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: E. 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

Jourdan Andersson, PhD
Pathology and Immunology, Baylor College of Medicine

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

Co-Mentor: Dr. Ashok Chopra, Microbiol. & Immunol., UT Medical Branch at Galveston

Co-Mentor: Dr. Vincent Tam, Pharmacy Practice and Translational Research, University of Houston College of Pharmacy

Host-directed therapeutics to combat antibiotic resistant pathogens.
Antibiotic resistant pathogens represent one of the most pressing public health concerns of the 21st century. With traditional drug development being insufficient to keep up with the current demand for newer drugs, drug repurposing offers a more rapid, alternative approach to identify novel therapeutics. Utilizing a drug repurposing screening approach, I previously identified three drugs that were broadly protective against a variety of pathogens, including Yersinia pestis, Clostridioides difficile, Klebsiella pneumoniae, and Salmonella Typhimurium. With no direct drug effects observed on these pathogens of interest, my project aims to optimize the protective effects of these drug leads as well as evaluate their impact on protective host defenses. The results of this study will identify previously unreported host pathways involved in disease pathogenesis and aid in development of targeted immunomodulation as an alternative option to combat antibiotic resistant pathogens.
**Luis Vega, PhD**  
Pediatrics, McGovern Medical School, University of Texas Health Science Center - 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.

**Cohort 2, Appointed July 1, 2020**

**Dierdre Axell-House, MD**  
Infectious Diseases, Baylor College of Medicine  
**Primary Mentor:** Dr. Cesar Arias, Department of Internal Medicine, Division of Infectious Diseases, The University of Texas Health Science Center at 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. 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.
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 *Clostridoides 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.