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Correlation between liver cancer occurrence and gene expression profiles in rat liver tissue

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ABSTRACT. Liver cancer (LC) is generally characterized by malignant cell proliferation and growth; it normally develops in stages that progress from non-specific injury of the liver to liver fibrosis, liver cirrhosis, dysplasia nodules, and liver carcinoma. We used a rat model of diethylnitrosamine (DENA)-induced LC; a Rat Genome 230 2.0 Array was used to detect gene expression profile of liver tissues from male rats 5, 8, 12, 16, and 18 weeks following the beginning of DENA-induced LC. We found 909 known genes, including 637 up-regulated, 270 down-regulated, and two up/down-regulated genes, that were significantly changed in expression. Among them, 108 genes were expressed at the 5th, 213 at the 8th, 516 at the 12th, 698 at the 16th, and 506 at the 18th week of DENA-induced LC. Methods in bioinformatics and systems biology were applied to explore the correlation between the gene expression profile of rat liver tissue and liver cancer occurrence at the transcriptional level; 23 physiological activities were found to be associated with LC. Among these, eight physiological activities, including stimulus response, inflammation and immune response, oxidative reduction, cell proliferation, differentiation, migration, adhesion, and angiogenesis were increased, implying that

they could play important roles in the occurrence and development of LC. In addition, carbohydrate, lipid, and organic acid metabolism were decreased, suggesting that liver injury induced by a carcinogenic agent has a negative effect on the metabolism of fundamental substances.

Key words: Liver cancer; Gene expression profile; Systems biology; Physiological activity

