Molecular Basis of Infectious Diseases (MBID)

Funded by the National Institute of Allergy and Infectious Diseases (NIAID), T32AI055449

Program Director: **Michael Lorenz**, PhD, Professor, Microbiology and Molecular Genetics, The University of Texas Health Science Center at Houston

Program Co-Directors: **Julian Hurdle**, PhD, Professor, Center for Infectious and Inflammatory Diseases (CIID), Texas A&M Health Science Center Institute of Biosciences & Technology
Natasha Kirienko, PhD, Associate Professor, Department of BioSciences, Rice University

https://www.gulfcoastconsortia.org/home/training/molecular-basis-of-infectious-diseases-mbid/

Meet the Trainees 2025-2026

Paula Rivera, Chemical, Physical and Structural Biology, Baylor College of Medicine

Appointment: September 1, 2025 – August 31, 2026
Mentor: Timothy Palzkill, PhD, Biochemistry and Molecular Pharmacology, Baylor College of Medicine

Project Title: Defining the Humoral Immune Landscape of Syphilis Infections through Genome-Scale Phage Display

Syphilis is a sexually transmitted disease (STD) caused by the spirochete bacterium *Treponema pallidum*, and it is the third most common bacterial STD. Syphilis is treatable with antibiotics, but if left untreated it can cause serious health issues. This is especially the case in congenital syphilis, where bacteria from a pregnant syphilis-infected person can cross the placenta and infect the fetus. The development of a vaccine is especially crucial for eliminating the risk of congenital syphilis. In this project, we aim to characterize the humoral immune response in individuals infected with *T. pallidum* by identifying common immunodominant epitopes. Our overarching goal is to define shared immunodominant and immunogenic epitopes that could inform the development of a syphilis vaccine and diagnostic tools. We will construct a comprehensive phage display library encoding overlapping peptides spanning across all ORFs of the *T. pallidum* genome. This phage display library will be used for affinity selection against Fc-immobilized antibodies isolated from the sera of syphilis-infected individuals. We will also utilize our phage display library to identify *T. pallidum* peptides with high affinity for extracellular matrix (ECM) components, including laminin, fibronectin, and collagen, which are key structural proteins also found in the human placenta. Uncovering novel binding partners and their interaction sites will significantly enhance our understanding of T. pallidum pathogenesis and its mechanisms of tissue invasion and dissemination. Overall, this extensive analysis will establish the groundwork for targeted vaccine development and improved stage-discriminative serodiagnostic tools by defining key antigenic targets of *T. pallidum*.

Teresa Sullivan, Microbiology and Molecular Genetics, University of Texas Health Science Center at Houston

Appointment: August 1, 2025 – July 31, 2026
Mentors: Anna Konovalova, PhD, Microbiology and Molecular Genetics, University of Texas Health Science Center at Houston

Project Title: Candida albicans biofilm formation in catheter-associated urinary tract infections

Antibiotics are drugs that kill bacteria during infection; however, bacteria can develop ways to resist these drugs. A group of bacteria, known as gram-negatives, have a protective layer called the outer membrane that works to keep antibiotics out. One way to avoid this challenge is to prevent assembly of important parts of the outer membrane by targeting a protein called BamA. BamA helps build and place proteins into the bacteria's outer layer and is important for survival, therefore it has become a popular target for new antibiotics. Our lab studies a compound named MRL-494 that targets and prevents BamA from functioning. I found several *E. coli* mutants that are able to survive in the presence of MRL-494. To understand how, I performed various experiments that uncovered that these mutants changed parts of the bacterial outer coating known as lipopolysaccharide (LPS) and increased the amount of LPS in the cell. I am currently testing a hypothesis that the cells are increasing LPS as a way to fill the void created by a lack of proteins in the outer membrane. My project will identify how the cells are able to accomplish this and whether this is a common trait among all gram-negative pathogens. By understanding how this resistance works, we can find ways to overcome it and better treat bacterial infections. With this project, I aim to elucidate the molecular mechanisms underlying this resistance and to assess its clinical relevance.

Larissa Tavizon, Microbiology and Molecular Genetics, University of Texas Health Science Center at Houston

Appointment: October 1, 2025 – September 30, 2026
Mentor: Danielle Garsin, PhD, Molecular Virology and Microbiology, University of Texas Health Science Center at Houston

Project Title: Elucidating the role(s) of ubiquitin-mediated proteolysis factors on SKN-1 during pathogen infection of C. elegans

Pathogens are becoming increasingly resistant to modern medicine resulting in untreatable infections. Rather than targeting the pathogen, an alternative option is to utilize the immune response to fight infection. A component of the protective immune response is the transcriptional regulator Nrf (humans)/SKN-1 (C. elegans). SKN-1 activity is protective against pathogen infection however, this activity is controlled by several regulatory mechanisms, one being the negative regulator WDR-23. Since this transcription factor plays a significant role in activating a protective response it is important to better understand how Nrf/SKN-1 regulates the immune response during infection. Doing so will address the critical need for new strategies for treating drug-resistant infections. A previous screen observing SKN-1 activity on pathogen identified a potential regulator, LIN-23. The objective of the research plan is to identify the mechanisms by which LIN-23 regulates SKN-1 activity during pathogen exposure and characterize the role of WDR-23 as a negative regulator of SKN-1. I hypothesize that LIN-23 targets WDR-23 for proteolysis and in doing so promotes SKN-1 activity. Upon completion of the proposed project, I expect to have shown a connection between LIN-23 and WDR-23 in a pathway to regulate SKN-1 activity. Understanding the mechanisms of these two regulators on a critical transcription factor will result in a positive impact on the field.

Meggie Wang, Biochemistry and Cell Biology, Rice University

Appointment: August 1, 2025 – July 31, 2026
Mentor: Natasha Kirienko, PhD, Biosciences Department, Rice University

Project Title: Characterizing the role of R pyocins in bacteria-bacteria and bacteria-host interactions

Antimicrobial resistance (AMR) is a phenomenon in which microorganisms develop resistance against previously effective antimicrobials; the CDC has reported that AMR infections are responsible for killing ~1.27 million people worldwide in 2019. One such pathogen, *Pseudomonas aeruginosa*, is problematic in hospital settings, especially in cystic fibrosis and immunocompromised patients, where certain sequence types (STs) such as ST111 and ST235 are more prevalent. *P. aeruginosa* produces R pyocins, phage tail-like protein complexes that are used for interspecies competition; our lab previously linked the production of R5 subtype pyocins to dominant STs of *P. aeruginosa.*

My current research focuses on understanding the genetic factors that drive strain dominance in bacteria-bacteria and host-pathogen interactions. Firstly, I have evaluated the sensitivity of a clinical isolate library towards each of the R pyocin subtypes. Next, I will evaluate genetic factors that contribute to the observed R pyocin resistance/sensitivity by generating gene deletion mutants and comparing sensitivity profiles. Once these genetic factors are identified, I will evaluate how these factors may confer advantages in bacteria-bacteria competition that shape ST dominance *in vitro*. Finally, I will evaluate these genetic factors in the well-established *Caenorhabditis elegans* model to understand host-pathogen interactions and test the efficacy of R pyocins as an antibacterial treatment. Overall, this research will provide insight into genetic factors that influence susceptibility to R pyocins and help guide the development of R pyocins as a targeted treatment against multidrug-resistant *P. aeruginosa* infections.