

CHARACTERIZATION OF GLOBAL DNA METHYLATION AT LINE-1 IN A COHORT OF URBAN ASTHMATIC CHILDREN WITH A GRADIENT OF EXPOSURE TO HIGHWAYS

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Background and Aims: Asthma is a complex chronic disease with heterogeneous clinical expression and waxing and waning activity over the life cycle. Epigenetic modifications may be a mechanism to explain clinical variability. However, the relationship between environmental exposures, epigenetic changes, and health outcomes is unclear, particularly in young vulnerable populations.

Methods: This study builds on an investigation of the impact of near-highway residence on the health of asthmatic children, "The Community Action Against Asthma (CAAA) Diesel Study." In this pilot study, we measured global DNA methylation in cells from saliva in a cohort of urban asthmatic children. Children aged 6-14 with asthma were recruited based on the proximity of their residence to highways. DNA was extracted from saliva samples from 79 children and assessed for degree of DNA methylation at four loci within LINE-1. We assessed the association between methylation and gender, age, and exposure to highways.

Results: Methylation of LINE-1 loci was heterogeneous and ranged from a mean of 66% at site 3, to 74% at site 2, with an overall mean of 70% across the four sites. Girls were hypomethylated at site 3 (65.64%) compared to boys (67.11%, $p=0.048$) and this difference remained significant after adjustment for gender, race, asthma severity, exposure to tobacco smoke, and highway exposure. Neither current highway exposure status nor asthma severity were significant independent predictors of methylation. However, changes in methylation pattern with age differed across exposure groups, showing a steeper declining gradient in the high diesel exposure group.

Conclusions: Differences in global methylation measured at LINE-1 are site-specific, present relatively early in life and may vary by exposure to roadway-associated air pollution. There may be important gender-specific differences in methylation. Expanded studies of the epigenome in exposed populations will help clarify the role of epigenetic modifications in asthma phenotype.