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Program: Oral and Poster Abstracts

- Stem Cells in ALD, Liver and Pancreatic Cancer
- Cell Death Regulation in ASH and Alcoholic Pancreatitis
- Novel Insights into Liver and Pancreatic Fibrogenesis
- Therapeutic Targets of ALPD and Cirrhosis
- Global Health: Impacts of Alcohol, Smoking and Obesity

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Occasional Alcohol Intake Promotes Nonalcoholic Steatohepatitis in Obese Rats

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The pathogenesis of nonalcoholic steatohepatitis (NASH) has been hypothesized to be a two-stage process in which steatosis is the first insult, and an unknown second “hit”. In order to investigate whether occasional alcohol intake could be a second hit to develop NASH from simple steatosis caused by obesity, 30 weeks old male Otsuka Long-Evans Tokushima Fatty (OLETF) rats (620 ± 10 g), which spontaneously develop steatosis and diabetes from 30 weeks old, were administered 10 ml of 10% ethanol or water using gavage tube five times, thrice, twice or once per week for 3 weeks. As control, male Otsuka Long-Evans Tokushima (OLET) rats (460 ± 15 g) were administered the same amount of ethanol or water. Both OLETF and OLET rats were sacrificed at the age of 10, 20 and 30 weeks to evaluate the induction of cytochrome P4502E1 (CYP2E1) through ageing. Massive steatohepatitis was observed in the livers of OLETF rats treated with ethanol once a week as well as five times, thrice and twice a week, while slight fatty degeneration was observed in OLETF rats received water. There was no fatty degeneration in OLET rats administered either ethanol or water. Both serum and hepatic triglyceride levels were significantly higher in all the groups of OLETF rats treated with ethanol compared to control OLETF rats received water. There was no difference in serum and hepatic triglyceride levels between LETO rats received ethanol or water. Immunohistochemical staining for CYP2E1 demonstrated dramatic increases in par with the increase of body weight in OLETF rats. 4-hydroxy-2-nonenal, a marker for reactive oxygen species (ROS) depicted remarkable staining in the hepatic tissue of OLETF rats treated with ethanol compared to OLETF rats received water. Our data indicates that occasional alcohol intake could be a second “hit” for the development of NASH in obese individuals.