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Inferred Cell-Type-Specific Methylation Quantitative Trait Loci for Cannabis Use

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Methylation Quantitative Trait Loci (meQTLs) are chromosomal regions that harbor genetic variants affecting DNA methylation levels. However, most meQTL studies to date utilize bulk methylation datasets and offer little insights on meQTL in specific cell types. Here, we developed a hierarchical Bayesian interaction model (HBI) to infer cell-type-specific (CTS) meQTLs from bulk methylation data and examined an association of CTS-meQTL with cannabis use among 431 individuals, in which genome-wide DNA methylation from peripheral blood mononuclear cells (PBMC) DNA and genotyping were available. We first inferred genome-wide CTS meQTL for five major cell types in PBMCs by applying HBI and identified 122,387 significant meQTLs in CD4+ T-cells, 34,310 in CD8+ T-cells, 25,020 in natural killer cells, 26,972 in B cells, 36,919 in monocytes. We examined the association between the CTS-meQTLs and cannabis use. We identified 91 meQTL in CD4+ T-cells, 53 meQTL in CD8+ T-cells, 15 meQTL in natural killer cells, 30 meQTL in B cells, and 93 meQTL in monocytes that are associated with cannabis use. The top cannabis use associated meQTLs are rs7720588 (natural killer cells specific meQTLs, mapped to an intron of XRCC4), rs13114536 (CD8+ T-cells specific meQTLs, mapped to an intron of ZNF827), and rs7099881 (monocytes specific meQTLs, mapped to an intron of BICC1). The results suggest that genetically-driving DNA methylation may contribute to peripheral mechanisms of cannabis use. Future study will further examine the causal relationship between CTS-DNA methylation and cannabis use using CTS-meQTL.