Branches of the NF-κB signaling pathway regulate proliferation of oval cells in rat liver regeneration

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ABSTRACT. The NF-κB (nuclear factor κB) pathway is involved in the proliferation of many cell types. To explore the mechanism of the NF-κB signaling pathway underlying the oval cell proliferation during rat liver regeneration, the Rat Genome 230 2.0 Array was used to detect expression changes of NF-κB signaling pathway-related genes in oval cells. The results revealed that the expression levels of many genes in the NF-κB pathway were significantly changed. This included 48 known genes and 16 homologous genes, as well as 370 genes and 85 homologous genes related to cell proliferation. To further understand the biological significance of these changes, an expression profile function was used to analyze the potential biological processes. The results showed that the NF-κB pathway promoted oval cell proliferation mainly through three signaling branches; the tumor necrosis factor alpha branch (TNF-α pathway), the growth factor branch, and the chemokine branch. An integrated statistics method was
used to define the key genes in the NF-κB pathway. Seven genes were identified to play vital roles in the NF-κB pathway. To confirm these results, the protein content, including two key genes (TNF and FGF11) and two non-key genes (CCL2 and TNFRSF12A), were analyzed using two-dimensional gel electrophoresis and MALDI-TOF/TOF mass spectrometry. The results were generally consistent with those of the array data. To conclude, three branches and seven key genes were involved in the NF-κB signaling pathway that regulates oval cell proliferation during rat liver regeneration.

**Key words:** Rat liver regeneration; NF-κB signaling pathway; Key genes; Oval cell proliferation; Gene expression profile