Title: Interactions between epigenetic modifications and associations with gene expression

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Abstract: Histone methylation and acetylation are critical in defining the epigenetic landscape of cells and tissues, and diverse patterns of histone modification combinations are found to be closely associated with genetic features including promoters, enhancers, and repressors. However, the rich diversities of epigenetic features along the genome of individual sample as well as the diversity at the same genomic region over different samples make the functional relevance of epigenetic features complicated. Aiming at uncovering the complete functional elements of the mouse genome, the ENCODE mouse project has generated a significant amount of data on histone modification, transcription factor binding, and gene expression in 80 cell and tissue types. In this study, we focus on how different histone marks interact with each other and how multiple histone marks act jointly to effect gene expression by integrating histone modification, transcription factor binding, and gene expression data on 11 samples from the ENCODE mouse project. We defined segments of genomic regions with enhanced epigenetic activity as “epigenetic hotspots”, and assigned “epi-genotypes” for individual marks and samples in the hotspots. Multiple regression models were used to study the interactions between different epigenetic marks and the association between epi-genotypes and gene expression. Both epi-genotypes that are proximal and distal to the genes were discovered as being strongly linked with gene expression. Our work presents a unique venue for integrating genetic and epigenetic data to study the interactions between epigenetic modifications in a genetic location-specific way. Our results suggest how patterns of epigenetic interactions affect gene transcription.