

Dynamics of enhancers in myeloid antigen presenting cells upon LPS stimulation

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Abstract

Background

Recent studies have underscored the role of enhancers in defining cell type-specific transcriptomes. Cell type-specific enhancers are bound by combinations of shared and cell type-specific transcription factors (TFs). However, little is known about combinatorial binding of TFs to enhancers, dynamics of TF binding following stimulation, or the downstream effects on gene expression. Here, we address these questions in two types of myeloid antigen presenting cells (APCs), macrophages and dendritic cells (DCs), before and after stimulation with lipopolysaccharide (LPS), a potent stimulator of the innate immune response.

Results

We classified enhancers according to the combination of TFs binding them. There were significant correlations between the sets of TFs bound to enhancers prior to stimulation and expression changes of nearby genes after stimulation. Importantly, a set of enhancers pre-bound by PU.1, C/EBP β , ATF3, IRF4, and JunB was strongly associated with induced genes and binding by stimulus-activated regulators. Our classification suggests that transient loss of ATF3 binding to a subset of these enhancers is important for regulation of early-induced genes. Changes in TF-enhancer binding after stimulation were correlated with binding by additional activated TFs and with the presence of proximally located enhancers.

Conclusions

The results presented in this study reveal the complexity and dynamics of TF-enhancer binding before and after stimulation in myeloid APCs.