

Antimicrobial Resistance Training Program in the Texas Medical Center (AMR-TPT)

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Program Director: **Cesar Arias**, MD, PhD, Professor, Internal Medicine, Infectious Disease, Houston Methodist Research Institute

Program Co-Directors: **Kevin Garey**, Pharm D, Professor and Chair, Department of Pharmacy Practice and Translational Research, University of Houston
Danielle Garsin, PhD, Professor, Department of Microbiology and Molecular Genetics, UTHealth

<https://www.gulfcoastconsortia.org/home/training/amr-tpt/>

Meet the Trainees



Andrew "Scott" Bray, PhD

Molecular Virology and Microbiology, Baylor College of Medicine

Appointment: July 1, 2025 – June 30, 2026

Primary Mentor: Katy Patras, PhD, Molecular Virology and Microbiology, Baylor College of Medicine

Co-Mentor: Indira Mysorekar, PhD, Infectious Diseases, BCM

Co-Mentor: Samuel Shelburne, PhD, Infectious Diseases, MDAnderson

Investigating the impact of a diabetic urinary environment on group B Streptococcus virulence and host response.

Group B Streptococcus (GBS) is a major cause of infections, particularly in newborns and adults with weakened immune systems. While antibiotics are commonly used to prevent and treat these infections, GBS is becoming increasingly resistant, making treatment more challenging. One group at high risk is individuals with type 2 diabetes, who are twice as likely to develop urinary tract infections (UTIs), often leading to more severe complications.

This study explores how the diabetic urinary environment influences GBS infections. Since diabetic urine contains high levels of sugar (glucose and fructose), we investigated whether this affects GBS survival and antibiotic resistance. Our preliminary research found that while these sugars do not make GBS grow faster, they do help the bacteria survive attacks from the immune system and increase their resistance to antibiotics like ciprofloxacin.

We identified two bacterial genes, *adhR* and *cydC*, that may play key roles in this process. To better understand their impact, we will create genetically modified strains of GBS and study their behavior in laboratory models, including diabetic mice. Additionally, we will analyze how high sugar levels in urine affect the body's immune response to GBS.

By uncovering how diabetes changes GBS infections, this research may lead to new, non-antibiotic treatments for diabetic patients. The findings could also help in combating other antibiotic-resistant bacteria that thrive in people with metabolic disorders.



Thanh Phuong Minh Le, Pharm D

Department of Pharmacy Practice and Translational Research, University of Houston
College of Pharmacy Appointment:

Appointment: July 1, 2025 – June 30, 2026

Primary Mentor: Kevin Garey, Pharm D, Pharmacy Practice and Translational Research, University of Houston College of Pharmacy Appointment

Co-Mentor: Julian Hurdle, PhD, Center for Infectious & Inflammatory Diseases, Texas A&M Health Science Center

Combining Structure and Genomics to Understand Fidaxomicin Resistance Development in Clostridioides difficile

Clostridioides difficile infection (CDI) is a CDC urgent threat level pathogen and leading cause of nosocomial antibiotic-associated diarrhea in the USA responsible for more than 12,800 death and \$1 billion attributable healthcare costs¹. Two antibiotics are recommended for CDI treatment: vancomycin and fidaxomicin, of which fidaxomicin is first-line therapy due to its narrow-spectrum activity on the gut microbiota and low recurrence rates. FDX use is increasing resulting in increased selection pressure for the emergence of FDX nonsusceptibility strains. Antibiotic susceptibility is not routinely done for *C. difficile* due to lack of appreciation of its importance and technically demanding methods, resulting in lack of knowledge of FDX resistance. The FDX binding site is located in the domain of RNA polymerase. Mutations that occur at or close to the binding pocket have been associated with FDX resistance. Our research uses the mechanistic understanding of FDX binding site to identify favorable mutations likely to confer FDX resistance and emergence in clinical settings. We will analyze whole genome sequencing data to predict FDX resistant strains using worldwide publicly available genomes. Using the clinically reflective mini-bioreactor models, we will determine which resistant strains are likely to propagate in the community. These findings will provide insights into the FDX mechanism of resistance and could be used as a predictive model for circulating FDX-resistant strains and monitor existing or emerging FDX resistance.



Henok Ayalew Tegegne, DVM, PhD.

Department of Pathology & Immunology, Baylor College of Medicine

Appointment: February 1, 2025 – January 31, 2026

Primary Mentor: Dr. Tor Savidge, Department of Pathology & Immunology, Baylor College of Medicine

Co-Mentor: Dr. Todd Treangen, Computer Science, Rice University

Co-Mentor: Dr. Blake Hanson, Epidemiology, Human Genetics & Environmental Sciences, UT Health

Rapid molecular diagnostic of microbiome dysbiosis to predict individual risk of Clostridioides difficile infection.

Clostridioides difficile poses a significant infectious disease threat as an antibiotic-resistant pathogen, particularly in healthcare settings where it causes severe gastrointestinal illness and burdens healthcare systems. However, because this bacterium commonly colonizes the intestine asymptotically, diagnosing pathogen-associated disease remains challenging due to the lack of a definitive test. To address this deficiency in the field we are working with bioMerieux to develop a conceptually different approach to diagnostic testing capable of identifying *C. difficile* infection based on distinct microbiome signatures identified in susceptible patients. This rapid multiplex PCR test could revolutionize patient care by enabling quicker treatment decisions and reducing pathogen spread in hospitals. My project goal is to develop and validate this point-of-care assay with samples from patients clinically diagnosed with *C. difficile* infection. Once validated, I'll proceed to evaluate its effectiveness in prospective studies. Additionally, I will craft user-friendly software to simplify result interpretation for healthcare professionals. Our efforts mark a prototypical shift in diagnostics to the battle against *C. difficile* infections.



Ryan Adam Valdez, PhD

Department of Microbiology and Molecular Genetics, University of Texas Health Science Center at Houston

Appointment: July 1, 2025 – June 30, 2026

Primary Mentor: Danielle Garsin, PhD, Department of Microbiology and Molecular Genetics, University of Texas Health Science Center at Houston

Co-Mentor: Blake Hanson, PhD, Department of Epidemiology, University of Texas Health Science Center at Houston

Co-Mentor: Natasha Kirieno, PhD, Department of BioSciences, Rice University

Deciphering the antibacterial effects of a fungal peptide

Antimicrobial resistance is one of the top threats to global public health and contributes to approximately 9% of all global deaths. Seven bacterial groups that are especially adept at developing antimicrobial resistance, the ESKAPEE pathogens, account for the majority of these deaths. Thus, it is imperative that we develop strategies to mitigate antimicrobial resistance and treat antimicrobial resistant bacterial infections.

Candidalysin, a peptide secreted by the human fungal pathogen *Candida albicans*, exhibits a protective effect against the bacterial pathogens *Enterococcus faecalis* and *Pseudomonas aeruginosa* in a *Caenorhabditis elegans* model of infection at low concentrations. Interestingly, candidalysin does not exhibit bactericidal or bacteriostatic effects on *E. faecalis* at these concentrations, suggesting a novel mechanism of protection. To better understand this effect and the potential of candidalysin as a therapeutic, this investigation aims to uncover the mechanism behind this protective effect. We hypothesize that candidalysin is altering the underlying physiology of the bacterial pathogens to exert this anti-virulence effect. We propose to use a transcriptomics approach to identify bacterial genes with altered expression in the presence of candidalysin, first in *E. faecalis* and then in *P. aeruginosa*, to identify metabolic and virulence pathways that may be impacted. To complement this approach, we will also leverage the two independently generated, ordered *E. faecalis* transposon mutant libraries available in the Garsin lab in a high-throughput forward genetics screen to identify genes implicated in candidalysin susceptibility. We anticipate this work will lay the foundation for the development of desperately needed antimicrobial therapeutics.



Katherine Jayne Wozniak, PhD

Department of Molecular Virology & Microbiology, Baylor College of Medicine

Appointment: July 1, 2025 – June 30, 2026

Primary Mentor: Robert Britton, PhD, Department of Molecular Virology & Microbiology, Baylor College of Medicine

Co-Mentor: Katy Patras, PhD, Molecular Virology and Microbiology, Baylor College of Medicine

Co-Mentor: Kevin Garey, Pharm D, Pharmacy Practice and Translational Research, University of Houston College of Pharmacy Appointment

Understanding Clostridioides difficile RT023 genetic features contributing to emergence of hypervirulent disease

Clostridioides difficile is a prevalent gastrointestinal pathogen that causes severe disease and frequently recurs, resulting in a continuous cycle of painful disease. Aside from fecal microbiota transplantation, the only line of treatment is antibiotic administration which often does not cure disease and can result in antimicrobial resistance. *C. difficile* can live in the environment as well as in human and animal hosts. Over time, *C. difficile* has been evolving to eat unique sugars from the host gut, which has led to prolonged *C. difficile* lifespan and enhanced ability to cause disease. Together, emerging *C. difficile* pose a severe healthcare burden. This project aims to understand the genes driving fitness and disease production in an effort to develop therapeutics for treatment of *C. difficile* infection.