

Identification of Toxicant-Specific Patterns of Gene Expression and Evaluation of Molecular Mechanisms in Cellular Responses to Environmental Toxicants Using by Radioactive cDNA Microarray

- As an example of gene expression profiling in workers exposed to polycyclic aromatic hydrocarbons or 2,3,7,8-tetrachlorodibenzo-p-dioxins using by microarray -

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Toxicogenomics is a scientific field that studies how the genome is involved in responses to environmental stressors and toxicants. Toxicogenomics combines studies of genetics, mRNA expression, cell and tissue-wide protein expression and metabonomics to understand the role of gene-environment interactions in disease.

To evaluate the effects of PAHs and dioxin on the genes expression, and to elucidate a possible mechanisms in cellular responses to these environmental toxicants, we investigated gene expression in automobile emission inspectors and waste incinerating workers using by radioactive cDNA microarray analysis. About 54 workers from three automobile emission inspection offices, 31 workers from waste incinerating company, and 84 matched, unexposed healthy subjects were enrolled in the study. Total RNA prepared from whole blood of these subjects was used to synthesize ³³P-labeled cDNAs by reverse transcription. This method using ³³P-labeled probes provided highly sensitive gene expression profiles including toxicants metabolism, and cellular signaling. The gene expression profiles showed that 11 genes were up-regulated and 4 genes were down-regulated in waste incinerating workers as compared with controls. Comparison rank analysis revealed that the expression of five genes related to oxidative stress, including CYP2F1, CYP2D6, anti-oxidant protein 2, glutathione S-transferase M1, and glutathione peroxidase 4 increased by more than 2.0 of the Z-ratio. Other genes up-regulated in waste incinerating workers are integrin-linked kinase, casein kinase 1, etc. which are known to be involved in general cell signaling pathway. It is interesting that genes related to oxidative stress were up regulated in waste incinerating workers. anti-oxidant enzymes that shift to anti-oxidation status in a free radical metabolism that is typical of oxidative stress. Up-regulation of these genes was confirmed in the proteomic analysis using by 2DE gel electrophoresis.

Consequently, we demonstrated that radioactive human cDNA microarray is highly efficient technology for evaluating the gene expression of PAHs or dioxin exposure and for identifying discriminating biomarkers for toxicity prediction by using high-throughput biotechnology.