

BISPHENOL A-ASSOCIATED EPIGENOMIC CHANGES IN PREPUBESCENT GIRLS FROM GHARBIAH, EGYPT

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Background and Aims: There is now compelling evidence that epigenetic modifications link adult disease susceptibility to environmental exposures during specific life stages, including pre-pubertal development. Animal studies indicate that bisphenol A (BPA) may impact health through epigenetic mechanisms. Epidemiological data associate BPA levels with metabolic disorders and reproductive effects. Here, we conducted an environmental epidemiology study of BPA exposure and epigenetics in pre-adolescent girls in Gharbiah, Egypt, hypothesizing that CpG methylation profiles will exhibit exposure-dependent trends.

Methods: Total urinary BPA was measured by the CDC for 46 girls aged 9 to 12. We concurrently evaluated genome-wide CpG methylation using the Infinium HumanMethylation27 array in saliva DNA samples. The Linear Models for Microarray Data (Limma) library in R program was used to model age, BMI, specific gravity, creatinine, and log BPA to predict % change in methylation. Top hits below a p-value of 0.05 were subjected to enrichment analysis including pathway and gene ontology via Molecular Concepts Map (MCM).

Results: Overall, urinary BPA levels were lower in Egyptian girls compared to similarly aged U.S. females as reported in NHANES. CpG methylation varied widely between girls, and BPA levels were associated with less genomic methylation. Pathway analyses indicated that genes with decrease in methylation % associated with BPA were involved in immune function, transport activity, metabolism, and caspase activity. In particular, hypomethylation of CpG targets on chromosome X was associated with BPA. Using the Comparative Toxicogenomics Database, we identified candidate genes with upregulated expression associated with BPA and found that many of the targets had BPA-associated hypomethylation in our sample, and visa versa.

Conclusions: Our data indicate that BPA may affect human health through specific epigenomic modification of genes in relevant pathways. Epigenetic epidemiology holds promise for the identification biomarkers of previous exposure and the development of epigenetic-based diagnostic and therapeutic strategies.