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Peroxisome Proliferator Activated Receptor γ Expression in two Animal Models of Chemically-Induced Liver Injury and Regeneration

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BACKGROUND-AIMS

Peroxisome proliferator activated receptors (PPARs) are members of the receptor family of ligand-activated transcription factors that include the steroid, retinoid and thyroid receptors. The mamalian PPAR family includes three subtypes PPARα, PPARβ and PPARγ. Agonist ligands for the PPARγ, as troglitazone, have been shown to induce terminal differentiation of adipocytes. In the present study we investigated the expression of hepatic PPARγ in two different rat models of injury and regeneration, induced by carbon tetrachloride (CCl_4) or thioacetamide (TAA) administration.

MATERIALS AND METHODS

Male Wistar rats were administered intraperitoneally with either 1 mL CCl_4 or 300 mg TAA/Kg of body weight. Toxicological end points and markers of hepatocellular regeneration were assessed at various time points (0, 12, 24, 36, 48, 60 and 72 h) after the injection of CCl_4 or TAA. The enzymatic activities of aspartate and alanine aminotransferases in serum, and the histological findings in the liver were used to estimate toxin-induced liver injury. The rate of tritiated thymidine incorporation into hepatic DNA, the enzymatic activity of liver thymidine kinase activity and the assessement of mitotic index and Ki-67 labeling index in hepatocytes were used as indices of regeneration. PPARγ was detected immunohistochemically in paraffin embedded liver tissue.

RESULTS

Toxin (CCl_4 or TAA) administration caused severe liver injury, followed by hepatocellular proliferation. In CCl_4-treated rats mild PPARγ immunoreactivity was prominent in centrilobular hepatocytes 12 h post-administration. At 24 h intense PPARγ expression was found in centrilobular hepatocytes and foam cells, while at 36 h, intense staining was found in hepatocytes in the vicinity of inflammatory sites. At further time points examined, moderate PPARγ expression was noted in proliferating hepatocytes and intense in the vicinity of inflammatory infiltrations. In TAA-treated rats no PPARγ expression was found at all time points examined, corresponding either to hepatic injury or regeneration.

CONCLUSIONS

Our data for first time describe alterations in the expression of PPARγ and implication of this receptor in toxin CCl_4-, but not TAA-induced liver injury and regeneration.