【P-33】

Toxicogenomics study of ENU-treated mouse liver using cDNA microarray

Sun-Hwa Lee, Seokjoo Yoon, Kyu-Hyuk Cho, Jae-Woo Cho, Sang-Seop Han and Chang-Woo Song

Laboratory of Toxicogenomics, Korea Institute of Toxicology (KIT), Korea Research Institute of Chemical Technology (KRICT), Korea

N-ethyl-*N*-nitrosourea (ENU), a toxin and carcinogen as well as a mutagen, has a variety of effects on mice. In the present study, we analyzed the expression patterns of cancer related genes in ENU-treated mouse liver. BALB/c mice were injected with phosphate-buffered saline or 250 mg/kg of ENU intraperitoneally. The mice were sacrificed at 4, 12, 24, and 48 hrs after treatment, respectively. Mouse 10K cDNA chip was used for gene expression profiling study in 24 and 48 hrs ENU treated mouse liver. Ninety genes were down-regulated and 37 genes were up-regulated in 24 hrs after treatment. Seventy-five genes were down-regulated and 32 genes were up-regulated in 48 hrsafter treatment. We found several up-regulated cancer related genes, such as growth hormone (GH) receptor, p53, metallothionein (MT) I & II. In order to validate the expression levels of these genes, we performed real-time PCR at each time point. The gene expression reached a peak (15~20 times higher than control) at 4 hrs after treatment. The expression level then gradually decreased,but still higher or equal to that of control. p53 and MT are well known tumor related molecular markers. Enhanced expression of p53 and MT at the 4 hrs ENU treatment showed that certain carcinogenetic actions occurred in early time. Interestingly, p53, MT, and GH receptor showed similar patterns in their gene expression. We hypothesized that up-regulated gene expression of GH receptor in ENU treatment is correlated with cancer progression. Additional experimental data, on these genes in carcinogenesis, are needed to elucidate the biological functions during ENU-induced cancer progression.

Keyword : ENU mutagenesis, carcinogenesis, cDNA array, gene expression