2018 Pilot Projects Summary

In 2018, four Pilot Projects were funded, for a total of $159,889.

1. **Near-Roadway Air Pollution Exposure and the Gut Microbiome During Pregnancy and Early Life: Implications for Childhood Obesity**

   **Co-Principal Investigators:**
   Claudia Toledo-Corral, MPH, PhD, Assistant Professor, California State University, Los Angeles, Department of Public Health/ Adjunct Assistant Professor of Research, Department of Preventive Medicine, Division of Environmental Health, Keck School of Medicine of USC
   Tanya Alderete, PhD, Postdoctoral Research Scholar, Department of Preventive Medicine, Division of Environmental Health, Keck School of Medicine of USC

   **Abstract:**
   Prenatal and early life environmental exposures to air pollutants have been associated with low birth weight and increased risk for childhood obesity. Additionally, results from the Children’s Health Study have shown that *in utero* near-roadway air pollution (NRAP) exposure is associated with increased childhood body mass index. While the mechanisms underlying these associations remain uncertain, animal studies and our recent preliminary data suggest that NRAP exposure may alter the gut microbiota and modify risk for obesity. Despite this, no studies have examined the potential impact of NRAP exposure on the human microbiome during critical periods of development, including pregnancy and early life. Therefore, we propose a pilot study that will examine a subset of pregnant Hispanic women from the ongoing Maternal and Developmental Risks from Environmental Stressors (MADRES) cohort, a newly established pregnancy cohort with an end-target of 1,000 predominantly Hispanic mother-child pairs living in the greater Los Angeles region. This pilot study will support the collection and analysis of stool samples needed to perform detailed gut microbial profiling in 40 women during pregnancy and 40 infants at 1 and 12 months of age. To our knowledge, this will be the first study to examine the relationships between prenatal and early life air pollution exposure and the gut microbiome, providing novel preliminary data for future grant applications. We postulate that increased NRAP exposure will be associated with alterations in the gut microbiome, which will contribute to alterations in infant growth trajectories in the first year of life. Results from the proposed pilot study will test the feasibility of stool collection in MADRES and will generate preliminary data for external grant applications aimed to examine these relationships in a larger cohort of mother-infant pairs with repeated stool sampling.

2. **Environmental Impacts on Cardiovascular Health Over the Lifecourse**

   **Principal Investigator:**
   Shohreh Farzan, PhD Assistant Professor, Department of Preventive Medicine, Division of Environmental Health, Keck School of Medicine of USC

   **Abstract:**
   Cardiovascular disease (CVD) accounts for the largest proportion of mortality and morbidity worldwide. While a strong body of evidence supports a role for long-term air pollution exposure in CVD among adults, relatively little is known about how air pollution exposures
during key developmental windows may affect subclinical markers of atherogenesis, and potential disease development, over the lifecourse. Early markers of these pathogenic processes, including measures of carotid artery intima-media thickness and arterial stiffening, can be measured in children and young adults and may provide insight into the beginnings of disease. The overall goal of this pilot is to generate key preliminary data for a competitive R01 submission to leverage existing cardiovascular health data from the Southern California Children’s Health Study (CHS) to inform the relationship between air pollution exposure and subclinical markers of CVD risk and begin to define how environmental air pollutants may relate to changes in cardiovascular risk from childhood and to early adulthood. We propose to recontact and reevaluate 20 CHS emerging adult participants, who provided carotid artery ultrasounds at age ~10. Using the childhood imaging data as a baseline measure of cardiovascular health, we will collect a second ultrasound scan from these participants to 1) calibrate newer instrumentation to enable longitudinal modeling of subclinical markers of CVD as measured by carotid ultrasound 2) explore calculation of echogenicity, a novel marker of arterial wall composition, from childhood ultrasound images and 3) begin to explore trajectories subclinical markers of atherosclerosis from childhood into adulthood and how these markers may relate to air pollution exposure over the lifecourse. These data will inform a larger study with a long-term goal to begin to characterize environmental contributions to early cardiovascular risk factors from childhood into early adulthood, which will be key to identifying those at risk to prevent later life disease.

3. Exposomic and metabolomic approaches to identifying risk factors for pediatric non-alcoholic fatty liver disease

**Principal Investigator:**
Leda Chatzi, MD, PhD, Associate Professor, Department of Preventive Medicine, Division of Environmental Health, Keck School of Medicine of USC

**Abstract:**
The prevalence of non-alcoholic fatty liver disease (NAFLD) in children has almost tripled over the past 20 years, currently affecting on average 8-12% of the general pediatric population and 34-40% of obese children in the US and in Europe. Mounting evidence suggests that early life environmental exposures contribute significantly to the genesis of metabolic diseases including NAFLD. Animal studies show hepatotoxic effects even at low levels of exposure to many endocrine disrupting chemicals (EDCs), and chronic exposures to ambient fine particulate matter have been shown to induce liver steatosis, inflammation and fibrosis in mice. Human evidence is limited to few cross-sectional studies in adults. We propose an innovative approach to evaluate the role of targeted environmental exposures measured prenatally in the subsequent development of childhood NAFLD. We will leverage the extraordinary existing resources of the “HELIX-The Human Early-Life Exposome” project, which includes harmonized prenatal geospatial data for air pollutants and targeted EDCs in 1200 pregnant mothers and children from 6 European countries. We propose to use archived blood samples collected during the childhood examination at ages 6-10 years to measure alanine aminotransferase (ALT), a validated surrogate biomarker for NAFLD in epidemiological studies of children, and cytokeratin-18 (CK-18), a marker of hepatocyte apoptosis. Existing omics signature data already measured in these samples will allow characterization of exposure associations with underlying mechanistic pathways of NAFLD, including metabolic, inflammatory and adipokine dysregulation pathways. Findings from this pilot project will be highly relevant to a planned R01 application to investigate further
the role of the “human exposome” and multi-omics signatures in pediatric liver disease. Our new multidisciplinary collaboration will also be relevant to future directions planned for the upcoming renewal of the Southern California Children’s Environmental Health Center and other major ongoing research projects at USC [e.g., MADRES and ECHO pregnancy cohort projects].

4. Indoor Particulate Matter and the Nasal and Gut Microbiota: Implications for Acute Lower Respiratory Tract Infection in Infants from Rural Bangladesh

**Co-Principal Investigators:**
Talat Islam, PhD, Assistant Professor, Department of Preventive Medicine, Division of Environmental Health, Keck School of Medicine of USC

Tanya Alderete, PhD, Postdoctoral Research Scholar, Department of Preventive Medicine, Division of Environmental Health, Keck School of Medicine of USC

**Abstract:**
In Bangladesh, acute lower respiratory infections (ALRI) have been estimated to cause 24% of deaths among children under five years of age. Increased exposure to particulate matter (PM) has been shown to contribute to ALRI. While the mechanisms underlying these associations remain uncertain, studies and our recently preliminary data suggest that PM exposure may alter the respiratory and gut microbiota, thereby modifying risk for ALRI. Despite this, no studies have examined the potential impact of PM exposure on the infant microbiota during critical periods of development, including the first year of life. Therefore, we propose a pilot study that will examine a subset of infants from the ongoing Bangladesh Pregnancy Cohort, which is evaluating the health effects of indoor PM exposure on ALRI in a large cohort (n=900) of women and their children. Through existing NIH funding (Fogarty), participants are already being extensively phenotyped for environmental exposures and infant health outcomes that include ALRI. This pilot study will support the analysis of respiratory and stool samples needed to perform detailed microbial profiling in 80 infants at 6 months of age. To our knowledge, this will be the first study to examine the relationships between the infant respiratory and gut microbiota and their associations with PM exposure and ALRI. Therefore, this pilot study will provide novel preliminary data for future grant applications. We hypothesize that increased PM exposure will be associated with alterations in the respiratory and gut microbiota, which will contribute to increased ALRI in the first year of life. Results from the proposed pilot study will test the feasibility of stool and nasal sample collection in the Bangladesh Pregnancy Cohort and will generate preliminary data for external funding applications that will examine these relationships in a larger cohort of participants with repeated microbiome sampling during the first year of life.