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 and Chair
Pharmacology, 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

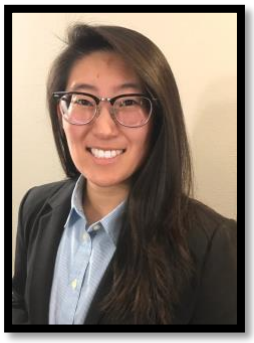
http://www.gulfcoastconsortia.org/home/training/training-in-precision-environmental-health-sciences-tpehs/

Meet the Trainees

Cohort 1, Appointed January 1, 2019 (Supported by institution)

MacKinsey Bach
Epidemiology, Human Genetics and Environmental Sciences (EHGES), University of Texas Health Science Center - Houston
Primary Mentor: Dr. Laura Mitchell, EHGES, UTHealth
Secondary Mentor: Dr. Mohammad Rahbar, EHGES, UTHealth
Effects of the Maternal Genome on Risk of Autism Spectrum Disorder: Utilization of Whole Genome Sequence Data for Genome-Wide, Gene-Based Analyses and Genetic Risk Scores
The etiology of autism spectrum disorder (ASD) is still largely unknown, with most cases likely resulting from combinations of genetic and environmental exposures. The maternal genome and preexisting maternal metabolic conditions modulate the fetal environment and thus potentially contribute to ASD risk and severity in her children, though prior studies on these types of maternal exposures have produced inconsistent results. Using whole genome sequencing data from the Simons Simplex Collection, I will use a genome-wide gene-based approach and analysis of maternal genetic risk scores for hypertension, obesity, and diabetes to investigate the role of the maternal genome in ASD. I will also explore interactions between maternal genes and/or GRS for these conditions and other exposures that can affect the fetal environment, such as substance use, age of the parents, the child's sex, and the child's genes, in relation to ASD.

Marzia Savini
Developmental Biology, Baylor College of Medicine
Primary Mentor: Dr. Meng Wang, Molecular and Human Genetics (BCM)
Secondary Mentor: Dr. Christophe Herman, Molecular and Human Genetics (BCM)
Tissue Cross-talk in Longevity Mechanism Regulation
The rate of aging can be modulated by nutritional, environmental and metabolic cues. How those signals are coordinated among different tissues is a fundamental question for understanding aging regulation. Recent work in our lab demonstrated that the intestine-specific induction of a lysosomal acid lipase *lipl-4* increases *C. elegans* lifespan by more than 40%. My project aims to identify through nutritional screening how the signal from the intestine (where *lipl-4* functions) is transmitted into the neurons (where the neuropeptide functions). I expect that my project will reveal novel regulatory mechanisms of longevity and diet-fat-neuron crosstalk, and have a broad impact on human health.



Lythou Melody Yeo
Biochemistry and Molecular Biology, Baylor College of Medicine
Primary Mentor: Dr. Richard Finnell, Center for Precision Environmental Health (BCM)
Secondary Mentor: Dr. Philip Lupo, Pediatrics (BCM)
Examining the Role of Folate Antagonism in Valproic Acid-Induced Neural Tube Defects
Anti-epileptic drugs (AEDs), despite having a well-established teratogenic potential, continue to be prescribed to women of reproductive age, leading to an elevated risk of adverse pregnancy outcomes such as neural tube defects (NTDs). Periconceptional maternal folate supplementation, shown to be effective at preventing NTDs in general, have also been found to counteract the teratogenic effects of valproic acid (VPA), the most commonly prescribed AED globally. However, some VPA-induced NTD cases appear to be non-folate responsive and persist despite folate supplementation, suggesting that the teratogenic mechanism of VPA involves disruption of proper folate utilization. Using next-generation sequencing techniques alongside both mouse and embryonic stem cell models, my project aims not only to establish the mechanism of action underlying VPA teratogenesis, but also to identify the cellular processes that are perturbed as a result of VPA exposure. Together, the results of this study will reveal the mechanism through which AEDs impair embryogenesis and ultimately promote the future development of non-teratogenic AEDs.

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

Eric Smith
Molecular and Cellular Biology, Baylor College of Medicine
Primary Mentor: Dr. H. Courtney Hodges, Molecular and Cell Biology (BCM)
Secondary Mentor: Dr. Rui Chen, Molecular and Human Genetics (BCM)
Lineage-specific epigenetic reprogramming induced by arsenic exposure to primordial germ cells
Description: Millions of people worldwide are exposed to naturally occurring inorganic arsenic through ingestion of contaminated food and water. Arsenic exposure not only has a broad impact disrupting several body systems, but it has also been shown to disrupt normal developmental processes and is associated with predisposition to cancer later in life. To make direct connections between arsenic-induced epigenetic changes and adverse health outcomes, we will combine single-cell approaches following the addition of arsenic to embryoid bodies, an in vitro 3D model of embryogenesis. We will use single-cell RNA-seq and single-cell ATAC-seq approaches to map out cell-type specific effects, as well as their persistence and reversibility following therapy. This intersection of a complex 3D model of embryogenesis and single-cell approaches will ultimately allow the determination of how early environmental exposure to arsenic affects development at a level of detail currently unavailable.

Lauren E. Swanson, DO
Department of Pediatrics, Section of Neonatology, Baylor College of Medicine
Primary Mentor: Dr. Bhagavatula Moorthy, Neonatology (BCM)
Secondary Mentors: Dr. Cheryl Walker, Center for Precision Environmental Health (BCM)
Dr. Krithika Lingappan, Neonatology (BCM)
Effect of Maternal Polycyclic Aromatic Hydrocarbon (PAH) Exposure on Neonatal Hyperoxic Lung Injury: Role of gut microbiome
Environmental exposure to polycyclic aromatic hydrocarbons (PAHs) during pregnancy has been shown to increase the risk of premature delivery. Bronchopulmonary dysplasia is a chronic lung disease of prematurity and one of the most common causes of morbidity and mortality in premature infants who require prolonged respiratory support; however, the specific effect of prenatal PAH exposure on neonatal lung development is largely unknown. There is increasing evidence that the intestinal microbiome influences the development of lung disease, a concept referred to as the gut-lung axis. We will test the hypothesis that mice exposed prenatally to a mixture of PAHs [Benzo[a]pyrene (BP), benzo(b)fluorene (BbF), and dibenz[a.h]anthracene (DBA)] will lead to augmentation of neonatal lung injury following postnatal hyperoxia, and that dysbiosis of the gut microbiome plays a mechanistic role in this phenomenon. We will also test the hypothesis that increased intestinal lactobacillus (LB) load via postnatal administration of LB, as a probiotic, will result in protection against neonatal lung injury. These studies should lead to the identification of novel mechanisms by which PAHs exacerbate neonatal lung injury in premature infants.

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.

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