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ABSTRACT: Pregnancy and Prenatal PAHs *and other* Environmental Exposures and Breast Cancer

Accumulating human and animal data support the hypothesis that breast cancer risk is modified during key windows of susceptibility. These include the prenatal and pregnancy windows, during which time the breast changes in structure and function and breast cells rapidly proliferate. The Columbia Center for Children's Environmental Health (CCCEH) birth cohort is one of the few cohorts in the world with extensive biospecimens and environmental monitoring data that are reflective of the contemporary environment collected during the pregnancy time period for mothers and during the prenatal period for children. In addition to multiple samples of urine throughout pregnancy and blood at the time of delivery, mothers wore a small backpack containing a personal ambient air monitor during the daytime hours for several days to measure personal air pollution exposures. The cohort is comprised exclusively of Hispanic Dominican and African-American women residing in New York City and their children, who were born in the Bronx or Northern Manhattan between 1998 and 2006 (N=543 mothers of whom 52.5% (N=285) are mother-daughter dyads). These families reflect our local community, as well as represent the population subgroups experiencing a rapidly increasing breast cancer incidence in young women. We propose to build on this unique birth cohort specifically by measuring breast tissue characteristics and breast density, a strong intermediate marker of breast cancer risk through optical spectroscopy (OS) for all mothers and daughters and mammography for mothers over 40 years of age (**Project 1**). We will collect clinical measures of breast tissue characteristics, anthropometry and biospecimens in the now adolescent girls (age range 10-16 years) and their mothers. There are few human studies in which exposures to the same pollutants have been measured to allow for simultaneous evaluation of their effect on both the mother's breast cancer risk and that of her daughter. We will focus on *Polycyclic Aromatic Hydrocarbons (PAH)*, by-products of combustion *classified as possible carcinogens by IARC and the US EPA*. We will couple our human study with robust animal experiments investigating the role of airborne PAH during gestation on altered mammary tissue and systemic DNA methylation and expression of genes important to DNA repair and apoptosis in mothers, their offspring, and their grandoffspring (**Project 2**). We also will investigate the role of PAH on PPAR α gene regulation, a gene important to lipid metabolism and associated with breast cancer risk, as well as examine mammary tissue alterations in both the animal and human models and compare genes that are methylated in humans with higher PAH exposure across both model systems. **Project 3** ties together both projects by building on the CCCEH Community Outreach and Translation Core to integrate our research findings with messages about environmental exposures and breast cancer prevention in our study participants and larger community in our Herbert Irving Comprehensive Cancer Center (HICCC) and Columbia University catchment area.