Prenatal Exposure to Phthalates and Cord Blood Mononuclear Cell DNA Methylation

Zhiyang Wang1, Zana Percy1, Liang Niu1, Shouxiong Huang1, Xiang Zhang1, Yuet-kin (Ricky) Leung2, Shuk-mei Ho2, Ann Vuong3, Stephani Kim4, Weili Yang1, Antonia Calafat5, Julianne Botelho5, Emily A. DeFranco6, Aimin Chen1

1 Department of Environmental Health, University of Cincinnati, 2 University of Arkansas Medical Center, 3 Department of Environmental and Occupational Health, University of Nevada, Las Vegas, 4 Nationwide Children’s Hospital, 5 Centers for Disease Control and Prevention, 6 Department of Obstetrics and Gynecology, University of Cincinnati

Introduction

• Phthalates are ubiquitous industrial plasticizers. Routes for human exposure include diet, inhalation, and dermal exposure.

• Prenatal exposure to phthalates may affect DNA methylation levels and lead to adverse developmental outcomes in children.

• This study investigated the association between prenatal phthalates exposure and cord blood mononuclear cell (CMBC) methylation in infants.

Methods

• We used data from 12 mother-newborn dyads in a Center for Environmental Genetics pilot project that enrolled pregnant women at delivery in the University of Cincinnati Medical Center.

• We included 13 metabolites of phthalates and phthalate alternatives: mBP, mBzP, mCNP, MCOCH, mCPP, MECPTP, MEHHTP, mEP, MHiNCH, miBP, mNP, MONP measured in maternal urine samples except DEHP metabolites that were deemed too high due to potential tube-related exposure in the delivery unit (Table).

• We associated phthalate metabolites with cord blood DNA methylation (Illumina 450K Methylation Beadchip) to identify differentially methylated regions (DMR) for each creatinine-standardized phthalate metabolite.

• We adjusted for maternal age, race, smoking status, gestational age, and infant sex.

• We selected the top 10 significant DMRs for each phthalate metabolite, with a false discovery rate of 0.1.

Results

• Three phthalate metabolites: MECPTP, mNP, and MONP were associated with DNA methylation, for a total of 30 function regions.

• We classified 30 function regions to seven classes: mRNA creation and processing, DNA repair, NADPH/NADH, Blastocyst development, Plasma membrane, Signal transduction, Catabolic & Metabolic processes.

• mRNA creation and processing was the most frequently noted functional class with 11 hits. All three phthalate metabolites were associated with this class.

Discussion

• We found an association between prenatal phthalate exposure and cord blood mononuclear cell DNA methylation, with relation to several biological functions.

• One limitation was the small sample size (n=12).

Acknowledgement

This CEG pilot project was supported by NIH/NIEHS P30ES006096.

Figure 1. Flow chart for the study

Figure 2. Differentially methylated regions associated with phthalate metabolites.