Training in Precision Environmental Health Sciences (TPEHS)

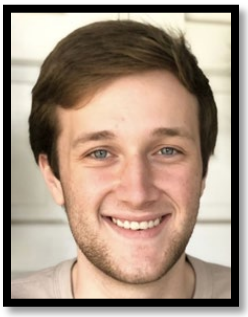
Program Director:
Cheryl Walker, PhD, Director, Center for Precision Environmental Health, Professor, Molecular & Cell Biology, and Medicine, Baylor College of Medicine

Program Co-Directors:
Swathi Arur, PhD, Professor, Genetics, MD Anderson Cancer Center;
Daniel Gorelick, PhD, Associate Professor, Cellular & Molecular Biology, Baylor College of Medicine, and
Craig Hanis, PhD, Professor, Epidemiology Human Genetics & Environmental Sciences, and Human Genetics Center, School of Public Health, UT Health Science Center at Houston.

http://www.gulfcoastconsortia.org/home/training/training-in-precision-environmental-health-sciences-tpehs/

Meet the TPEHS Trainees

The following trainees are supported by T32ES027801, an NIEHS T32 program:



Noah Powell

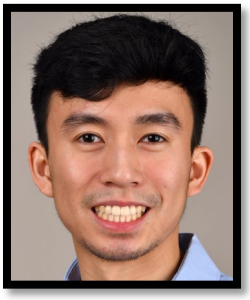
Appointed: February 1, 2025 – January 31, 2026 (Grant year 06)
Program in Cancer and Cell Biology, Baylor College of Medicine
Primary Mentor: Dr. Jason Lee, Molecular and Cellular Biology, BCM
Secondary Mentors: Dr. Swathi Arur, Genetics, MDA; Dr. Ronald Parchem, Molecular and Cellular Biology, BCM
The Functional Tunability of Membrane-less Organelles in Response to Environmental Stressors
In response to environmental stresses, such as heat or arsenic exposure, cells employ an acute compartmentalization mechanism that changes how mRNAs are organized and utilized within minutes of exposure. This acute compartmentalization of mRNAs is governed by the striking formation of membrane-less organelles, such as mRNA processing(P)-bodies. Extensive research into membrane-less organelles has been conducted over the last decade to uncover their dynamics and composition; however, many of their functions are still unclear. Therefore, the overarching goal of my research is to develop novel assays to uncover the function of membrane-less organelles, specifically when cells are exposed to different environmental stresses.

Ellen Thompson

Appointed: February 1, 2025 – January 31, 2026 (Grant year 06)
Program in Development, Disease Models, and Therapeutics, Baylor College of Medicine
Primary Mentor: Dr. Susan Rosenberg, Molecular and Human Genetics, BCM
Secondary Mentor: Dr. Robert Britton, Molecular Virology and Microbiology, BCM
Uncovering the Relationship Between Transcription and Antibiotic-Induced Mutations
In 2019, five million individuals died globally in relation to antimicrobial resistance (AMR), and by 2050 AMR mortality is expected to rise to ten million people. Antimicrobial resistance results

from the horizontal transfer of resistance genes or from new mutations that decrease bacterial sensitivity to one or more antibiotics. Adding to this problem, antibiotics can induce increased mutagenesis themselves thus, increasing the probability of bacteria developing new resistant mutations. My project aims to investigate the role of RNA polymerase transcriptional fidelity and its role in *E. coli* mutagenic DNA break repair of double-strand breaks caused by low-dose exposure to ciprofloxacin (cipro). Cipro-induced double-strand breaks are repaired by homologous recombination which induces the SOS DNA-damage response in all cells causing a cascade of molecular events that lead to increased mutagenesis in a 20-30% subpopulation. We know that RNA polymerase transcription is needed for cipro-induced mutagenesis, so I aim to answer whether the pausing, location, and/or processivity of RNA polymerase has any effect on cipro-induced mutations.

Adya Verma
Appointed: June 1, 2025 – May 31, 2026 (Grant year 06)
Program in Development, Disease Models, and Therapeutics, Baylor College of Medicine
Primary Mentor: Dr. Margot Williams, CPEH, BCM
Secondary Mentor: Dr. Daniel Gorelick, CPEH, BCM
Characterizing the Role of Folate Receptors in Neural Tube Closure
When the brain or spinal cord does not develop properly in the first trimester of pregnancy, babies are born with neural tube defects like spina bifida – these are some of the most common birth defects worldwide. Large-scale population level studies have shown that prenatal supplementation with folic acid can prevent up to 70% of neural tube defects through a mechanism that remains largely unknown. To determine how folate deficiency disrupts morphogenetic cell behaviors driving neural tube closure, I will use a live imaging approach to directly observe neural tube closure at a cellular resolution in living zebrafish embryos lacking folate receptor proteins. Additionally, I will interrogate how folate receptor binding interacts with other pathways that are known to be important in neural tube closure. By determining folate's developmental mechanisms and gene-environment interactions, we will address a long-standing gap in neural tube defect research and gain insight into functional pathways underlying the role of folate in neural tube closure.



Xing Zhang
Appointed: February 1, 2025 – January 31, 2026 (Grant year 06)
Program in Genetics and Epigenetics, MD Anderson Cancer Center
Primary Mentor: Dr. Georgios Karras, Genetics, MDA
Secondary Mentor: Dr. Chad Huff, Epidemiology, MDA
Interrogating Environmental Determinants of HSP90-Buffered Phenotypes
Predicting the clinical pathogenicity of germline mutations is challenging due to gene-environment interactions that contribute to the incomplete penetrance and variable expressivity of phenotypes. The protein-folding chaperone HSP90 may account for much of this phenotypic variation, as it can suppress or "buffer" the deleterious effects of mutations at the cost of rendering phenotypic expression conditional on proteotoxic stressors in the environment. Using the genome instability-associated DNA repair genes FANCA and BRCA1 as models, my project aims to identify common proteotoxic stressors found in the environment that can reveal HSP90-buffered phenotypes. Moreover, it will determine the impact of HSP90-mediated gene-environment interactions on clinical phenotypes, such as cancer, in the general population.

Han Bit Baek, PhD
Appointed: June 1, 2025 – May 31, 2026 (Grant year 06)
Department of Genetics, MD Anderson Cancer Center
Primary Mentor: Dr. Swathi Arur, Genetics, MDA
Secondary Mentor: Dr. Daniel Gorelick, CPEH, BCM
***The Role of Flavonoids in Regulating Oocyte Development in* C. elegans**
Maternal nutrition is a critical factor that influences the quality of her eggs and the health of her offspring. In humans, eggs develop in utero within the fetal gonad. Therefore, starvation and/or dietary exposure to environmental toxins can adversely affect the health of not only her child, but of her grandchildren. To investigate how maternal nutrition regulates egg development, I use *C. elegans* to assess how flavonoids, a class of bioactive compounds found in fruits and vegetables, affect chromosomal dynamics during oogenesis. Given the importance of proper chromosome segregation during egg formation and the potential for flavonoids to affect this process, my work will uncover how flavonoids affect egg development, which will deepen our understanding of how maternal nutrition influences egg quality.

Ty Gadberry, PhD
Appointed: February 1, 2025 – January 31, 2026 (Grant year 06)
Center for Precision Environmental Health, Baylor College of Medicine
Primary Mentor: Dr. Rachel Arey, CPEH, BCM
Secondary Mentor: Dr. Kristina Whitworth, CPEH, BCM
***Understanding Gene-Environment Interactions in PFAS-Induced Neural Toxicity Using* Caenorhabditis Elegans**
Per- and poly-fluoroalkyl substances (PFAS) are a class of persistent and ubiquitous environmental pollutants, with >98% of humans exhibiting detectable levels in circulation. Various legacy and emergent PFAS are associated with adverse health outcomes across species, yet the specific mechanism(s) underlying neurodevelopmental impairments remain poorly understood. *C. elegans* are soil-dwelling nematodes that serve as a powerful model organism for assessing cellular and multi-omic responses to environmental toxicants thanks in part to their rapid lifecycles, translucence, and invariant nervous systems with highly conserved/orthologous function with humans. Therefore, this project will assess the effects of PFAS exposure in *C. Eelgans* on neuronal gene expression across critical developmental stages and over time, explore how natural variations across genetically diverse strains can confer selective susceptibility or resilience to discrete compounds, and determine if exogenous supplementation of candidate antioxidants can mitigate toxicity.

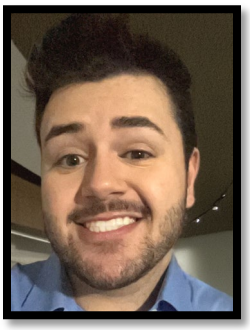
Khushali Patel, PhD
Appointed: June 1, 2025 – May 31, 2026 (Grant year 06)
Department of Molecular and Human Genetics, Baylor College of Medicine
Primary Mentor: Dr. Chonghui Cheng, Genetics, BCM
Secondary Mentor: Dr. H. Courtney Hodges, CPEH, BCM
The Role of Environmental Pollutants in Epigenetic Regulation of Transposons and Cancer Development
Environmental stressors such as arsenic and bisphenol A can disrupt gene regulation – not only by causing DNA mutations but also by acting as molecular switches that turn genes on or off. My research focuses on their effects on a relatively obscure part of the genome called transposons. These repetitive DNA elements are typically silenced, but we have discovered novel transposon-derived RNA transcripts that are differentially expressed during epithelial-mesenchymal transition, a crucial process in development and cancer. In this project, I will investigate the global impact of arsenic and BPA exposure on transposon activity and explore how transposon-derived transcripts alter normal cellular processes to increase risk for diseases such as cancer. This research will reveal the molecular mechanisms linking environmental pollutants to transposon expression and disease.

The following TPEHS trainees receive financial support from their home institutions:

Julia Enterria Rosales

Appointed: February 1, 2025 – January 31, 2026 (Grant year 06)
Program in Development, Disease Models, and Therapeutics, Baylor College of Medicine
Primary Mentor: Dr. Richard Finnell, CPEH, BCM
Secondary Mentor: Dr. Ronald Parchem, Molecular and Cell Biology, BCM
Evaluating the Impact of Semaglutide on Pregnancy Outcomes in a Diabetic Mouse Model

Diabetes during pregnancy is a high-risk situation for both the mother and the baby. While insulin is a common treatment, newer medications like semaglutide, commonly known as Ozempic or Wegovy, have gained popularity for managing diabetes and promoting weight loss. However, the effects of semaglutide on pregnant women with preexisting diabetes or the developing fetus have not been adequately characterized. My project aims to determine whether semaglutide can alleviate diabetes-induced pregnancy complications, such as macrosomia, preterm delivery, and congenital defects, by evaluating gestational parameters in diabetic C57BLKS/J mice. Additionally, the study will examine fetal development and the potential long-term effects on offspring exposed to semaglutide during pregnancy. The research will also include an analysis of semaglutide's biodistribution in maternal plasma, placenta, and fetal tissues, providing insight into its potential developmental toxicity and informing safety guidelines for its use during pregnancy in women with preexisting diabetes.



Joshua Lindenberger

Appointed: June 1, 2025 – May 31, 2026 (Grant year 06)
Department of Genetics and Epigenetics, MD Anderson Cancer Center
Primary Mentor: Dr. Guillermina (Gigi) Lozano, Genetics, MDA
Secondary Mentors: Dr. Han Xu, Epigenetics and Molecular Carcinogenesis, MDA; Dr. Bin Wang, Genetics, MDA
Characterization of Metastatic Cellular Dormant Tumor Cells and Microenvironment from Mutant Trp53 Driven Breast Cancer

My project leverages a mutant p53 driven murine breast cancer to study metastatic cellular dormancy. By studying the transcriptome in the context of spatial localization, we can begin to understand this rare cell population. Beyond this, clinical data show patient obesity impacts tumor recurrence, and we will model this in mice to observe impacts on dormancy.

Llaran Turner

Appointed: June 1, 2025 – May 31, 2026 (Grant year 06)
Program in Genetics and Epigenetics, MD Anderson Cancer Center
Primary Mentor: Dr. George Eisenhoffer, Genetics, MDA
Secondary Mentor: Dr. Swathi Arur, Genetics, MDA
The Role of Sphingosine-1-Phosphate 2 Receptor (S1PR2) in Regulating Cytoskeletal Dynamics Under Environmental Stress of Epithelial Cells During Extrusion

My research explores how cancer cells may hijack the natural process of epithelial cell extrusion to invade surrounding tissue. Building on previous findings that S1P signaling coordinates actin dynamics to regulate extrusion, my in vivo data suggest that interfering with S1PR2 causes cells to extrude basally—mimicking early events in cancer metastasis. My two specific aims focus on identifying how S1PR2 disruption affects F-actin reorganization and whether this promotes basal extrusion of oncogenic cells. Completion of these aims will define the impact of S1PR2 signaling in driving basal cell extrusion and provide insight into how environmental exposures can encourage aberrant actin reorganization in cancer cells to facilitate escape from the tissue. Basal cell extrusion could serve as a potential therapeutic target, and agents that attenuate extrusion may provide new treatment options to reduce metastatic spread.

Udhaya Kumar Siva Kumar, PhD
Appointed: February 1, 2025 – January 31, 2026 (Grant year 06)
Department of Medicine, Baylor College of Medicine
Primary Mentor: Dr. Zheng Sun, Medicine, BCM
Secondary Mentor: Dr. Cristian Coarfa, CPEH, BCM
Intergenerational Effects of Paternal Arsenic Exposure

Extensive air, water, and soil pollution has resulted from urbanization and industrialization. While some progress has been made in reducing pollution, its long-term effects on future generations and their risk for chronic diseases remain unclear. Our study focuses on inorganic arsenic (iAs), a common environmental pollutant in drinking water, to investigate how it impacts health across generations. Male mice exposed to iAs had female offspring with impaired blood sugar regulation and disrupted hypothalamic-pituitary-gonadal (HPG) axis, while male offspring showed lower liver lipid content and triglyceride levels. We found that iAs exposure altered DNA methylation and non-coding RNAs in sperm, which regulate genes linked to hormones and lipid metabolism. We hypothesize that iAs-induced DNA methylation and gene expression changes in the HPG axis can explain the metabolic phenotype in the female offspring. I will use whole genome bisulfite sequencing to analyze DNA methylation in the pituitary. I will use CRISPR-guided epigenome editing to manipulate DNA methylation at specific loci with differential methylation levels in the pituitary. We also will profile RNA modifications in the paternal sperm and early embryos and address their function in epigenetic and phenotypic changes in the offspring. Our study will improve our understanding of how environmental pollutants contribute to chronic diseases like diabetes and fatty liver, helping address the global rise in metabolic disorders.

The TPEHS program is Administered by the:

Gulf Coast Consortia
QUANTITATIVE BIOMEDICAL SCIENCES

www.gulfcoastconsortia.org

The GCC is a collaboration of:
Rice University
Baylor College of Medicine
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