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Comprehensive Analysis of Differential Gene Expression Profiles on Carbon Tetrachloride-induced Rat Liver Injury and egeneration

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Microarray analysis of RNA from carbon tetrachloride (CCl₄)-administered rat livers was performed at various time points to establish a global gene expression profile during injury and regeneration stages. A single dose of 1 ml/kg of CCl₄ was given by ip injection, and the liver samples were obtained after 6 h, 24 h, 48 h, and 2 wk. Histopathologic studies of liver tissues, liver function tests (serum AST, ALT levels) and PCNA analysis enabled the classification of the CCl₄ effect into injury (6 h and 24 h) and regeneration (48 h and 2 wk) stages. The expression levels of 5,180 clones on a custom rat gene microarray were analyzed and the results were confirmed by semi-quantitative RT-PCR. Out of 2,256 clones that gave reliable data, 587 clones (26%) yielded changeable gene expression on at least single time point. One hundred seventy nine clones were classified as injury-specific clones, while 38 clones as regeneration-specific clones. Characteristic gene expression profiles could be associated with CCl₄-induced gene expression with the disruption of lipid metabolism, which is known to cause the fatty liver induced by CCl₄ treatment. In addition, induction of the transcripts for many ribosomal proteins was detected during the injury stage, particularly at the 24 h time point, despite the previous report of decreased protein synthesis rate upon CCl₄ treatment. Several genes with known functions were also identified as CCl₄-regulated genes. In conclusion, we report microarray analysis results in rat liver upon acute CCl₄ administration with a full chronological profile that not only covers injury stage but also later points of regeneration stage. This work was supported by the grant from the National Institute of Toxicology Research, Korea (to Gu Kong).

Keyword : histopathology, toxicogenomics, microarray analysis, fatty liver