Texas Medical Center Training Program in Antimicrobial Resistance (TPAMR)

Funded by the National Institute of Allergy and Infectious Diseases (NIAID), T32 AI141349

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

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 Clostridoides 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:

Gulf Coast Consortia
QUANTITATIVE BIOMEDICAL SCIENCES

www.gulfcoastconsortia.org

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