhe3, Dra, and Sglt1 contribute to diarrhea during *Clostridioides difficile* infection. *Gut Microbes*. 2023;15(1):2225841. PMCID: PMC10291935.

Future VDDRC Core Use

We will continue to use the MS/Omics, Cell Imaging, and Flow Cytometry Cores to support our independent and collaborative projects on elucidating and defining the structural basis for gastrointestinal microbial toxins, as well as the Translational Analysis Core to evaluate our mouse models of infection.