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Cell-Type Specific Epigenome-Wide Analysis Reveals Unique DNA Methylation Patterns Associated with Tobacco Use

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Tobacco use is known to strongly influence DNA methylation (DNAm) and gene expression alterations, which have been associated with negative health consequences. Previous Epigenome-wide association studies (EWAS) have identified CpG sites associated with tobacco use in blood cells in bulk, providing limited insights into cell-type specific DNAm patterns linked with tobacco use. Tobacco use is recognized for its impact on immune cell function and composition. Methylation alterations due to smoking in particular cell types may signify distinct sensitivities to exposure and different mechanisms among cell lineages, potentially influencing cell-type-specific disease development or the early detection of disease. In this study, we aim to identify differentially methylated CpG sites for tobacco use in six cell types using Yale Stress Center Cohort Study (YSCCS) (N=502) and two publicly available datasets from Gene Expression Omnibus database [GSE53045 (N=111) and GSE131989 (N=371)]. DNAm in blood or peripheral blood mononuclear cells was deconvoluted by Tensor Composition Analysis (TCA). Cell-type EWAS of tobacco use was performed in each cohort separately and a meta-EWAS was conducted followed by gene set enrichment analysis. We identified cell-type-specific CpG sites associated with tobacco use in each cohort. Cell-type level meta-EWAS revealed distinct patterns of tobacco use-associated differential CpG methylation. Cell-type EWAS of tobacco use was performed in each cohort separately, followed by meta-EWAS and gene set enrichment analysis. Our findings revealed cell-type specific CpG sites associated with tobacco use in each cohort, with distinct patterns of tobacco use-associated differential CpG methylation observed in the meta-EWAS at the cell-type level.