

DEMOGRAPHIC AND LIFESTYLE FACTORS AFFECTING GENOMIC BLOOD DNA METHYLATION BIOMARKER LEVELS

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Background and Aims: Levels of DNA methylation can be altered by environmental exposures and have been shown to be important molecular markers in disease etiology. Several methodologies are available to determine genomic DNA methylation including overall genomic DNA methylation and repetitive DNA methylation measurements. It is not clear what the determinants of these methylation measures are in healthy individuals. The aim of this study was to examine whether age, gender, smoking status, and ethnicity are associated with several DNA methylation measurements in white blood cell (WBC) DNA of healthy individuals.

Methods: Individual data from three studies including a total of 1300 healthy subjects were combined. WBC genomic and repetitive element DNA methylation was quantified by three different assays: Luminometric Methylation Assay (LUMA) for genomic DNA methylation levels, and PCR-pyrosequencing (*LINE-1*) and MethyLight (*LINE-1* and *Sat2*) for repetitive element DNA methylation. Demographic and lifestyle characteristics were evaluated in relation to the epigenetic biomarkers.

Results: Smoking status was associated with a decreased in genomic DNA methylation by LUMA. Current smokers had lower levels of DNA methylation than never and former smokers (66.3% vs. 68.3%, $p=0.0132$). No gender or age differences were observed for any of the biomarkers under study. Repetitive element DNA methylation levels were lower in Caucasian women than other ethnicities (*Sat2*: 38.5% vs. 49.7% ($p=0.005$) and *LINE-1*: 73.9% vs. 75.2% ($p<0.0001$)). Statistically significant correlations were found for LUMA and *LINE-1* measurements (Spearman coeff=0.11 ($p=0.04$)), but not *Sat2*.

Conclusions: Genomic DNA methylation levels vary in relation with smoking status and ethnicity. Differential correlation between repetitive sequences and global measurements of DNA methylation suggests contributions of the different biomarkers might be different to global genomic DNA methylation levels. These findings need to be considered in designing epidemiological studies aimed at identifying associations between DNA methylation, disease and environmental exposures.