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Toxicogenomics Study on Bromobenzene Treated Mouse Liver with Histological and Blood Biochemical Non-Hepatotoxic Doses

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Bromobenzene (BB) is well known hepatotoxicant. Also, BB is an industrial solvent that arouses toxicity predominantly in the liver where it cause centrilobular necrosis. BB is subjected to Cytochrome P450 mediated epoxidation followed by either conjugation with glutathione, enzymatic hydrolysis or further oxidation. In this study, we focused on BB-induced gene expression at non-hepatotoxic dose. Usually, hepatotoxic doses show fulminant changes in gene expression and pathology. We supposed that non-hepatotoxic dose has effect on initiation of hepatotoxicity. C57BL/6 mice (12wks-old) were injected with corn oil or 40, 400 mg/kg of BB intraperitoneally. The mice were sacrificed at 24 hrs after treatment. Mouse 7.4K twin chip (Digitalgenomics, Korea) was used for toxicogenomics study. Liver isolated for RNA preparation and histopathology (H&E staining). Blood samples (serum) were collected for blood biochemical study (AST and ALT). Histopathological and blood biochemical data show that hepatotoxic evidence is not shown at the doses. Cell growth and maintenance related genes (Fatty acid binding protein, anillin, apolipoprotein, epidermal growth factor receptor, etc.) were down regulated with BB treatement. Stress-related genes (Serum amyloid A3, Tumor necrosis factor, Heat shock 70kD protein, etc.) were down regulated with the treatment. The down regulation pattern was also found in transcription related gene groups (GATA binding protein, Hepatic nuclear factor 4, Zinc finger homeobox, etc.). Down regulation pattern at the non-hepatotoxic dose of BB showed that certain physiological actions occurred with BB treatment. Additional study is needed to elucidate the physio-and pathological function on non-hepatotoxic dose BB treatment.

Keyword : Toxicogenomics, non-hepatotoxic dose, gene expression, Bromobenzene