

Triglyceride-Associated Epigenetic Markers and Diet and Lifestyle Habits in the Framingham Heart Study

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Objectives: The current evidence has shown that environmental and lifestyle factors (e.g., diet, physical activity, tobacco smoking, alcohol) are associated with DNA methylation patterns. However, the mechanisms underlying the relation between diet and other exposures and epigenetic profiles are not well understood. To reduce such knowledge gap, we investigated the links between lifestyle, including diet, and methylation marks with plasma triglyceride concentrations (TG).

Methods: We first conducted an epigenome-wide association study (EWAS) (Illumina HumanMethylation450 BeadChip) for TG in the Framingham Heart Study Offspring population (n = 2,178). We then examined the relationships between dietary and lifestyle-related variables, collected over 13 years, and differential DNA methylation marks associated with the last TG measures (exam 8). Second, we conducted a mediation analysis to examine the potential causal relationship between diet-related variables and TG.

Results: The EWAS analyses revealed 28 TG-associated DNA methylation sites at 19 regions (e.g., ABCG1, CPT1A, DHCR24, PHGDH, SLC7A11, SLC43A1, SREBF1, TXNIP). Within those methylation sites, we identified 427 significant associations between these DNA methylation sites and one or more dietary and lifestyle-related variables after accounting for multiple testing. The two most significant and consistent associations between TG-associated DNA methylation markers and diet were alcohol (g/day) and carbohydrate intake (% total energy), with P-values ranging from 10^{-4} to 10^{-56} . Mediation analyses demonstrated that alcohol and carbohydrate intake independently affect TG via DNA methylation markers as mediators. For seven of the 19 identified differential DNA-methylation regions, higher alcohol intake was associated with decreased methylation and higher TG. In contrast, increased carbohydrate intake was associated with higher DNA methylation at two epigenetic loci (CPT1A and SLC7A11) and lower TG.

Conclusions: Our findings indicate that dietary factors (i.e., alcohol and carbohydrate) are associated with specific DNA methylation markers that could mediate some of the observed associations between diet and cardiometabolic risk factors.

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