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, 2023
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.

Chase Hutchins
Appointed November 1, 2022 – October 31, 2023
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 funcitonal and biophysical assays to examine both membrane dynamics and potential druggability of the two proteins.

Joan Jacob
Appointed December 1, 2021 – November 30, 2023
Biochemistry and Cell Biology Graduate Program, University of Texas Health Science Center at Houston (UTH)
Primary Mentor: Dr. Kendra Carmon, IMM-Center for Translational Cancer Research, UTH
Secondary Mentor: Dr. Mary Estes, Molecular Virology and Microbiology, Baylor College of Medicine

Targeting EREG for the Treatment of Colorectal Cancer

Epiregulin (EREG) is a ligand protein found highly expressed in treatment resistant colorectal cancers (CRC) of various mutation statuses and in both differentiated and undifferentiated cancer stem cell (CSC) populations. The goal of my project is to understand the role of EREG in tumor progression and create an EREG-targeted antibody-drug conjugate (ADC) that functions like a guided missile to deliver a cytotoxic drug to EREG-expressing tumors without harming healthy tissue. I will also generate a bispecific ADC co-targeting EREG and LGR5, to determine if it is more effective in targeting CRC cell plasticity. I will test our ADCs for safety and efficacy against a panel of CRC cell lines and patient-derived tumor and healthy organoid models.

Thi Thu Trang Luu
Appointed January 1, 2022 – December 31, 2023
Biochemistry and Cell Biology Graduate Program, University of Texas Health Science Center at Houston (UTH)
Primary Mentor: Dr. Guangwei Du, Integrative Biology and Pharmacology, UTH
Secondary Mentor: Dr. John Hancock, Integrative Biology and Pharmacology, UTH

Identifying proteomic responses to acute sphingolipid synthesis inhibition

Imbalanced levels in sphingolipids strongly relate to several human diseases, such as cancer and inflammation. The current sphingolipid inhibitors have not generated satisfactory therapeutic outcomes due to toxic side effects and low efficacy. Currently, the studies focus on the long-term cellular responses after sphingolipid inhibition, which are often secondary or indirect. Very little is known about how cells respond shortly after sphingolipid metabolism inhibition. We hypothesized that one type of early response to sphingolipid metabolism inhibition is changes in abundance or subcellular localizations of some proteins. We will identify these proteins shortly after sphingolipid synthesis inhibition and evaluate whether their inhibition can be used together with sphingolipid synthesis inhibitors to improve the current therapies.

Kevin Wilhelm
Appointed November 1, 2022 – October 31, 2023
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 Houston
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