ties were significant. In addition, AROD and immunodetectable CYP1A-like protein were also significantly correlated. This indicates that the CYP1A-like protein is involved in the AROD activities. In P. largha, immunodetectable CYP3A-like protein was significantly correlated with AROD. This suggests that the CYP3A-like protein in this seal is also responsible for catalytic activities of AROD. Immunodetectable CYP2B-like protein was not correlated to any activities. The CYP2B-like protein may be unlikely to participate in the substrate metabolism. As immunodetectable CYP1A- and CYP3A-like proteins in P. largha were also correlated with TH activity, these CYP subfamilies may be associated with TH. (5) In P. largha, a growth-dependent increase of EROD activity was found in male seals. In contrast, female seals showed a decreasing pattern in EROD activity. Such specific patterns of EROD activity in male and female seals were found to be similar to those of organochlorine accumulation, implying a potential for induction of seal P450 by environmental pollutants.

Generation of Reactive Oxygen Species and Decrease of Liver Catalase in Long-Evans Cinnamon Rats Predisposed to Hepatitis and Hepatoma.

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The Long-Evans Cinnamon (LEC) rat, an inbred mutant rat derived from the Long-Evans strain, is characterized by spontaneous hepatitis due to gross accumulation of hepatic Cu. We have studied generation of reactive oxygen species, superoxide anions, hydrogen peroxide, and catalase, which could be a reduction enzyme of H2O2, in LEC and Wistar rat livers. Generation of superoxide anions was higher in the liver of female LEC rats than in that of Wistar rats at 14 wk (acute stage) of age. However, generation of superoxide anions was lower in the liver of male LEC rats than in that of Wistar rats at 16 (acute stage) and 24 wk (chronic hepatitis stage) of age. Generation of hydrogen peroxide was higher in the liver of LEC rats than in that of Wistar rats. Of the enzymes examined, hepatic catalase was markedly decreased in LEC rats. Western-blot analysis revealed that the content of catalase in the liver of LEC rats was 44%, 39%, 23%, and 26% of the control values at 9 (normal stage), 14 (acute hepatitis stage), 16 (acute hepatitis stage), 24 (chronic hepatitis stage) wk of age, respectively. These results suggest that cellular accumulation of ·OH from H2O2 in the presence of Cu, causes cellular damage leading to hepatitis and hepatoma.