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

Giuseppe Buda de Cesare, PhD
Department of Microbiology and Molecular Genetics, University of Texas Health Science Center at Houston

Appointment: July 1, 2026 – June 30, 2027

Primary Mentor: Mike Lorenz, PhD, Microbiology and Molecular Genetics
Co-Mentor: Dimitrios Kontoyiannis, MD, Internal Medicine, MDAnderson
Co-Mentor: Tor Savidge, PhD, Pathology and Immunology, BCM

Characterization of Activity and Mechanism of Action of the Enterococcus faecalis Bacteriocin EntV on Fungal Pathogens.

This project investigates EntV, a peptide derived from *Enterococcus faecalis*, which reduces fungal virulence and infection severity by altering the production and properties of fungal extracellular vesicles (EVs) rather than directly killing the fungus.

The research aims to define how EntV-modified EVs influence host immune responses and fungal clearance, identify the molecular mechanisms underlying its activity, and evaluate its effectiveness against drug-resistant *Candida* strains alone and in combination with existing antifungal therapies. These studies will support the development of EntV as a novel broad-spectrum antifungal therapeutic.

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, 2027

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 costs[1]. 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.

Ryan Adam Valdez, PhD
Department of Microbiology and Molecular Genetics, University of Texas Health Science Center at Houston

Appointment: September 1, 2025 – Aug 31, 2027

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, 2027

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.