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/

Meet the Trainees

Chrystine Gallegos
Appointed November 1, 2022 – October 31, 2024
Neuroscience Graduate Program, University of Texas Health Science Center at Houston (UTH)
Primary Mentor: Dr. Carmen Dessauer, Integrative Biology and Pharmacology, UTH
Secondary Mentor: Dr. Edgar Walters, Integrative Biology and Pharmacology, UTH
Effects of satellite glial cell activation on DRG nociceptors
Satellite glial cells (SGCs) are support cells in the dorsal root ganglion (DRG) that can become activated in chronic pain states, such as after spinal cord injury (SCI). SGC activation may contribute to the development and maintenance of a pro-chronic pain environment, as well as promoting nociceptor dysfunction involving reduced opioid sensitivity and increased hyperexcitability. SCI is also associated with the prolonged elevation of neuroactive signaling molecules, including cytokines and growth factors. The goal of my project is to determine how factors that are upregulated after SCI drive SGC activation, and how activated SGC's in turn induce opioid insensitivity and nociceptor hyperexcitability.

Peyton High
Appointed January 1, 2024 – December 31, 2024
Biochemistry & Cell Biology Graduate Program, University of Texas Health Science Center at Houston (UTH)
Primary Mentor: Dr. Kendra Carmon, Institute of Molecular Medicine, UTH
Secondary Mentor: Dr. Jin Wang, Biochemistry & Molecular Pharmacology, BCM
EGFR-mediated regulation of LGR5 expression and strategies to enhance the efficacy of antibody-drug conjugates
Antibody-drug conjugates (ADCs) are an emerging class of anti-cancer therapeutics that specifically hone cytotoxic payloads to tumor cells while sparing normal tissue. Our lab has generated ADCs targeting leucine-rich repeat-containing G-protein coupled receptor 5 (LGR5), a positive definer of colorectal cancer stem cells (CSCs). Upon treatment, LGR5-directed ADCs promote tumor regression, yet relapse following ADC withdrawal is a major obstacle to sustained tumor elimination. Notably, therapies targeting epidermal growth factor receptor (EGFR), an oncoprotein overexpressed in colorectal cancers (CRCs), have been shown to increase LGR5 *mRNA* and protein levels. Additionally, LGR5 genetic ablation sensitized CRC cells to EGFR-targeted

therapy. The goals of my project are two-fold: (1) determine the mechanism underpinning EGFR-mediated regulation of LGR5 expression; and (2) assess the effect of EGFR-LGR5 dual-targeted therapeutic approaches versus monospecific LGR5 ADC treatment on anti-tumor efficacy and tumor relapse.

Chase Hutchins
Appointed November 1, 2022 – October 31, 2024
Biochemistry and Cell Biology Graduate Program, University of Texas Health Science Center at Houston (UTH)
Primary Mentor: Dr. Alemayehu Gorfe, Integrative Biology and Pharmacology, UTH
Secondary Mentor: Dr. Jeffrey Frost, Integrative Biology and Pharmacology, UTH
Membrane Dynamics and Potential Druggability of Small GTPases Rheb and RhoA
Aberrant activity of small GTPases of the Ras superfamily is prevalent in a variety of cancers. All GTPases of this family are membrane bound proteins anchored to the membrane by a lipid tail at the end of an intrinsically disorded linker region, and move in 3D space around the membrane adopting specific orientation states relative to the membrane. The goal of my project is to determine how these membrane dynamics influence signaling, and then explore how each protein can be drugged in their native membrane bound forms through a combined experimental and computational approach. I will be using molecular simulations in conjunction with experimental functional and biophysical assays to examine both membrane dynamics and potential druggability of the two proteins.

Thao K. Nguyen
Appointed November 1, 2023 – October 31, 2024
Immunology, Therapeutics and Pharmacology Graduate Program, University of Texas Health Science Center at Houston (UTH)
Primary Mentor: Dr. Zhiqiang An, Institute of Molecular Medicine, UTH
Secondary Mentor: Dr. Kai Xu, Institute of Molecular Medicine, UTH
LILRB5 as an immune-checkpoint target during Mycobacterial tuberculosis infection
Immune checkpoint pathways aid the survival of *Mycobacterium tuberculosis* (*M.tb*) inside the host, but they are also vital in controlling *M.tb*-induced pathologies. Therefore, our therapeutic strategies for *M.tb* infection must target only the immune checkpoint factors exploited by the pathogen. Our preliminary data identified the LILRB5 receptor on human immune cells binding to *M.tb*-secreted molecules. Therefore, my goal is to investigate how the activation of LILRB5 limits the human immune response against *M.tb* and its potential as a therapeutic target. Our lab also generated monoclonal IgG antibodies targeting the LILRB5 receptor. They allow us to evaluate the immune-modulating effects of LILRB5 activation during primary *M.tb* infection by blocking the receptors and will facilitate immediate translation from biomedical research to therapeutic applications.

Kevin Wilhelm
Appointed November 1, 2022 – October 31, 2024
Genetics and Genomics Graduate Program, Baylor College of Medicine (BCM)
Primary Mentor: Dr. Olivier Lichtarge, Molecular and Human Genetics, BCM
Secondary Mentor: Dr. Theodore Wensel, Biochemistry and Molecular Biology, BCM
Developing genomics-based tools for drug repurposing
Gene-disease association studies can find candidates for drug repurposing by finding new uses for FDA-approved drugs. Recently, our lab developed multiple algorithmic methods for gene-disease association using evolutionary history and machine learning. I will test new ways of

combining these methods to prioritize identified genes using voting algorithms and PubMed knowledge graphs. I will then rank potential drug repurposing candidates by studying the genes' drug interactions, mechanisms of action, and association to the investigated disease. The result of this study will provide a disease-agnostic method to find new genes influencing disease risk and identify drugs that can be repurposed.

The TIPS program is administered by the:

Gulf Coast Consortia
QUANTITATIVE BIOMEDICAL SCIENCES

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The GCC is a collaboration of:
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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
Houston Methodist Research Institute