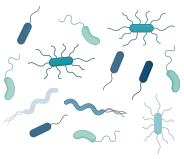
Member: D. Borden Lacy, PhD
Rank: Professor
Department: Pathology, Microbiology and Immunology, and Biochemistry
VDDRC Status: Full Member
Research Group: GII





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
R37AI095755	Structural mechanisms of *Clostridioides difficile* pathogenesis	05/01/2021-04/30/2026	$360,000
Veterans Administration IK2BX005699	Gastrointestinal cell type-specific signaling and *C. difficile* toxin pathogenesis	10/01/2021-09/30/2026	Listed under Contact PI

Summary of Digestive Disease Research

My laboratory's primary focus has been understanding the three toxins produced by *C. difficile* and their roles in pathogenesis, 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. More recently, we have 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

New Associate Director, VDDRC
Co-Director, Scientific Catalyst Program
Strategic Planning Committee, collaborating VI4 Institute
Former Pilot & Feasibility Award Recipient
Retreat Speaker
Retreat Poster Judge

VDDRC Collaborations

We collaborate with Drs. Algood, Byndloss, Coffey, Goldenring, Kaji, Kordus, Lau, Markham, Nicholson, Olivares-Villagomez, Shrubsole, 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 Cell Imaging, Flow Cytometry, and MS/Omics 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.