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Genes directly regulated by NF-κB in human hepatocellular carcinoma HepG2

Wei Dai
Southeast University, China

It has been well-known that over activation of NF-κB has close relationship with hepatitis and hepatocellular carcinoma (HCC). However, the complete and exact underlying molecular pathways and mechanisms still remain not fully understood. By manipulating NF-κB activity with its recognized activator TNFα and using ChIP-seq and RNA-seq techniques, this study identified 699 NF-κB direct target genes (DTGs) in a widely used HCC cell line, HepG2, including 399 activated and 300 repressed genes. In these NF-κB DTGs, 216 genes (126 activated and 90 repressed genes) are among the current HCC gene signature. In comparison with NF-κB target genes identified in LPS-induced THP-1 and TNFα-induced HeLa cells, only limited numbers (24~46) of genes were shared by the two cell lines, indicating the HCC specificity of identified genes. Functional annotation revealed that NF-κB DTGs in HepG2 cell are mainly related with many typical NF-κB-related biological processes including immune system process, response to stress, response to stimulus, defense response and cell death and signaling pathways of MAPK, TNF, TGF-β, chemokine, NF-κB and toll-like receptor. Some NF-κB DTGs are also involved in hepatitis C and B pathways. It was found that 82 NF-κB DTGs code secretory proteins, which include CCL2 and DKK1 that have already been used as HCC markers. Finally, the NF-κB DTGs were further confirmed by detecting the NF-κB binding and expression of 14 genes with ChIP-PCR and RT-PCR. This study thus provides a useful NF-κB DTG list for future studies of NF-κB-related molecular mechanisms and theranostic biomarkers of HCC.

Biography

Wei Dai has completed her Master's degree from Anhui Agricultural University, China. She is a Doctor of the State Key Laboratory of Bioelectronics, Southeast University, China. She has published several papers in reputed journals with impact factor more than 15.

dw0710@126.com

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