National Institute of General Medical Sciences

# Training Interdisciplinary Pharmacology Scientists (TIPS)

Program Director: **Carmen Dessauer,** PhD, Professor, Integrative Biology and Pharmacology, The University of Texas Health Science Center at Houston
Program Co-Director: **Timothy Palzkill**, PhD, Professor and Chair Pharmacology and Chemical Biology, Baylor College of Medicine
*http://www.gulfcoastconsortia.org/home/training/pharmacological-science-tps/*

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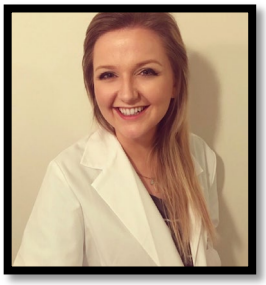
## Meet the Trainees

**C. Ulises Gonzalez**
Appointed November 1, 2020 – October 31, 2021
Biochemistry and Cell Biology, University of Texas Health Science Center – Houston (UTH)
**Primary Mentor:** Dr. Vasanthi Jayaraman, Biochemistry & Molecular Biology, UTH
**Secondary Mentor:** Dr. Seung-Hee Yoo, Biochemistry & Molecular Biology, UTH
***How is the NMDA receptor involved in triple negative breast cancer***
Brain localized N-methyl D- Aspartate receptor (NMDAR) is a tetrametric ionotropic glutamate receptor able to obtain different biophysical properties based on subunit composition. Recently, NMDAR mRNA expression has been identified outside the central nervous system (CNS) and in triple negative breast cancer (TNB). I propose to find subunit composition differences in TNB using molecular techniques as well as verify their functionality using electrophysiology. Furthermore, I will use subunit specific inhibitors to measure decrease in proliferation of TNB. This will allow us to use NMDAR as a handle to pharmacologically target TNB.

**Harmon Greenway**
Appointed December 1, 2020 – November 30, 2021
Chemical, Physical, and Structural Biology, Baylor College of Medicine (BCM)
**Primary Mentor:** Dr. Jin Wang, Pharmacology and Chemical Biology, BCM
**Secondary Mentor:** Dr. Bert O'Malley, Molecular & Cellular Biology, BCM
***Anti-tumor efficacy of alternative splicing inhibitors as HER2-targeted antibody-drug conjugates***
The presentation of neoantigens is an important driver of antitumor immunity and a significant correlate of the clinical outcome for both checkpoint blockade and adoptive T-cell therapies. Dysregulation of pre-mRNA alternative splicing has been implicated in many cancers and produces a class of neoantigen which may yield viable immunotherapeutic targets. Small-molecule inhibitors of alternative splicing machinery have been developed to increase neoantigen burden and demonstrate a selective, cytotoxic effect on tumors. To improve the safety and efficacy of these treatments, we will develop spliceosome inhibitors as antibody-drug conjugates targeted to HER2+ and triple negative breast cancer. Utilizing cancer immunotherapies, we will evaluate the role of neoantigens produced by alternative splicing in T cell-mediated antitumor response.



**Allison Judge**
Appointed November 1, 2019 – October 31, 2021
Biochemistry and Molecular Biology, Baylor College of Medicine (BCM)
**Primary Mentor:** Dr. Timothy Palzkill, Pharmacology, BCM
**Secondary Mentor:** Dr. BVV Prasad, Biochemistry & Molecular Biology, BCM
***Structure, Function, and Inhibition of CTX-M Antibiotic Resistance Enzymes***
My project addresses the most commonly found antibiotic resistance genes, CTX-M family β-lactamases. The first aim employs a novel, high-throughput method for finding amino acid interactions (cooperativity) within an enzyme. This method can be used to gather basic information about structural and functional requirements in CTX-Ms. The second aim will use a DNA-encoded library (DEL) of small molecules to develop inhibitors against a clinically relevant CTX-M enzyme.

**Miranda Lewis**
Appointed November 1, 2020 – October 31, 2021
Molecular Virology and Microbiology, Baylor College of Medicine (BCM)
**Primary Mentor:** Dr. Mary Estes, Molecular Virology and Microbiology, BCM
**Secondary Mentor:** Dr. Timothy Palzkill, Pharmacology and Chemical Biology, BCM
***Combating chronic human norovirus by evaluating nitazoxanide in ex vivo stem cell-derived human intestinal organoids and a clinical trial***
Human norovirus is the predominant cause of vomiting and diarrhea and can establish a chronic infection in immunocompromised people, leading to years of diarrhea which can be life threatening. Currently, there are no licensed therapeutics to treat norovirus. My goal is to determine if nitazoxanide is an effective antiviral for human norovirus, discover its mechanism of action, and determine if norovirus can become resistant to nitazoxanide. These studies will be done utilizing human intestinal organoid cultures as well as samples from an ongoing clinical trial evaluating nitazoxanide treatment in chronically infected patients. This work will support nitazoxanide as the potentially first licensed therapeutic for norovirus infection.

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