National Institute of Environmental Health Sciences

The University of Texas Health Science Center at Houston

Baylor College of Medicine

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 Trainees

Appointed June 2019 (Supported by TPEHS)

Samantha Decker
Neuroscience, Baylor College of Medicine
Primary Mentor: Dr. Ronald Parchem, Neuroscience, BCM
Secondary Mentor: Dr. Richard Finnell, CPEHS, BCM
MicroRNA regulation of neural tube closure in maternal diabetes
Pregestational diabetes increases risk of neural tube closure defects (NTDs) which can range from embryonic lethal anencephaly to debilitating spina bifida. The mechanism underlying the maternal environment's impact on the genetic regulation of neural tube closure is not fully understood. My project aims to study the role of a micro RNA (miR-290) in the context of the diabetic maternal environment. I will use a miR-290 mouse model and induce maternal pregestational diabetes. Then I will be able to characterize the NTD phenotype of embryos that have miR-290 knocked out compared to their WT littermates. I also plan to use multiple sequencing methods to identify which genes are being regulated by miR-290 to potentially identify genes that are misregulated due to the diabetic maternal environment that leads to increased prevalence of NTD.

Ahmet Yavuz, PhD
Huffington Center on Aging, Baylor College of Medicine
Primary Mentor: Dr. Meng Wang, Huffington Center on Aging (BCM)
Secondary Mentor: Dr. Rui Chen, Molecular and Human Genetics (BCM)
Metabolic Fate of Saturated and Unsaturated Dietary Lipids
Lipid molecules act not only as energy resources or physical barriers, they are also actively involved in regulating cellular signaling, membrane trafficking, and the transcriptional network. Aberrations in lipid intake is an environmental factor impairing the lipid metabolism and contributing to the pathology of various human diseases including obesity, nonalcoholic fatty liver diseases, cardiomyopathy, and type II diabetes; however, the molecular mechanisms regulating physiological and pathological functions of different types of fatty acids are not clearly understood. Using the model organism C. elegans, I will dissect the molecular mechanisms that regulate the incorporation of different types of fatty acids into lipid droplets, special cell compartments excess fatty acids are stored in, through high-throughput forward genetic screening. I will create a novel pipeline to analyze the mutant candidates from the screen and identify causal mutations with whole genome sequencing, as an alternative to the current methods that require backcrossing.

Appointed June 2020 (Supported by TPEHS)

Shinhye Chung
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
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.

Amal Rammah, PhD
Center for Precision Environmental Health, Baylor College of Medicine (BCM)
Primary Mentor: Dr. Elaine Symanski, Center for Precision Environmental Health, BCM
Secondary Mentors: Dr. Chris Amos, Institute of Clinical and Translational Medicine, and Quantitative Science, BCM; Dr. Kristina W. Whitworth, Center for Precision Environmental Health, BCM
Air pollution, residential greenness and metabolic dysfunction among pregnant women
Metabolic disorders of pregnancy, such as impaired glucose tolerance (IGT), gestational diabetes mellitus (GDM) and dyslipidemia, have short- and long-term implications for the health of both mother and child. Previous investigations of the association between air pollution and metabolic dysfunction in pregnancy have generally assessed GDM based on the birth record without examining subclinical disturbances (such as IGT or dyslipidemia) and have also relied on crude air pollution exposure assessment methods. Further, despite growing recognition of the importance of the built environment in influencing maternal health, no studies have examined the combined effects of air pollution and residential greenness on metabolic function in pregnant women. This will be the first study to evaluate the combined effect of air pollution (fine particulate matter ($PM_{2.5}$) and nitrogen dioxide (NO_2)) and residential greenness on the risk of metabolic dysfunction during pregnancy, drawing on a large population-based cohort with extensive sociodemographic, diet and health history data linked to electronic medical records (the Spanish INfancia y Medio Ambiente (INMA) project). To reduce misclassification errors present in prior studies, we will also apply novel exposure assessment methods that produce weekly NO_2

exposure estimates and incorporate satellite data with geographic, meteorological and air monitoring data to produce highly resolved weekly $PM_{2.5}$ exposure estimates based on each mother's residential history throughout pregnancy.

John Steele, PhD
Center for Precision Environmental Health, Baylor College of Medicine
Primary Mentor: Dr. Richard Finnell, Center for Precision Environmental Health (BCM)
Secondary Mentors: Dr. Robert Cabrera, Center for Precision Environmental Health (BCM)
Dr. Cristian Coarfa, Center for Precision Environmental Health (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.

Appointed June 2020

Harlie Cope
Genetics and Genomics, Baylor College of Medicine
Primary Mentor: Dr. Cheryl Walker, Molecular and Cell Biology (BCM)
Secondary Mentor: Dr. Cristian Coarfa, Molecular and Cellular Biology, (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
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, Dan L Duncan Cancer Institute, 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-occuring 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.

Jun Xu
Epidemiology, Human Genetics and Environmental Sciences (EHGES), 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.

Appointed July 2020 (Supported by TPEHS)

Alyssa Alaniz
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.

The TPEHS program is Administered by the:

Gulf Coast Consortia
QUANTITATIVE BIOMEDICAL SCIENCES

www.gulfcoastconsortia.org

Questions: Contact Vanessa Herrera
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The GCC is a collaboration of:
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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