C/EBPy HAS A STIMULATORY ROLE IN THE TRANSCRIPTION OF PROINFLAMMATORY CYTOKINE AND CHEMOKINE GENES

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CCAAT/enhancer binding protein y (C/EBPy) is a ubiquitously expressed member of the C/EBP family of transcription factors that was originally described as an inhibitor of C/EBP transactivation potential. Previously, we reported that C/EBPy augments the activity of C/EBPP in lipopolysaccharide (LPS) induction of the interleukin-6 (IL-6) and IL-8 promoters in a B lymphoblast cell line. This ability of C/EBPy to augment C/EBPp transactivation potential is dependent upon its dimerization with C/EBPP and is potentiated by coactivation of NF-KB. Here, we demonstrate a profound deficit in LPSinduced cytokine and chemokine expression in C/EBPy-deficient mouse embryonic fibroblasts (MEFs) when compared to wild type (wt) MEFs. Chromatin immunoprecipitation analysis of two C/EBP target genes, IL-6 and IL-ip showed defective LPS-induced recruitment of C/EBPp and C/EBP5 to the target promoters of these genes in C/EBPy-deficient MEFs. These same promoters showed reduced LPSinduced NF-KB p65 occupancy. Furthermore, LPS-induced expression of several cytokine and chemokine genes was reduced in a tissue-specific manner in C/EBPydeficient mice when compared to wt mice. These findings demonstrate that C/EBPy plays an important role in LPS-induced transcriptional activation of many cytokine and chemokine genes.