Dynamic metabolic epigenome landscape in human tissues from Korea Epigenome Project

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Abstract

Type 2 Diabetes (T2D) is common complex disease with heterogeneous disease etiology. Genome wide association study has revealed >86 candidate markers that only mildly increases the risks of T2D by 10~30%. To overcome poor risk prediction, complementation research using epigenetic or environmental factor is required. To unravel epigenomic causality on diabetes, KNIH's Korea Epigenome Project generated 70 epigenome data sets so far on diabetes related purified target cells including beta, islet, ductal, acinar, adipocyte, preadipocyte, mesangial, tubule and podocyte from pancreas, fat and kidney tissues. Here, we performed combined analysis among whole genome bisulfite sequencing, Infinium450K DNA methylation chip, mRNA-Seq and miRNA-Seq data with 70 diabetic epigenomes and plan to add Histone modification data in near future. First of all, we identified tissue type specific, cell type specific and diabetes specific epigenome markers in WGBS and mRNA-Seq data. To analyze further into association between WGBS methylation and RNA expression, we applied MeQTL analysis using MatrixEQTL method, revealing significant epigenome-wide interactions between blocks of DNA methylation and gene expression. Taken together, our result will help to uncover novel association between DNA methylation and gene expression in addition to target epigenome variation which will help to identify causal factors on metabolic diseases. Further study on combined analysis with IHEC data set will be discussed in detail.