Texas Medical Center Training Program in Antimicrobial Resistance (TPAMR)
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Program Director: **Cesar Arias, MD, PhD**, director and founder of the Center of Antimicrobial Resistance and Microbial Genomics (CARMiG) at McGovern Medical School and director of the Center for Infectious Diseases at the School of Public Health, University of Texas Health Science Center at Houston

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

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

Meet the Trainees

Cohort 1, Appointed July 1, 2019

Luis Vega, PhD
Pediatrics, McGovern Medical School, The University of Texas Health Science Center at Houston
Primary Mentor: Dr. Anthony Flores, McGovern Medical School, UTHSC- Houston
Co-Mentor: Dr. Samuel Shelburne, Department of Infectious Diseases, Division of Internal Medicine, The University of Texas MD Anderson Cancer Center
Co-Mentor: Dr. Cesar Arias, Department of Infectious Diseases, Division of Internal Medicine, The University of Texas Health Science Center at Houston

Characterization of relationships between pathogenesis and antimicrobial resistance in Group A Streptococcus
Group A Streptococcus (GAS) can, like most other bacteria, transfer resistance to antibiotics between strains using mobile genetic elements. In addition to making bacteria resistant to antibiotics, mobile genetic elements may affect the ability of bacteria to cause disease. My research project tests the hypothesis that, by changing GAS gene expression, mobile genetic elements may enhance transmission and disease. Using GAS as a model to study how mobile genetic elements that carry antibiotic resistance change the ability of bacteria to infect and transmit across people, my research will enhance our understanding of the emergence and spread of antibiotic resistance.

Dierdre Axell-House, MD
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Co-Mentor: Dr. Cecilia Truc Tran, Department of Internal Medicine, Division of Infectious Diseases, The University of Texas Health Science Center at Houston

LiaX As A Surrogate Marker of Daptomycin Susceptibility In Multidrug-Resistant Enterococcus faecium in patients with cancer
Enterococcus faecium (E. faecium) are usually harmless gut-residing bacteria. They also frequently become "superbugs", which are bacteria resistant to one or more antibiotics. Sometimes *E. faecium* leave the gut and enter the bloodstream, causing life-threatening infections. Daptomycin is a drug of last resort that is used for these serious infections, but now resistance to daptomycin is increasing and of major concern. Traditional methods for detecting whether *E. faecium* are resistant to daptomycin have been shown to be unreliable. These methods are based on the growth of *E. faecium* in the presence of daptomycin, not whether they have a mechanism that results in daptomycin resistance. Only recently has the mechanism been uncovered – a novel protein designated LiaX is released into the environment by enterococci, senses daptomycin, and changes the composition of the outer layer of the organism to disable killing by daptomycin. My project will test the hypothesis of whether quantifying LiaX accurately detects daptomycin resistance compared to traditional methods. The test is most likely to help patients with reduced immune systems at risk for developing *E. faecium* bloodstream infections from the gut, and may improve patients' outcomes. Within this group, patients who receive chemotherapy or immunotherapy for leukemia and lymphoma, or types of blood and bone marrow cancer, are at the highest risk. Because the source of blood infections is the gut for these patients, this "LiaX test" can also be performed on stool samples to test for bacteria before it develops into a bloodstream infection.

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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.

Shantanu Guha, PhD, MPH
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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.