01. OVERVIEW OF CENTER SPECIFIC AIMS
Childhood obesity is one of the most critical issues of our time. The prevalence of obesity in U.S. children has increased markedly during the last forty years and now exceed 25%. The current level of childhood obesity threatens the health of a generation of children because childhood obesity is a major risk factor for important childhood and adult diseases including type 2 diabetes, non-alcoholic fatty liver disease and cardiovascular diseases (CVD). Projections based on these adverse consequences of childhood obesity indicate that obesity has the potential to cause unprecedented levels of morbidity and mortality that could lead to a lower life expectance in our children and bankrupt the health care system. Given these facts, major efforts have been launched to reverse these ominous trends. However, the effectiveness of these interventions is uncertain because the determinants of childhood obesity and its consequences are not fully understood. Over nutrition and inadequate physical activity clearly play a role, but emerging evidence shows that the determinants of obesity clearly extend beyond energy imbalance. Given the magnitude of the problem, the difficulty in treating obesity once established and the severe long-term consequences of the epidemic of obesity, there is an urgent need to identify additional determinants of obesity that could be targets for effective interventions.

A rapidly developing literature has identified wide spectrum of environmental exposures as potentially important yet understudied causes obesity and its metabolic consequences. Recent studies suggest that early life and childhood environmental exposures, including ambient particulate air pollution, contribute to childhood obesity. In the Southern California Children’s Health Study (CHS), we reported that growth trajectory of body mass index (BMI), risk of obesity were associated with traffic density and near-roadway air pollution (NRAP) exposure across childhood. In this applications we present provocative new findings showing that high NRAP during the in utero period increased the risk for obesity at age 5 years by 70% (see figure X) and that childhood exposure increased visceral adipose tissue (VAT), the fat depot most strongly associated with adverse metabolic and inflammatory effects. The metabolic and inflammatory effects of air pollution in overweight or obese children has yet to be determined but may be important as this group is at greatest risk of the adverse consequences of obesity in adult life. In this regard, we present new findings that NRAP is associated with increased fasting blood glucose, triglycerides, systemic inflammation and adverse effects on pancreatic beta cell function. Taken together, the emerging science supports the hypothesis that traffic-related air pollutants contribute to the development of obesity and progression of metabolic and inflammatory abnormalities that increase the risk type 2 diabetes and cardiovascular diseases. Because NRAP has potentially obesogenic components and exposure is pervasive, increasing and unregulated, it offers a novel modifiable target for intervention. However, before efficacious science-based interventions can be developed, many questions that arise from this broad hypothesis need to be answered.

To address the clear need for research to assess this broad hypothesis and the urgent need for novel solutions for these problems, we have organized Southern California Children’s Environmental Health Center (SCCEHC) around the theme: Air pollution, childhood obesity and metabolic consequences. The broad scientific and public health objectives of the SCCEHC are to 1) define the role of air pollution in the development and progression of childhood obesity and it associated metabolic and inflammatory consequences, 2) rapidly translate the emerging science to key groups to facilitate science-based interventions to prevent and reduce the consequences of childhood obesity and metabolic abnormalities and 3) foster the next generation of CEH investigators.

We have identified a set of key research questions that provide focus and integration for the Projects and Cores. We propose to investigate NRAP as the primary air pollutant mixture of interest based on our preliminary findings, level of exposure in children and toxicological properties of components. The key questions are:

1) Does NRAP cause childhood obesity? If so when and how?
2) Does NRAP affect fat distribution and cause adipose tissue inflammation to produce more detrimental fat phenotypes or increased ectopic fat?
3) Does NRAP affect metabolic function and outcomes that drive risks for diabetes and CVD including glucose homeostasis, lipid profile, systemic inflammation and the metabolic syndrome?
4) Are effects of NRAP on metabolic and inflammatory outcomes the result of changes in fat distribution and and/or adipose tissue inflammation?

The SCCEHC has organized an experienced and productive multidisciplinary team with broad expertise in CEH, obesity and metabolism to conduct an integrated program of population-based, clinical and experimental research that employs state-of-the art methods to answer these questions.