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Cholestatic liver injury results from the accumulation of toxic bile salts within the liver. The aim of the present study was to understand the mechanism of bile salts-induced hepatocellular apoptosis in bile duct-ligated (BDL) rats, using Western blot and immunohistochemical analysis. The mechanisms of hepatoprotective effects of *Salvia miltiorrhiza* (SM) was also studied in this model. Apoptotic cell death was increased five-fold after three days of BDL, decreased over two weeks and remained constant thereafter. Total cellular Bax protein was increased three days after BDL and decreased over time thereafter. We observed the translocation of Bax to mitochondria and subsequent release of cytochrome c. Nuclear p53 increased three days after BDL, but most p53 was expressed in the cytoplasm after one week. The expression of c-Myc was inhibited by three days, but increased at later stages following BDL. Bcl-2 was increased over time in BDL rats. Fas expression was not changed and activation of caspase 8 did not occur. Fas immunoreactivity was exclusively observed in the cytoplasm of hepatocytes, indicating that Fas expressed in rat hepatocytes is predominantly a soluble form. Thus our data suggest that nuclear p53 regulates the expression of Bax in BDL rats. The translocation of Bax to mitochondria supports the hypothesis that this may lead to release of cytochrome c and transduce the signal for apoptotic death of hepatocytes by toxic bile salts. The lack of changes in Fas suggests that Fas may not be playing a role in apoptosis in this model.

Salvia miltiorrhiza BUNGE, a traditional chinese herbal medicine, has been commonly used to treat chronic hepatitis and liver fibrosis. However, the mechanism of action is not yet fully understood. The treatment of extract of SM to BDL rat reduced the number of TUNEL positive cells to the control level after 10 days of BDL. The expression of Bax was reduced with time by the treatment of SM. The treatment of SM accelerated the cytoplasmic sequestration of p53. The expression of Bcl-2 was increased, hence the Bax to Bcl-2 ratio was decreased significantly. These results suggest that SM may be used as hepatoprotective agent in extrahepatic cholestasis model.

[PA3-12] [10/18/2001 (Thr) 14:00 – 17:00 / Hall D]

Effect of gamma radiation on steroidogenesis and testicular function in adult mice

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The effect of radiation on testis are related to the irradiated dose resulting in temporary or permanent inhibition of spermatogenesis depending upon the radiation damaged cell types. We examined changes in testosterone production in the testis of male mice after wholebody gamma-irradiation. Eight-week-old male ICR mice were irradiated with 6.5 or 10 Gy. At days 1, 2, 3, 4 and 5 after irradiation, testes were removed and processed for paraffin sections and isolation of mRNA. We calculated the gonad index from body and testis weight, and checked testosterone levels per testicular volume. Hormonal analysis in serum and testis was performed by means of radioimmunoassay. Semiquantitative RT-PCR techniques were used to evaluate the expression kinetics of the apoptotic gene after irradiation. Gamma-irradiation in the mice showed that body weight and testosterone concentration and differential expression of the apoptotic gene were reduced compared to that of non-irradiated ones. These results demonstrate that gamma-radiation induces impairment of testicular function somewhat in adult mice.

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Levels of PCB congeners and organochlorine pesticides in Korean adipose tissue, liver and whole blood

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