

**DEPARTMENT OF INTERNAL MEDICINE
COLLEGE OF MEDICINE****SUMMER RESEARCH OPPORTUNITIES FOR UNDERGRADUATE students****FOR APPLICATION YEAR: 2025****PROJECT TITLE: Pathogen factors in Clostridioides difficile - PMN interactions and their impact on CDI recurrence.**

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Project Description

Clostridioides difficile infection (CDI) is a significant public health concern, causing healthcare-associated diarrhea and colitis. Although antibiotic treatment for the initial episode of CDI is effective, recurrence rates remain high. Host inflammatory response to CDI is characterized by colonic Neutrophil infiltration. Although neutrophils are perceived to form the primary defense against C. difficile through phagocytosis and release of anti-microbial molecules, somewhat paradoxically the risk of recurrence is increased in patients with higher neutrophil count at first CDI. Therefore, we posit that C. difficile must have devised mechanism(s) to survive the neutrophil attack and find safe heavens far from the reach of antibiotics to cause recurrence (rCDI). However, we know nothing about how C. difficile survives neutrophil attacks.

This research project aims to unravel the role of neutrophils in CDI recurrence. The study hypothesizes that C. difficile utilizes its virulence factors to evade neutrophil responses, contributing to recurrence. Preliminary data indicate that neutrophils fail to clear C. difficile and, intriguingly, may enhance toxin production and spore entry into intestinal epithelial cells. The project comprises two key aims: (i) Investigate the protective role of virulence factors in C. difficile survival during neutrophil responses in vitro and in vivo; (ii) Examine whether neutrophils facilitate spore entry into intestinal tissue, influencing CDI recurrence. The research strategy involves in vitro and in vivo experiments and employing advanced techniques like flow cytometry and confocal microscopy. The anticipated results promise a deeper understanding of pathogen factors involved in C. difficile survival and the contribution of neutrophils to CDI recurrence, laying the groundwork for future comprehensive investigations.