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Deconvolution of bulk DNA methylome and a cell type specific epigenome-wide association study for HIV infection

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Background: Epigenome-wide association analysis (EWAS) has been applied to identify mostly none-tissue/cell specific signals for complex disease. It has been challenging to profile cell type specific methylome due to high costs of cell sorting and methylation profiling. Here, we present a cell type specific EWAS for HIV infection from a subset of Veteran Aging Cohort Study samples by computationally deconvoluting cell-type-specific methylome. DNA methylation in blood (N=718) was measured by using Illumina DNA methylation 450K Beadchip.

Results: A total of 408,366 CpG sites were analyzed after quality control. Bulk DNA methylome for each sample was deconvoluted into 6 cell-type-level methylomes by using Tensor Composition Analysis (TCA) and an EWAS for HIV infection was conducted in each cell type. We found a number of significant CpG sites associated with HIV infection in different cell types that were consistent with signals in bulk DNA methylome. For example, we identified a significant association of cg16411857 located on the promoter of *NRLC5* for HIV infection in CD4 T cells (p=9.37E10-7), granulate cells (p=3.81E10-12), and monocytes (p=8.06E10-12) but not in B, CD8 and natural killer cells. cg16272981 on *LPCAT1*, previously associated with HIV infection in blood methylome, showed significant association with HIV infection only in B cells (p=3.87E10-9) and granule cells (p=2.36E10-9).

Conclusion: Applying TCA to bulk DNA methylome, we have demonstrated that DNA methylation associated with HIV infection is differential by cell type.