**Specific Aims**

This application leverages and builds upon an existing, population-based, longitudinal cohort to investigate ways in which adverse environmental early life exposures negatively affect two ECHO pediatric health outcomes, neurodevelopment and obesity. We capitalize on our currently active, ongoing population-based prospective longitudinal study known as the Family Life Project (FLP). The FLP follows a cohort of children (N=1292) and their primary caregivers, from birth, oversampled for poverty and African American ethnicity in predominantly low-income, non-urban counties in Pennsylvania and North Carolina. A primary focus of the FLP in all phases of data collection has been the prospective investigation of associations between adverse non-chemical environmental exposures at the social/behavioral level (early life stress) and neurodevelopment in the area of self-regulation (including executive function, emotion regulation, the control of attention, the ability to delay gratification), ADHD and learning disability (LD). We now extend the focus of our inquiry to include obesity risk. Obesity risk and neurodevelopment are highly interrelated and profoundly influenced by exposure to a host of environmental chemical and non-chemical stressors. In prior phases of the FLP, we collected biospecimens and multi-method, multi-measure demographic, typical development, and patient-reported outcome data at 8 time points between 0-5yrs and 6 time points between 5-12yrs. We acquired comprehensive data on the physical and psychosocial environment of the home, parenting and care, the stress response, genes, anthropometry, feeding practices, nutrition, and physical growth, along with measures of many other constructs. This application extends our prior data collection both retrospectively and prospectively in order to amplify and enhance our focus on adverse chemical as well as non-chemical environmental exposures and neurodevelopment and obesity outcomes. Doing so will allow us to integrate this unique landmark prospective cohort of an underserved, understudied rural poor US population with the ECHO synthetic pooled cohort for future multi-cohort protocols.

In the UG3 retrospective phase we expand our investigation to include chemical exposures. Specific Aims are 1) Assay saliva samples collected at child ages 7, 15, 24, & 48mos for cotinine a biological maker of tobacco smoke exposure. 2) Link previously collected GIS data on children’s homes and childcare settings 0-5yrs to community level data and quantify exposures 3) Obtain children’s health record data 0-5yr and quantify blood lead levels. 4) Prepare genetic data collected from children and primary caregiver at child age 3 years for ECHO consortium specific assays and analyses. Milestones for the UG phase include the completion of each of these aims in ways that ensure ECHO Consortium access to FLP data and biospecimens, demonstrate feasibility and high rates of success in data collection, data management, and data analysis, and provide an evaluation of the robustness and quality of the data for contributions to the prospective multi-cohort protocol by estimating relations between environmental exposures and neurodevelopment and obesity risk collected in early and middle childhood.

Specific aims for the UH3 prospective phase are

1) Collaborate with ECHO directorship and consortium partners to design protocols for data collection with FLP participants at 15 and 17yrs. We propose to use a combination of behavioral-cognitive assessments and biospecimen assays (broad spectrum metabolomics, neurotransmitter levels, immune markers) to identify clearly defined neurodevelopmental and obesity phenotypes.

2) Collect data on environmental chemical and psychosocial (non-chemical) stressor exposure from children and primary caregiver at 15 and 17 years.

3) Test hypotheses regarding the unique effects of timing (early, mid, late) and type (psychosocial, chemical) of exposure on neurodevelopment and obesity phenotypes from early childhood through late adolescence, with a specific focus on increasing stability in outcomes from 15 to 17 years.

4) Test hypotheses in which unique effects of timing and type of exposure on neurodevelopment and obesity phenotypes are mediated through biological mechanisms including salivary cortisol, alpha amylase, and cardiovascular reactivity measured 0-5 years and through immune markers and the stress response measured at age 11-13.

5) Test hypotheses in which unique effects of timing and type of exposure on neurodevelopment and obesity phenotypes are moderated by later occurring experiences in neighborhood, family, peer, and school contexts.

6) Collaborate with ECHO consortium partners and CHEAR and PRISMS resources to develop innovative approaches (genomics, epigenomics, metabolomics, exposomics) to develop and test novel hypotheses.