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Differential Gene Expression Profiles in the Fibrosis / Steatosis Model of Rat Liver by Chronic Administration of Carbon Tetrachloride

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Global gene expression profile was analyzed by microarray analysis of rat liver RNA chronically administered with carbon tetrachloride (CCl4). Chronic intermittent injection of CCl4 was performed continuously, and the liver samples were obtained after 0 d, 30 d, 60 d and 90 d of injection. Histopathologic studies of liver tissues enabled the classification of the CCl4 effect into mild and severe fatty liver (30 d and 60 d, respectively) and fibrosis/cirrhosis (90 d) stages. The expression levels of 4,900 clones on a custom rat gene microarray were analyzed and the results were confirmed by semi-quantitative RT-PCR. Four hundred thirty one clones (8.8%) yielded changeable gene expression on at least single time point. Multiple genes involved in lipid metabolism showed differential transcript levels upon chronic CCl4 administration. In addition, various genes responsible for fibrosis gave altered RNA expression. Several genes with known functions but not involved in steatosis or cirrhosis were also identified as CCl4-regulated genes. In conclusion, we report microarray analysis results in rat liver upon chronic CCl4 administration with a full chronological profile that not only covers steatosis but also later points of fibrosis/cirrhosis. These data will provide the insight of specific gene expression profiles that is implicated in the multistep process of liver fibrosis/cirrhosis and steatosis upon chronic hepatotoxins exposure. This work was supported by the grant from the National Institute of Toxicology Research, Korea (to Gu Kong).
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