National Institute of Environmental Health Sciences

Baylor College of Medicine
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The University of Texas Health Science Center at Houston

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:
Richard Finnell, PhD, Professor, Center for Precision Environmental Health, Baylor College of Medicine;
Craig Hanis, PhD, Professor, Epidemiology Human Genetics & Environmental Sciences, and Human Genetics Center, School of Public Health, UT Health Science Center at Houston: and
Rui Chen, PhD, Professor, Molecular and Human Genetics, Baylor College of Medicine

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

Meet the TPEHS Trainees

The following trainees are support by T32ES01781, an NIEHS T32 program:

Danielle Gonzales, MD
Appointed: June 1, 2021 – May 31, 2022 (Grant year 03)
Department of Clinical Fellow- Section of Neonatology, Baylor College of Medicine
Primary Mentor: Dr. Bhagavatula Moorthy, Molecular and Cell Biology, BCM
Secondary Mentor: Dr. Abiodun Oluyomi, Epidemiology and Population Sciences, Department of Medicine, BCM
Prenatal Exposure to Heavy Metals in Living Proximity to Superfund Sites and Associated Maternal and Neonatal Complications
Preterm birth has been a source of research for decades. Harris county, Texas has a preterm birth rate that is higher than the national average. Many factors contribute to preterm birth, including maternal health complications. Certain heavy metals have been associated with an increased risk of preterm birth and pre-eclampsia but there are many others that remain to be studied. In addition, Superfund sites have been known to have many contaminants of concern, including heavy metals, but their impact on preterm birth and maternal complications have not been studied. A biospecimen suppository will be used to measure heavy metal levels in cord blood samples in two cohorts of women based on living proximity to Superfund sites. Further, using geospatial analysis, distribution of those who experience preterm birth and certain maternal complications, such as pre-eclampsia, will be analyzed in relation to the environmental hazard.

Kevin C. Klatt, PhD, RD
Center for Precision Environmental Health (CPEH), Baylor College of Medicine
Appointed: June 1, 2021 – May 31, 2022 (Grant year 03)
Primary Mentor: Dr. Cheryl Walker, Molecular and Cell Biology, CPEH, BCM
Secondary Mentor: Dr. Richard Finnell, Molecular and Cell Biology, CPEH, BCM
Fetal Programming By Tributyltin: A Placental Perspective. Early life environmental exposures, including nutrition and industrial chemicals, have the potential to influence fetal development and subsequent adult risk of disease. Tributyltin is a persistent industrial chemical with well-described endocrine-disrupting properties found as a contaminant in the diet, primarily seafood

and drinking water. Emerging links between developmental exposure to this organotin compound and risk of adult hepatic steatosis have spurred investigations into the molecular etiology of this relationship. Research from the Walker Lab is actively investigating epigenetic and gene expression signatures of early life TBT exposure and has identified a conserved hepatic molecular signature of disease risk across the postnatal life-course, extending out to 10 months of age. To further this work, I will be investigating the presence of such a molecular signature, utilizing RNA-Seq and ChIP-Seq approaches, in fetal tissues, including the fetal liver and placenta, a readily available tissue with the potential to serve as both a mediator and surrogate marker of pregnancy-related exposures ad later disease risk.

John Steele, PhD

Appointed: June 1, 2020 – May 31, 2022 (Grant years 02-03)
Center for Precision Environmental Health (CPEH), Baylor College of Medicine
Primary Mentor: Dr. Richard Finnell, CPEH, BCM
Secondary Mentors: Dr. Robert Cabrera, CPEH, BCM; Dr. Cristian Coarfa, CPEH, BCM
Environmental Intervention Strategies for Folic Acid-Resistant Neural Tube Defects

Neural tube defects (NTDs) are severe congenital anomalies caused by disrupted development of the embryonic brain or spinal cord. The etiologies of these birth defects are complex, influenced by compounding genetic and environmental factors. Many NTD cases are fatal; but even treatable NTDs, such as spina bifida, generally result in permanent damage and life-long disability. Thus, public health research has emphasized prevention by identifying the underlying genetic and environmental risk factors. It is well known that maternal dietary folate status is the greatest factor associated with risk for an NTD-affected pregnancy, and that a significant proportion of NTDs can be prevented through dietary fortification with this essential vitamin in the form of folic acid (FA). While FA fortification and supplementation programs have proven successful in preventing over a million birth defects globally these last two decades, the public health burden of NTDs has not been eliminated. In fact, many NTDs have proven FA-resistant, presenting an urgent need to understand the mechanisms underlying these FA-resistant defects and to develop novel intervention strategies targeting this population. My project aims to dissect metabolic mechanisms underlying NTDs in FA-resistant genetic mouse models using both untargeted metabolomic analysis and targeted stable isotope tracing of embryonic metabolism. These same techniques will be used to assess the efficacy of proposed intervention strategies for preventing FA-resistant NTDs in these models. By elucidating mechanisms of FA-resistance and establishing alternative intervention strategies, this study will yield valuable knowledge needed to target and prevent these previously unpreventable birth defects.

Alyssa Alaniz Emig

Appointed: June 29, 2020 – June 28, 2022 (Grant years 03-04)
Department of Molecular and Cellular Biology, Center for Precision Environmental Health (CPEH), Baylor College of Medicine
Primary Mentor: Dr. Margot Kossmann Williams, Molecular and Cell Biology, CPEH, BCM
Secondary Mentor: Dr. Richard Finnell, Molecular and Cell Biology, CPEH, BCM
Genetic Drivers of Neural Tube Morphogenesis and Their Role in Environmental Risk of Birth

Congenital conditions arise from atypical embryonic development and are among the most common causes of childhood death and loss of pregnancy worldwide. These conditions include the malformation of the future brain and spinal cord, which arise during early development and are shaped by highly conserved cell movements that extend the head-to-tail axis and close them into a tube. Holoprosencephaly (HPE) is a result of the improper formation of the brain and facial structures due to mutations affecting these conserved cell movements through the Nodal signaling pathway. In addition to Nodal signaling mutations, exposure to toxic environmental factors (pesticides, herbicides and hyperthermia) has been correlated with HPE risk, but it is unknown why some individuals with the same genetic mutation are more likely than others to develop a severe form of the condition. By utilizing nodal mutant zebrafish as a model for HPE in combination with RNA sequencing and environmental toxicant screening, we will identify key modifier genes that interact with environmental toxicants to increase the severity of brain and spinal cord related congenital conditions.

Shinhye Chung
Appointed: June 1, 2020 – May 31, 2022 (Grant years 02-03)
Department of Epidemiology, Human Genetics and Environmental Sciences (EHGES), University of Texas Health Science Center - Houston
Primary Mentor: Dr. Goo Jun, EHGES, UTHealth
Secondary Mentor: Dr. Craig. L. Hanis, EHGES, UTHealth
Diet by Genomic Interactions in Determining Metabolic Traits and Profiles Among Mexican Americans in Starr County, Texas
Prediabetes is a condition of higher blood sugar level than normal, but not high enough to be type 2 diabetes. It is important to prevent it from progressing to type 2 diabetes, stroke, and heart disease. Diet is one of the essential modifiable factors on glycemic traits, but it is still unknown how different nutrients can affect glucose metabolism in conjunction with genes. Recently, metabolomics has been studied as a new tool to find genetic and environmental associations. Thus, the goal of this project will identify how different nutrients can affect glycemic traits with the human gene via plasma metabolites from the metabolomic profiles in Mexican Americans. This study could provide scientific evidence of how diet can affect glycemic traits with individual gene variation.

Phillip Erice
Appointed: June 1, 2020 – May 31, 2022 (Grant years 02-03)
Department of Immunology, Baylor College of Medicine
Primary Mentor: Dr. Antony Rodriguez, Department of Medicine, Immunology, Allergy, and Rheumatology, BCM
Secondary Mentor: Dr. H. Courtney Hodges, Molecular and Cell Biology, BCM
Mechanisms of Let-7 microRNA in immune cells as a genetic modifier of emphysema
Chronic inhalation of cigarette smoke and air pollutants are major causes of sterile inflammation and pulmonary emphysema. While the molecular mechanisms underlying emphysema pathophysiology are incompletely defined, evidence of the contributions of the let-7 microRNA regulatory network is emerging. We will test the hypothesis that let-7 miRNA operates within distinct immune cell compartments as a molecular brake to inflammation in emphysema. Our approach makes use of genetically manipulated mice in combination with preclinical models of emphysema to identify the cell-intrinsic role of let-7. We will assess the immune response and lung injury of our murine models after exposure to cigarette smoke or nanoparticulate carbon black, a component of smoke and air pollution, and utilize transcriptomic profiling of sorted lung immune cells to interrogate the direct post-transcriptional targets of let-7.

Rachel Keuls
Appointed: July 1, 2021 – June 30, 2022 (Grant year 04)
Department of Development, Disease Models and Therapeutics, Baylor College of Medicine
Primary Mentor: Dr. Ronald Parchem, Molecular and Cell Biology, BCM
Secondary Mentor: Dr. Richard Finnell, CPEHS, BCM
MicroRNAs regulate maternal-fetal nutrient exchange during neural tube closure
Neural tube closure is the first step in central nervous system formation that begins early during embryonic development before the placenta and embryonic vasculature are established. Many neural tube closure defects (NTDs) are lethal, but even if the fetus survives, lifelong disability results. Approximately 300-500 babies are born each day with an NTD. NTDs are of complex etiology resulting from both environmental and genetic factors. Neural tube closure requires a precise input of a variety of metabolites, such as folic acid, glucose, and lipids. How metabolic pathways are regulated to ensure neural tube closure is not well understood. During neural tube closure, the yolk sac serves as the primary site of maternal-fetal nutrient exchange. Previously it has been demonstrated that microRNA mediated gene silencing is required for neural tube closure, yolk sac formation, and proper embryonic metabolism. My research aims to understand how microRNAs promote the proper uptake and processing of nutrients within the yolk sac and the embryo to ensure neural tube closure. This work will reveal mechanisms that could be used to prevent or correct neural tube closure defects in-utero.

Gabriel Tukeman
Appointed: July 1, 2021 – June 30, 2022 (Grant year 04)
Department of Molecular and Cellular Biology, Baylor College of Medicine
Primary Mentor: Dr. Richard Finnell, CPEHS, BCM
Secondary Mentor: Dr. Daniel Gorelick, CPEHS, BCM
Cellular response to HIV integrase inhibitor dolutegravir with varying folate status
Dolutegravir (DTG) is a medication use in the treatment and management of Human Immunodeficiency Virus (HIV). It is the number one recommended treatment of HIV by the World Health Organization, regardless of age and sex. In 2018, DTG was flagged as a potential factor that could result in neural tube defects (NTDs) when taken at the onset of pregnancy. Post- market surveillance studies in Botswana as of 2020 have shown that mothers taking dolutegravir from the beginning of their pregnancy were twice as likely to have a pregnancy resulting in an NTD birth defect. DTG has previously been shown as a partial antagonist to folate receptor 1, and folate supplementation is a long known modifier to against NTD risk. My project aims to study cellular response to DTG in natural and synthetic folate environments and identify potential mechanisms leading to increased NTD risk. I will utilize primary mouse embryonic fibroblasts harvested from wildtype, FOLR1$^{+/-}$, and FOLR1$^{-/-}$ embryos and treat with step-wise concentrations of DTG supplemented with either natural 5-methyl-tetrahydrofolate (5-MTHF) or synthetic folic acid. I will then stain and visualize cells for structural changes as well as look at changes in the transcriptome and methylome between conditions. These experiments will reveal processes impaired with the addition of DTG and if such impairment can be rescued with additional folic acid or 5-MTHF.

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

Sofia Ivana Aramburu
Appointed: July 1, 2021 – June 30, 2022 (Grant year 04)
Program in Development Disease Models and Therapeutics, Baylor College of Medicine
Primary Mentor: Dr. Susan M. Rosenberg, MHG, BCM
Secondary Mentor: Dr. Cristian Coarfa, Molecular and Cellular Biology, BCM
Identifying human proteins that protect the cell from DNA damage
Cells are subject to an estimated 70000 DNA-damaging events every day, stemming from both internal and external sources. Although these events are usually repaired correctly, inefficient, or low-fidelity repair can lead to mutations. Mutation accumulation during aging causes loss of cellular function, thus increasing the risk of age-related diseases. Water bears and stress resistant organisms possess proteins that protect them from damage. We have identified human proteins with shared biochemical and structural properties and used DNA damage markers that show them to reduce DNA damage when over-produced in human cells. The goal of this project is to determine what kinds of DNA damage are reduced and how these proteins reduce damage. Moreover, because the ultimate goal of preventing DNA damage is reducing the accumulation of mutations in cells, we will measure whether mutations are decreased by the over-production of the protein candidates to identify those that can maintain a low number of mutations. This project will provide valuable insight into disease development and open the door to new potential disease prevention strategies.

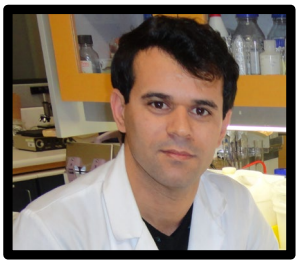
Harlie Cope
Appointed: June 1, 2020 – May 31, 2022 (Grant years 02-03)
Department of Genetics and Genomics, Baylor College of Medicine
Primary Mentor: Dr. Cheryl Walker, Molecular and Cell Biology, CPEH, BCM
Secondary Mentor: Dr. Cristian Coarfa, Molecular and Cellular Biology, CPEH, BCM
Role of Non-coding RNAs in Epigenomic Reprogramming by TBT
Tributyltin (TBT) is an environmental contaminant associated with adverse health outcomes in rodent models and humans, including non-alcoholic fatty liver disease (NAFLD). NAFLD prevalence is increasing in the U.S., making understanding NAFLD onset and progression a critical public health concern. For my project, I will be studying the potential for the epigenome to be reprogrammed in response to an early life exposure to TBT. I will be focusing on the role of non-coding RNAs, which despite making up

70% of the genome and having diverse biological roles, have been historically overlooked in toxicology studies. I will be examining the role of non-coding RNAs as both targets of reprogramming by TBT, and as mediators of environmental health effects.

Rowland Pettit

Appointed: June 1, 2020 – May 31, 2022 (Grant years 02-03)
Department of Quantitative and Computational Biosciences, Baylor College of Medicine
Primary Mentor: Dr. Chris Amos, Institute for Clinical and Translational Research, BCM
Secondary Mentor: Dr. Christian Coarfa, Molecular and Cellular Biology, CPEH, BCM
Determining Causality and the Shared Genetic Architectures between Phenotypes, Environmental Exposures, Co Morbidities and Lung Cancer

Lung cancer is the leading cause of cancer-related deaths. Currently, no genetic-based lung cancer screening tool exists, however, co-occurring phenotypic traits can potentially serve as surrogate risk markers. My work will focus on identifying novel phenotypes associated with lung cancer and determining if they play a causal role in disease development. Cross-trait linkage disequilibrium score regression (LDSR) is a genome-wide association based regression method that is particularly useful for identifying genetic correlations between phenotypes and a disease process. Mendelian randomization is an epidemiological tool that can infer causality between exposures and outcomes by creating cohorts of people based on individual genetics – 'randomizing' them by their shared genes. Using LDSR and Mendelian randomization, I aim to demonstrate a genetic basis and causal role between environmental factors, phenotypic traits, and disease co-morbidities with lung oncogenesis.



Vahid Zadmajid, PhD

Appointed: July 1, 2021 – June 30, 2022 (Grant year 04)
Department of Molecular and Cellular Biology, Center for Precision Environmental Health (CPEH), Baylor College of Medicine
Primary Mentor: Dr. Daniel A Gorelick, Molecular and Cell Biology, CPEH, BCM
Secondary Mentor: Dr. Margot Kossmann Williams, Molecular and Cell Biology, CPEH, BCM
Endocrine disruption through membrane steroid receptors

Endocrine-disrupting chemicals (EDCs) are exogenous small molecules that mimic endogenous hormones and alter the functions of the endocrine system. EDCs alter endocrine functions by activating or inhibiting steroid hormone receptors. So far, the field has been focused on how EDCs bind to nuclear hormone receptors such as estrogen receptors alpha and beta. To date, data on EDC engagement with membrane steroid receptors, such as G protein-coupled estrogen receptor, is limited. Here, I hypothesize that EDCs act via membrane steroid receptors, in addition to previously defined nuclear steroid receptors, to cause adverse effects on embryonic development. I will expose zebrafish embryos to multiple classes of EDCs (estrogens, progestins, androgens) and assay morphological phenotypes. I will then test whether the phenotype is rescued in zebrafish with mutations in the corresponding membrane steroid receptor versus nuclear steroid receptor. Results from this study will increase our understanding of the molecular and cellular mechanisms by which EDCs influence embryonic development.

Jun Xu

Appointed: June 1, 2020 – May 31, 2022 (Grant years 02-03)
Epidemiology, Human Genetics and Environmental Sciences (EHGES), The University of Texas Health Science Center - Houston
Primary Mentor: Dr. Craig Hanis, EHGES, UTHealth
Secondary Mentor: Dr. Goo Jun, EHGES, UTHealth
The Functional Roles of the Gut Microbiome in Type 2 Diabetes and Obesity: A Metagenomics Analysis within The Mexican American Population of Starr Country, TX

Although many studies have revealed associations between the gut microbiota composition and host metabolism, the functional gene and gene families and related biological pathways, which are actually contributed to human physiology and pathobiology remains largely unexplored. Multiple molecular mechanisms of gut

microbiota and their interactions with environmental exposures, such as diet, contributed to metabolic disease. Microbiota modulates inflammation, interacts with dietary constituents, affects gut permeability, glucose and lipid metabolism, insulin sensitivity and overall energy homeostasis in the host. Function-driven metagenomics analysis offers great possibilities to discover new classes of genes with specific functions. Using whole genome sequencing profiling data from human gut microbiome of participants in Starr County, TX, I will evaluate associations between glycemic status and obesity and functional profiling from metagenomics data to identify gene families and metabolic pathways. I will also explore the interactions between the identified gene families/metabolic pathways and dietary factors associated diabetes and obesity.

The TPEHS program is Administered by the:

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The GCC is a collaboration of:
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