Diet quality associated peripheral blood DNA methylation signatures

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Abstract

Leukocyte DNA methylation patterns associated with habitual diet may reveal molecular mechanisms involved in the pathogenesis of diet-related chronic diseases and highlight targets for prevention and treatment. We aimed to examine peripheral blood derived leukocyte DNA methylation signatures associated with diet quality. We meta-analyzed epigenome-wide associations between diet quality and DNA methylation levels at over 400,000 cytosine-guanine dinucleotides (CpGs). We conducted analysis primarily in 6,662 European ancestry (EA) participants and secondarily in a group additionally including 3,062 participants of non-European ancestry from five population-based cohort studies. DNA methylation profiles were measured in whole blood, CD4 + T-cells, or CD14 + monocytes. We used food frequency questionnaires to assess habitual intake and constructed two diet quality scores: the Mediterranean-style diet score (MDS) and Alternative Healthy Eating Index (AHEI). Our primary analysis identified 32 diet-associated CpGs, 12 CpGs for MDS and 24 CpGs for AHEI (at FDR < 0.05, corresponding p-values = 1.2×10^{-6} and 3.1×10^{-6}, respectively) in EA participants. Four of these CpGs were associated with both MDS and AHEI. In addition, Mendelian randomization analysis indicated that seven diet-associated CpGs were causally linked to at least one of the CVD risk factors. For example, hypermethylation of cg11250194 (*FADS2*), which was associated with higher diet quality scores, was also associated with lower fasting triglycerides concentrations (p-value = 1.5×10^{-14}) and higher high-density lipoprotein cholesterol concentrations (p-value = 1.7×10^{-8}). Transethnic meta-analysis identified nine additional CpGs associated with diet quality (either MDS or AHEI) at FDR < 0.05. Overall quality of habitual diet was associated with differential peripheral leukocyte DNA methylation levels of 32 CpGs in EA participants. The diet-associated CpGs may serve as biomarkers and targets for preventive measures in CVD health. Future studies are warranted to examine diet-associated DNA methylation patterns in larger, ethnically diverse study samples.

Conflict of Interest

There is no conflict of interest