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## GENES DIRECTLY REGULATED BY NF- $\kappa$ B IN HUMAN HEPATOCELLULAR CARCINOMA HEPG<sub>2</sub>

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It has been well-known that over activation of NF- $\kappa$ B 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- $\kappa$ B activity with its recognized activator TNF $\alpha$  and using ChIP-seq and RNA-seq techniques, this study identified 699 NF- $\kappa$ B direct target genes (DTGs) in a widely used HCC cell line, HepG2, including 399 activated and 300 repressed genes. In these NF- $\kappa$ B DTGs, 216 genes (126 activated and 90 repressed genes) are among the current HCC gene signature. In comparison with NF- $\kappa$ B target genes identified in LPS-induced THP-1 and TNF $\alpha$ -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- $\kappa$ B DTGs in HepG2 cell are mainly related with many typical NF- $\kappa$ B-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-beta, Chemokine, NF-kappa B, and Toll-like receptor. Some NF- $\kappa$ B DTGs are also involved in Hepatitis C and B pathways. It was found that 82 NF- $\kappa$ B DTGs code secretory proteins, which include CCL2 and DKK1 that have already been used as HCC markers. Finally, the NF- $\kappa$ B DTGs were further confirmed by detecting the NF- $\kappa$ B binding and expression of 14 genes with ChIP-PCR and RT-PCR. This study thus provides a useful NF- $\kappa$ B DTG list for future studies of NF- $\kappa$ B-related molecular mechanisms and theranostic biomarkers of HCC.

### Biography

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