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Program: Oral and Poster Abstracts

- Stem Cells in ALD, Liver and Pancreatic Cancer
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- Novel Insights into Liver and Pancreatic Fibrogenesis
- Therapeutic Targets of ALPD and Cirrhosis
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Mechanism of the pathogenesis of hepatocellular carcinoma during chronic administration of ethanol in mice

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Epidemiological evidence indicates that chronic intake of alcohol increases the risk of carcinogenesis in liver and gastrointestinal tract. However, the mechanism of ethanol induced hepatocarcinogenesis is not clear. In order to elucidate the effects of ethanol on the pathogenesis of hepatocellular carcinoma (HCC), male ICR mice were administered ethanol through drinking water over a period of 60 and 70 weeks at a concentration of 5% on the first week, 10% during the next 8 weeks, and 15% thereafter. The control group received equal amount of water without ethanol. Some of the control and treated mice were sacrificed at 60 weeks and the remaining at 70 weeks. At 60th week, 40% of ethanol group had visible white nodules (5-10 mm) in the liver, while such nodules were totally absent in control mice. At 70th week, several larger nodules (5-22 mm) were present in the livers of 50% mice in ethanol group. In control group, one mouse (10%) developed a single nodule. All nodules were histologically trabecular HCC composed of eosinophilic and vacuolated cells. In the livers of both control and ethanol group, a few foci were present with cellular aberration. The size of the foci in ethanol group was significantly larger than those in the control group. In order to obtain an insight of the mechanism of pathogenesis of ethanol induced HCC, immunohistochemistry was performed in paraffin embedded liver sections of control and ethanol treated mice for cytochrome P4502E1 (CYP2E1), 4-hydroxy-nonenal (HNE), a marker for reactive oxygen species (ROS), and c-Myc. There was dramatic upregulation of all these molecules in the foci where cellular aberration was present. The results indicated that chronic administration of ethanol upregulates CYP2E1 which results in the production of ROS that in turn induces c-Myc and triggers the development of HCC in mice. Our data suggest that ethanol acts as a promoter for the pathogenesis of HCC.