

Multivariate analysis of high throughput methylation screening identifies methylation sites associated with exposure to pesticides

Tamar Sofer, Harvard University

Eighty individuals from the Agricultural Health Study were selected for a pilot study of methylation based on high and low levels of exposure to organophosphates (OPs). The goal of the study is to detect associations between exposure to OPs and methylation levels in blood. Methylation was measured on the 450K Infinium Illumina beadchip. The data was corrected for batch effects and normalized. We developed the A-clustering algorithm, to detect clusters of co-regulated, adjacent methylation sites based on high correlations. We studied the properties of the A-clustering algorithm via correlation-preserving simulations of methylation data. The A-clustering algorithm was applied on the data set, and then all detected clusters were tested for association with exposure using generalized estimating equations (GEEs) assuming constant effect size of exposure on the methylation sites in the cluster. After FDR corrections, 4 clusters were significantly associated with exposure.