Integrative analysis to reveal transcriptional regulation of NF-κB

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Cellular differentiation is a time-dependent process and regulated by sequential activation of transcription factors. Such transcriptional regulation is closely associated with the epigenetic changes of chromatin structure, histone modifications and DNA methylation. Super-enhancer (SE) has been suggested to determine cell specificity through generation of a threshold gene expression response, quantitatively different from the graded response controlled by typical-enhancers (TEs). Today I will introduce our integrated NGS data analysis approach to identify quantitative relationship between chromatin status, SE formation and SE-mediated transcription. NF-κB plays an important role for antigen-dependent B cell differentiation. We collected the dataset of NF-κB (RelA)-DNA binding, H3K27Ac modification, chromatin accessibility using assay for transposase-accessible chromatin using sequencing (ATAC-seq) and single cell mRNA expression using mouse B lymphocyte stimulated with anti-IgM for 1 hour. Our analysis show that chromatin opening is essential for SE formation, significant NF-κB binding and switch-like gene expression whereas the chromatin closing induced the loss of SE, NF-κB dissociation and steep gene down-regulation. A small change in chromatin structures contributed for TE formation and graded small transcriptional response. The study indicates that the degree in open-close chromatin selects the enhancer modes and quantitatively regulates gene expression. We further applied this analytical method to a model of hematopoietic cell differentiation and identified transcription factors might be responsible for cellular transition.