Title: Epigenetic interactions between histone modifications affecting 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 an individual tissue as well as the diversity at the same genomic region over different tissues 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 to jointly affect gene expression by integrating histone modification, transcription factor binding, and gene expression data on 11 samples from the ENCODE mouse project. We defined “epi-genotypes” as the combination of individual marks at each genomic location in each tissue. Multiple linear regressions were applied to detect interactions between different epigenetic marks that were associated with gene expression. Both epi-genotypes that are proximal and distal to the genes were discovered as being strongly linked with gene expression, and our results show how patterns of epigenetic interactions affect transcript abundance. Our approach can be directly extended to include genotype information in addition to epi-genotype to study how genetic variants and epigenetic states combine to regulate gene expression.