【P-34】

Gene Expression Analysis in the Acetaminophen Treated Mouse Liver at Histological and Blood Biochemical Non-Hepatotoxic Doses

Sun Young Jung, Jung Sun Lim, Jae Woo Cho, Han Jin Park, Dal Sun Cha,
Yong Bum Kim, Moon Koo Chung, Sang Seop Han,
Chang Woo Song and Seokjoo Yoon
Korea Institute of Toxicology, KRICT, P.O Box 123, Yuseong, Daejeon, Korea

Acetaminophen (APAP) is one of the extensively used analgesic all over the world. We studied the gene expression pattern at the non-hepatotoxic doses. Sometimes high dose of acetaminophen induced severe hepatotoxicity. Usual therapeutic doses of APAP are not hepatotoxic, because the biotransformed metabolites conjugate with glucuronide or sulfate. We focused on the initialization of hepatotoxicity even at the non-hepatotoxic doses (therapeutic dose). Some of biochemical cascades might start in the early time response. C57BL/6 mice (12wks-old) were injected with saline or 30, 300mg/kg of APAP intraperitoneally. The mice were sacrificed at 6 and 24 hrs after treatment. Mouse 7.4K twin chip (Digitalgenomics, Korea) was used for gene expression analysis. 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 showed that hepatotoxic evidence is not shown at the doses. Basically we selected up- or down-regulated genes more than 2 folds change. In the functional category for cell growth and maintenance, some of genes (Anillin, Insulin-like growth factor binding protein, etc.) were up-regulated all APAP treated groups. Some of genes (Apolipoprotein, Aquaporin, etc.) from same category were down-regulated with APAP treatment. Stress-related gene, Serum amyloid A3, was up-regulated with the treatment. The down-regulation pattern also found in transcription related gene groups. However, the down-regulated transcription related genes were not matched among the groups. We supposed that some response occur to stress even at non-hepatotoxic dose of APAP treatment. Down-regulation pattern at the non-hepatotoxic dose of APAP showed that certain actions occurred with APAP treatment. Further study is needed to elucidate the biological function on non-hepatotoxic dose APAP treatment.

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