Program Nr: 509 from the 2001 ASHG Annual Meeting

Loss of Tyrosine Aminotransferase may Contribute to the Pathogenesis of Hepatocellular Carcinoma. *X.Y. Guan, Y.W. Xie, J.S.T. Sham.* Dept Clinical Oncology, Univ Hong Kong, Hong Kong, China.

Loss of material at chromosome arm 16q is one of the most frequent alterations in hepatocellular carcinoma (HCC) detected by comparative genomic hybridization and loss of heterozygosity studies. It suggests that the frequent deleted region at 16q may contain a tumor suppressor gene. cDNA subtraction strategy was applied to isolate down-regulated gene at 16q. cDNAs from the surrounding non-tumor liver tissue was subtracted with cDNAs from its matched primary HCC tumor and a gene at 16q22, tyrosine aminotransferase gene (TAT), was isolated. RNA expression of the TAT gene in 8 primary HCC tumors with 16q deletion was analyzed by northern blot hybridization and reverse transcriptase-polymerase chain reaction. Absence and marked reduction expression of TAT gene was detected in 5 and 2 tumors, respectively, as compared with tumor surrounding liver tissues. Homo-deletion of genomic DNA sequence of TAT gene was observed in two cases detected by PCR. Tyrosine aminotransferase is the rate-limiting enzyme for the tyrosine catabolic pathway and the deficiency of TAT gene may result in elevation of tyrosine level. Prolonged elevation of intracellular tyrosine concentrations may disrupt normal functions of hepatocytes and initiate local inflammatory responses, leading to liver diseases including HCC. Therefore, loss of TAT gene may contribute to the pathogenesis of HCC.