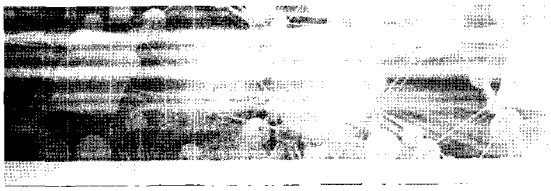

S10-4

Differential gene expression profiles of acute and chronic injury and recovery in rat liver steatosis-fibrosis/cirrhosis model

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Microarray analyses of RNA from carbon tetrachloride (CCl_4)-administered rat livers were performed to establish a global gene expression profile during acute and chronic intoxication regimens. In an acute model, a single dose of 1 ml/kg of CCl_4 was given by i.p. injection, and the liver samples were obtained after 6 h, 24 h, 48 h, and 2 wk. Histopathologic, biochemical, and immunohistochemical studies enabled the classification of the CCl_4 effect into injury (6 h and 24 h) and regeneration (48 h and 2 wk) stages. A custom rat gene microarray was analyzed and 587 clones yielded changeable gene expression on at least single time point. In addition to the differential expression of genes associated lipid metabolism, many ribosomal protein genes were induced during the injury stage despite the previous report of decreased protein synthesis rate upon CCl_4 treatment.

In the chronic intoxication model, rats received 0.5 ml CCl_4/kg three times a week, and the liver samples were obtained after 0, 30, 60, and 90 d of injection. The CCl_4 effect was classified into mild and severe fatty liver/steatosis (30 and 60 d, respectively) and fibrosis/cirrhosis (90 d) stages. The same custom rat gene microarray was analyzed and 438 clones were differentially expressed at one or more time points. Multiple genes involvedin lipid metabolism and ribosome biogenesis showed differential transcript levels upon chronic CCl_4 administration asseen in acute model. In addition, a total of 149 clones were identified as fibrosis/cirrhosis-specific genes by either fold changes or Significance Analysis of Microarrays.

In conclusion, we established a global gene expression profile utilizing microarray analysis in rat liver upon acute or chronic CCl_4 administration with a full chronological profile that covers injury and regeneration stage or fatty liver/steatosis and fibrosis/cirrhosis, respectively. These data will provide the insight of specific gene expression profiles that is implicated in the multistep process of fatty liver/steatosis and fibrosis/cirrhosis after acute or chronic hepatotoxin exposure.