P126  Dysregulation of genes involved in iron metabolism in chemical carcinogen-induced liver tumors.

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Liver tumors have iron deficient phenotype. But, its mechanisms are not clearly known. We investigated whether reduction of iron in tumors is associated with altered expression of iron metabolism related genes. The liver tumor mice were established by diethylnitrosamine. Analysis of iron content and iron regulatory genes was also performed.

Decreased iron level in tumor was confirmed through AAS. But, there was no significant difference in serum iron compared to control with similar mRNA level of Tf. The mRNA of iron uptake transporters DMT1(IRE+) and TfR2 were downregulated in tumor although their expression levels were not changed in non-tumor regardless of iron overloading. Another transporter TfR1 mRNA was increased in tumor, but much higher in non-tumor. In addition, HFE, which mediates iron influx, was upregulated in non-tumor though it was unchanged in tumor. In the case of DMT1 (IRE-) and HFE 2, there was no significant alteration even at iron overloaded. Iron storage protein ferritin displayed differential expression levels in its two subunits. The mRNA level of Ferritin H was unchanged regardless of iron treatment, but Ferritin L, main subunit of liver ferritin, was downregulated in tumor and induced in overloaded liver. Iron exporter MTP1 and iron efflux-involved Hepcidin displayed reduced mRNA in tumor, but recovered at iron overloading.

These findings suggest reduced iron in liver tumor might be induced by decreased expression of iron uptake related genes including DMT1 (IRE+), TfR2 and increased mRNA level of iron efflux related Cp. However, DEN-induced tumors sense iron depletion and respond to it in such a way to keep tissue iron level within normal physiological range with reduced expression of iron exporter MTP1.

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P127  Comparison of transformation activities of arsenic compounds in Bhas 42 cells with those in BALB/c 3T3 cells

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A cell transformation assay is a unique system among in vitro assays to predict chemical carcinogenicity. The two-stage BALB/c 3T3 cell transformation assay, which simulates a two-stage carcinogenicity test in vivo, has been used for detection of tumor initiators and promoters. The two-stage BALB/c 3T3 cell transformation assay is simplified, using Bhas 42 cells which are established from the BALB/c 3T3 cells transfected by v-H-ras gene. The Bhas 42 cell transformation assay is superior in cost, labor and assay period and appropriate for the routine screening assay of carcinogens. Inorganic arsenic compounds have epidemiologically defined to be carcinogenic in human. Although their mutagenicity is weak, they were reported to increase transformation frequency in various assays. In this study, we performed the Bhas 42 cell transformation assay of arsenic compounds. Sodium arsenite was positive and sodium arsenate was negative in the initiation assay. Both sodium arsenite and sodium arsenate were positive in the promotion assay. These results accord with the data reported in BALB/c 3T3 assays. Initiation and promotion assays of organic arsenic compounds are ongoing. In the presentation, we will discuss the equivalence between the Bhas 42 assay and the BALB/c 3T3 assay.

Bhas 42細胞におけると素化合物の形質転換活性のBALB/c 3T3細胞における報告との比較
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