## Developmental exposures altered epigenetic signatures across tissues in offspring

Early life exposure to lead and phthalates altered epigenetic signatures in brain, blood, and liver tissues, according to an NIEHS-funded study in mice. Epigenetic signatures reflect the chemical marks on genes that affect gene function but do not change the underlying genetic sequence. The research may help advance studies in humans by providing insight into whether epigenetic signatures in more accessible tissues, such as blood, can help predict effects in hard-to-access tissues, like the brain.

As a part of the Toxicant Exposures and Responses by Genomic and Epigenomic Regulators of Transcription (TaRGET II) Consortium, the researchers orally exposed female mice to either lead or phthalates throughout gestation and weaning. Then, they examined changes in DNA methylation, a type of epigenetic modification, in the offspring's brain, blood, and liver tissues at five months of age. They compared the epigenetic signatures in exposed and unexposed mice to identify differentially methylated regions (DMR) of genes. The researchers were particularly interested in DMRs on imprinted genes, which are important for healthy growth and development. Precise DNA methylation is critical for the proper expression of imprinted genes, and early disruption of this process can result in developmental disorders.

Brain tissues contained the majority of DMRs for both lead and phthalate exposure. Across all tissues, DMRs appeared in gene regions responsible for regulation of gene expression. DMRs were most prevalent on imprinted genes in exposed mice. Two imprinted genes, which have been associated with developmental disorders, contained a significant number of exposure-associated DMRs and displayed similar signatures across tissues.

According to the authors, results suggest that imprinted gene epigenetic signatures in blood may be useful biomarkers of exposure in brain and liver tissues, two commonly studied organs that are often inaccessible in human population studies.

*Citation:* Morgan RK, Wang K, Svoboda LK, Rygiel CA, Lalancette C, Cavalcante R, Bartolomei MS, Prasasya R, Neier K, Perera BPU, Jones TR, Colacino JA, Sartor MA, Dolinoy DC. 2024. Effects of developmental lead and phthalate exposures on DNA methylation in adult mouse blood, brain, and liver: a focus on genomic imprinting by tissue and sex. Environ Health Perspect 132(6):67003.