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Incorporating local ancestry into methylation quantitative trait loci (meQTL) mapping for tobacco smoking in the African American population

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The effects of tobacco smoking on DNA methylations have been widely reported, however, few studies focused on the African American (AA) population and incorporated local ancestry information with genotyping data to investigate the potential ancestry-specific inheritance patterns. Here we report an epigenome-wide association study (EWAS) on smoking followed by the methylation quantitative trait loci (meQTL) mapping among 487 AA participants in the Veterans Aging Cohort Study (VACS). We performed the EWAS on smokers versus non-smokers using DNA methylation in whole blood samples. Demographics, clinical variables, cell-type composition, and batch effects were adjusted for in the association model. We identified 26 CpG sites significantly associated with smoking ($p\text{-value} < 1E-7$). We then estimated the number of variations with European or African ancestral origin at each genetic locus and performed meQTL mapping to obtain ancestry-specific meQTL coefficients. In total, we identified 82 meQTLs for 16 smoking-associated CpG sites. Among the identified meQTLs, 10 were African allele-specific, 54 were European allele-specific, and 18 had significant effects in both ancestries. We compared the ancestry-specific coefficients for the identified meQTLs and 55 of 82 meQTLs had significantly different allelic effects between the two ancestries. Our results suggest that for a subset of meQTLs, the local ancestry designation of the genetic variation had a significant effect on methylation. Our findings indicate that local ancestry holds the promise of improving the resolution and mechanistic interpretation of meQTL mapping in epigenetic studies.