

Toxicogenomics Concepts and Applications to Develop New Pharmaceuticals

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The recent DNA microarray technology enables us to understand a large number of gene expression profiling. The technology has potential possibility to comprehend mechanism of multiple genes were related to compounds which have toxicity in biological system. So, microarray system has been used for the prediction of toxicity through gene expression induced toxicant and has shown that compounds with similar toxic mechanisms produce similar changes in gene expression *in vivo* and *in vitro* system. Recently, many pharmaceutical companies and research groups are making databases of gene expression related to toxic mechanism induced by compounds that were well characterized. These collected databases of microarray associated with toxicity will shorten the toxicity evaluation steps that are often the rate-limiting step in the discovery and development of new pharmaceuticals. Therefore, the toxicogenomics through this technology may be very powerful for understanding the effect of unknown toxic mechanisms in biological system.

In this study, a rat 4.8K cDNA microarray which contains approximately 4,800 toxicity-related genes has designed. Twenty different compounds have analyzed for the toxicogenomic studies. Toxicity in livers of all of the treated animals with histological examinations were performed. In order to determine gene expression profiles associated with chemical exposure, liver total RNA was extracted after exposures to the compound. To reduce variability in the level of gene expression of rats treated with vehicle, control total RNA has pooled and used for hybridizations on the 4.8K cDNA microarray.

One of the challenging issues in Toxicogenomics is the construction of intelligent database management system which can deal with heterogeneous and complex data from many different experimental and information sources. Therefore, toxicogenomic database system was constructed for focusing on the connectivity of heterogeneous data and the query system which enables users to obtain relevant useful information related toxicology. The database dealt with four kinds of information; compound, histopathology, gene expression, and annotation information.

Expression analyses with tens of different chemicals suggested that such results will provide valuable informations for further studies of the classification of compound associated signature. Therefore, gene expression profiling using DNA microarray may prove to be a highly sensitive technique for safety screening of drug candidates in level of transcription in rodent system.