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, and
Program Co-Director: **Timothy Palzkill**, PhD, Professor and Chair, Biochemistry and Molecular Pharmacology, Baylor College of Medicine

http://www.gulfcoastconsortia.org/home/training/pharmacological-science-tps/

Meet the Trainees



Maya Cappellino
Appointed January 1, 2027 – December 31, 2027
Molecular and Translational Biology Graduate Program, University of Texas Health Science Center at Houston (UTHealth Houston)
Primary Mentor**:** Dr. Kendra Carmon, Institute of Molecular Medicine, UTHealth Houston
Secondary Mentor: Dr. Ali Azhdarinia, Institute of Molecular Medicine, UTHealth Houston
Dual-targeting LGRs and EREG using Bispecific Antibody-based Approaches for the Treatment of Colorectal Cancer

Colorectal cancer (CRC) remains a leading cause of cancer-related mortality, in part due to tumor heterogeneity and cellular plasticity, which drive therapeutic resistance. This project focuses on developing and validating a novel bispecific antibody-drug conjugate (bsADC) targeting leucine-rich repeat-containing G protein-coupled receptor 5 (LGR5) and the EGFR ligand epiregulin (EREG), two complementary tumor-associated targets implicated in CRC progression, metastasis, and recurrence. Preliminary findings demonstrate LGR5 and EREG co-internalize and that dual-targeting antibody-based approaches exhibit enhanced cytotoxicity compared with individual targeting strategies.

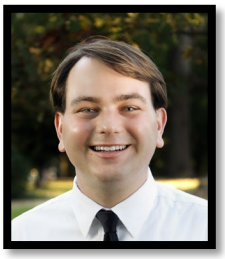
We hypothesize that EREG and LGR5 are inversely regulated, potentially driving resistance to EGFR/MAPK-directed therapies, and that dual-targeting will improve antitumor efficacy. First, we will investigate the mechanisms regulating EREG and LGR5 expression and treatment response. We will then generate and validate EREG×LGR5 bispecific antibodies and use the lead candidate to develop a bsADC, which will be evaluated for safety and efficacy in preclinical CRC models. This therapeutic strategy has the potential to improve treatment durability and reduce relapse in CRC.



Jazmine Grant
Appointed November 1, 2025 – October 31, 2027
MD/PhD student in the Therapeutics and Pharmacology PhD Program, UTHealth Houston
Primary Mentor: Dr. Xiaodong Cheng, Integrated Biology and Pharmacology (IBP), UTHealth Houston
Secondary Mentor: Dr. Alex Gorfe, IBP, UTHealth Houston
Discovery of Paralog-Specific Pharmacological Probes for the EPAC Pathway

The cAMP signaling pathway is a fundamental second messenger system that regulates vital cellular and physiological processes necessary for survival. Exchange protein activated by cAMP (EPAC) was recently discovered as a PKA-independent cAMP effector that acts as a guanine exchange factor for the small GTPase family Rap. EPAC has emerged as a promising therapeutic target for various diseases, particularly in chronic pain. Its paralogs, EPAC1 and EPAC2, while sharing nearly 70% sequence homology, exhibit differences in cellular localization, tissue distribution, and function. Progress in defining EPAC paralog-specific roles in pathophysiological conditions has been limited by the lack of suitable pharmacological probes. Few existing agonists are solely paralog-preferential, and there are no highly selective antagonists with favorable drug-like properties.

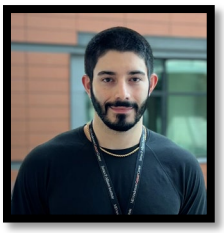
Therefore, the primary objective of my project is to identify potent, paralog-specific small molecules to characterize the pathophysiological roles of EPAC paralogs in chronic pain. To achieve this, we are leveraging past experimental screening datasets and computational drug discovery methods, including quantitative structure-activity relationship (QSAR) models, AI/ML molecular generation, in silico modeling, and molecular dynamics simulations. A hybrid approach integrating ligand- and structure-based drug design will advance our understanding of EPAC paralogs by revealing key protein–ligand interactions, defining conformational states, and characterizing the binding pockets of selected compounds. Establishing new pharmacological tools that target EPAC in a paralog-specific manner will enable investigation of the distinct contributions of EPAC paralogs to various pathophysiological conditions.



Franklin Kennedy
Appointed January 1, 2027 – December 31, 2027
Biochemistry and Cell Biology Graduate Program, Rice University
Primary Mentor: Dr. Natasha Kirienko, BioSciences, Rice University
Secondary Mentor: Dr. Hyun-Eui Kim, Integrated Biology and Pharmacology, UTHealth Houston
Investigating Novel Small Molecules as Promoters of Proteostasis

Neurodegenerative diseases (NDDs) such as Alzheimer's, Parkinson's, and Huntington's diseases continue to rise in prevalence around the world. These disorders are associated with toxic protein aggregates that negatively affect mitochondrial metabolism and function. The accumulation of damaged mitochondria leads to cellular stress, accelerating disease progression and negatively impacting neurons, which do not undergo cell division. Molecules enhancing mitochondrial function (e.g., urolithin A) have been shown to improve NDD-related symptoms, so the identification of more effective drugs for improving mitochondrial function may lead to future therapeutics.

A screen of 250,000 novel small molecules yielded 13 hits belonging to two distinct structural clusters. Because these compounds were not commercially available, we purchased structurally related analogs. Some analogs reduced protein aggregation, ROS levels, and lipid content in worms, without showing toxicity. However, we do not yet know how these compounds function. My research will resolve this question so that we can better understand their potential for future development as NDD preventatives.



Mason Ruiz
Appointed November 1, 2025 – October 31, 2027
Therapeutics and Pharmacology Graduate Program, UTHealth Houston
Primary Mentor: Dr. Zhiqiang An, Institute of Molecular Medicine, UTHealth Houston
Secondary Mentor: Dr. Anil Sood, Gynecologic Oncology, UT MD Anderson Cancer Ctr
A Novel MSMP Neutralizing Antibody Inhibits Angiogenesis-mediated Metastasis in High-grade Serous Ovarian Cancer

High-grade serous ovarian cancer (HGSC) is the most lethal gynecologic malignancy, marked by aggressive growth and frequent recurrence. HGSC tumors depend on VEGF-driven angiogenesis to sustain proliferation and metastasis. Anti-VEGF agents provide initial benefit, but most patients relapse as tumors adapt through alternative angiogenic programs.

This project focuses on MSMP, a tumor-associated pro-angiogenic protein implicated in VEGF-independent angiogenesis. We generated novel fully human anti-MSMP antibodies from a phage scFv library to use as probes for investigating MSMP's biological function. Lead candidate M14, selected on affinity, EC50, and dominant epitope blocking, inhibited endothelial tube formation *in vitro* and showed anti-tumor and anti-angiogenic activity in ovarian cancer xenograft models. We have also developed bispecific constructs pairing anti-MSMP with a VEGF trap, PD-1 blockade, or both to exploit known angiogenic–immunotherapy synergy, for evaluation in immunocompetent models. This work addresses VEGF resistance and aims to advance anti-MSMP antibodies toward preclinical development for VEGF-refractory tumors.

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Alexis Sarne
Appointed January 1, 2027 – December 31, 2027
Neuroscience Graduate Program, UTHealth Houston
Primary Mentor: Dr. Carmen Dessauer, Integrated Biology and Pharmacology, UTHealth Houston
Secondary Mentor: Dr. Jiaqian Wu, Neurosurgery, UTHealth Houston

Satellite Glial Cells as a Novel Therapeutic Target in Chronic Pain

Over half of patients with spinal cord injury (SCI) develop severe and lifelong pain that greatly impact quality of life. Current drug treatments are inadequate in treating this kind of pain; this includes opioids, a highly addictive class of drugs that has dangerous side effects. Specialized neurons (nociceptors), that reside outside of the spinal cord in dorsal root ganglia, respond to painful cues or stimuli. In a healthy person, nociceptors do not fire at rest, but in a pain state, nociceptors fire spontaneously without a pain stimulus, persisting long after recovery from SCI.

My project investigates the role of specialized support cells, satellite glial cells (SGCs), that wrap around nociceptors. We have found that these support cells change after injury and release molecules that may drive abnormal nerve activity. My project will identify these secreted factors, determine how they affect pain-sensing neurons, and uncover new ways to block these harmful signals. Ultimately, this work aims to uncover new targets for safer, more effective treatments for chronic neuropathic pain after spinal cord injury.

The TIPS Program is administered by the

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QUANTITATIVE BIOMEDICAL SCIENCES

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University of Texas MD Anderson Cancer Center
Institute of Biosciences & Technology at Texas A&M HSC
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