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#3584 Ethanol and aging promote pathogenesis of hepatocellular carcinoma in mice.

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Background & Aims: Chronic intake of alcohol increases the risk of gastrointestinal and hepatic carcinogenesis. The present study was focused to investigate the incidence and mechanism of pathogenesis of hepatocellular carcinoma (HCC) during aging and chronic ingestion of alcohol without any additional hepatic injury.

Methods: Ethanol was administered to ICR male mice through drinking water for 70 weeks at concentrations of 5% (first week), 10% (next 8 weeks), and 15% thereafter. The animals were sacrificed at 60 weeks and 70 weeks, the livers were examined for hepatic tumors, and evaluated for foci of cellular alteration. Immunohistochemical staining was performed in the liver sections for cytochrome P4502E1 (CYP2E1), 4-hydroxy-nonenal, and proto-oncogene, c-Myc

Results: At 60th week, 40% of mice in the ethanol group had visible white nodules (5-10 mm) in the liver, but not 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 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, several foci with cellular alteration were present, which were significantly higher in ethanol group. Staining for CYP2E1, 4-hydroxy-nonenal and c-Myc depicted marked upregulation of all these molecules in the foci of cellular alteration.

Conclusions: Our data demonstrated that upregulation of CYP2E1 and subsequent production of reactive oxygen species along with the persistent expression of c-Myc play a significant role in the pathogenesis of HCC during chronic ingestion of ethanol. Furthermore, aging is also a risk factor for development of HCC.* Presenting author

Citation Format

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