



National Institute of
Allergy and
Infectious Diseases



Texas Medical Center Training Program in Antimicrobial Resistance (TPAMR)

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Program Directors: **Anthony Flores**, MD, PhD, Associate Professor, Pediatrics, Infectious Disease, The University of Texas Health Science Center at Houston; and **Cesar Arias**, MD, PhD, Professor, Internal Medicine Infectious Disease, The University of Texas Health Science Center at Houston

Program Co-Directors: **Kevin Garey**, Pharm D, Professor and Chair, Department of Pharmacy Practice and Translational Research, University of Houston; and **Lynn Zechiedrich**, PhD, Professor, Molecular Virology and Microbiology, Baylor College of Medicine

<https://www.gulfcoastconsortia.org/home/training/tpamr/>

Meet the Trainees



Taryn Eubank, PharmD

Pharmacy Practice and Translational Research, College of Pharmacy, University of Houston; Infectious Disease, Houston Methodist

Appointment: July 1, 2021 – June 30, 2022

Primary Mentor: Dr. Kevin Garey, Department of Pharmacy Practice and Translational Research, College of Pharmacy, University of Houston

Co-Mentor: Dr. Barbara Trautner, Department of Medicine, Baylor College of Medicine

Co-Mentor: Dr. Blake Hanson, Department of Epidemiology, School of Public Health, The University of Texas Health Science Center at Houston

Co-Mentor: Dr. Julian Hurdle, Center for Infectious and Inflammatory Diseases, IBT, Texas A&M University

Emerging Antimicrobial Resistance in Clostridioides difficile

Clostridioides difficile infection (CDI) is the most common healthcare-associated infection in the United States with 223,900 estimated cases and 12,000+ deaths. *C. difficile* is inherently resistant to most antibiotic classes although the most commonly used antibiotic to treat CDI, vancomycin, is generally considered pan-susceptible. Recently, a SNP change in the *vanG* gene cluster was shown to decrease vancomycin susceptibility. This study aims to explore the molecular epidemiology of isolates with decreased vancomycin susceptibility with a focus on the *vanG* gene cluster, assess clinical outcomes associated with these reduced susceptibility strains, and develop a model to understand the pharmacokinetic-pharmacodynamic relationship of this emerging resistance mechanism.



Shantanu Guha, PhD

Microbiology & Molecular Genetics, McGovern Medical School, The University of Texas Health Science Center at Houston

Appointment: September 1, 2020 – August 31, 2022

Primary Mentor: Dr. Danielle Garsin, Department of Microbiology & Molecular Genetics, The University of Texas Health Science Center at Houston

Co-Mentor: Dr. Michael Lorenz, Department of Microbiology & Molecular Genetics, The University of Texas Health Science Center at Houston

Co-Mentor: Dr. William Miller, Division of Infectious Diseases, The University of Texas Health Science Center at Houston

Co-Mentor: Dr. Timothy Palzkill, Department of Pharmacology & Chemical Biology, Baylor College of Medicine

Development of novel antifungals against Candida based on an antifungal peptide produced by Enterococcus faecalis
Fungal antimicrobial resistance to commonly used medicines is a growing public health threat. The most common cause

of dangerous, bloodstream fungal infections are *Candida* species, and there are emergent strains of *Candida* resistant to all current antifungals; this highlights a dire need for novel antifungals. The basis of this project in developing novel antifungal agents is a secreted bacterial peptide (EntV) which is produced by *Enterococcus faecalis* and restricts *C. albicans* to a non-virulent form. This investigation aims to identify the minimal structural features necessary for EntV activity, generate a combinatorial peptide library using the truncated peptide as a template, conduct high-throughput screening to determine gain-of-function peptide variants, and test EntV and its variants in preclinical models to determine its effectiveness and potential usage. We hypothesize that by rationally varying specific residues in combination, we will generate more potent antifungal peptides than the template sequence through synthetic molecular evolution.



Kara Hood, PhD

Pathology and Genomic Medicine, Houston Methodist Research Institute

Appointment: October 1, 2021 – September 30, 2022

Primary Mentor: Dr. Cesar A. Arias, Pathology and Genomic Medicine, Houston Methodist Research Institute

Co-Mentor: Dr. Anna Konovalova, Assistant Professor, Microbiology and Molecular Genetics, UT Health Science Center at Houston

Co-Mentor: Dr. Yousif Shamoo, Ralph & Dorothy Looney Professor, BioSciences, and Vice Provost for Research, Rice University

Molecular Characterization of Transmembrane Proteins of the Lia System Involved in Daptomycin Resistance in Enterococci

Enterococci are gram-positive commensals that can cause life-threatening bacteremia in immunocompromised patients. Susceptible infections are treated with vancomycin, but the rise of vancomycin-resistant enterococci (VRE) is a serious threat to public health. VRE can be treated with daptomycin but the development of daptomycin resistance is often rapid and dramatic; therefore, resistance mechanisms must be understood to circumvent their development. Mutations that confer daptomycin resistance in *Enterococcus faecalis* are often found in the three-component signaling system LiaFSR. LiaFSR regulates the organization of the lipid membrane to divert daptomycin away from the cell septum and prevent disruption of cell division. This project aims to directly measure LiaF's activation of LiaS, the putative interaction LiaF with its proposed inhibitor LiaX, and how other downstream proteins mediate the cell's membrane remodeling response once the pathway has been triggered.



Eva Preisner, PhD

Molecular Virology and Microbiology, Baylor College of Medicine

Appointment: July 1, 2020 – June 30, 2022

Primary Mentor: Dr. Robert Britton, Department of Molecular Virology and Microbiology, Baylor College of Medicine

Co-Mentor: Dr. Kevin Garey, Department of Pharmacy Practice and Translational Research, University of Houston

Co-Mentor: Dr. Anthony Maresso, Department of Molecular Virology and Microbiology, Baylor

College of Medicine

Characterization of simplified microbial communities as a safe antimicrobial treatment option in Clostridioides difficile infections

Antibiotic resistance has emerged as a huge problem leading to an increase in the investigation of non-antibiotic treatment options. Diarrhea caused by infection with *Clostridioides difficile* (*C. difficile*) is most often a result of antibiotic use in hospital or nursing homes. This antibiotic associated disease has the potential for serious complications, including bloody diarrhea, significant chance of relapse, and death. Once *C. difficile* infection (CDI) recurs, many patients get into a vicious cycle of antibiotic therapy and relapse. Fecal transplants from a healthy person have been effectively used to combat recurrent CDI. Microbes in stool help to restore natural gut communities and its protectiveness against enteric infections. However, this treatment can be dangerous due to the many unknown organisms in stool and their potential for adverse side effects. This study is exploring the idea of restoring the protective gut microbiome by using just a few

known and well-studied organisms. This beneficial consortium is aiming to be used as a safeguard when taking certain CDI risk associated antibiotics, but also shortening and lessening the severity once diagnosed. We started by diluting stool, with the idea that through a series of dilutions some of the microbes would be lost, resulting in a community with fewer organisms that were then screened for their resistance to *C. difficile*. The key of the project is the development of a protective community that can eliminate pathogens without the use of antibiotics, lessening the use of antibiotics and preventing unwanted antibiotic resistance.

The TPAMR program is administered by the:



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The GCC is a collaboration of:

Rice University

Baylor College of Medicine

University of Houston

University of Texas Health Science Center at Houston

University of Texas Medical Branch at Galveston

University of Texas MD Anderson Cancer Center

Institute of Biosciences & Technology at Texas A&M Health Science Center