activated proteins. Currently, we are investigating the mechanism of downregulation at the transciption level.

[PC3-3] [04/18/2003 (Fri) 09:30 - 12:30 / Hall P]

The Antiproliferative Effects of Bile Acids and Their Derivatives on HT-29 Human Colon Cancer Cells

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The antiproliferative effects of bile acids and their derivatives on HT-29 human colon cancer cells were investigated. Ursodeoxycholic acid (UDCA) and its synthetic derivatives, HS-1030 and HS-1183, and chenodeoxycholic acid (CDCA) and its synthetic derivatives, HS-1199 and HS-1200 were employed for this study. General evaluations focusing on cell cycle were conducted in HT-29 human colon adenocarcinoma cell line (p53 mutant type). Although UDCA and CDCA exhibited no significant effect on the cell viability and growth, their synthetic derivatives highly decreased their viability in a concentration- and time-dependent manner as assessed by MTT assay and cell growth study. Flow cytometric analysis demonstrated that the synthetic bile acid derivatives increased G1/S population. Western blotting showed that the expressions of cyclins, cyclin dependent kinase were down-regulated. The cyclin dependent kinase inhibitor, p21, was up-regulated in a p53-independent manner. These findings suggest that these cytotoxic effects of novel bile acid derivatives on human colon adenocarcinoma cells were mediated via apoptosis through a p53-independent pathway.

[PC3-4] [04/18/2003 (Fri) 09:30 - 12:30 / Hall P]

4-Hydroxy nonenal (HNE) Induces Endothelial cells Apoptosis via iNOS mediated ONOO- generation

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Among the aldehydes derived from lipid peroxidation, 4-hydroxynonenal (HNE) that can be produced from arachidonic acids, linoleic acids, or their hydroperoxides in relatively large amounts in response to oxidative insult. Therefore, HNE might be an important mediator of oxidative stress-induced apoptosis. To study the hypothesis that HNE may induce apoptosis, we estimated cytotoxicity of HNE on YPEN-1 rat prostatic endothelial cells. Anti-proliferative effects were examined by morphological changes and MTT assay after exposure to different concentration (5 ~ 15 μM) of HNE. As results, we observed apoptotic bodies with propidium iodide staining and detected induction of apoptosis by HNE with flow cytometry assay. We also studied apoptosis related events with Western blotting. Cells exposed to HNE for 24 hr resulted in increased poly(ADP-ribose) polymerase cleavage and up-regulation of Bax. In addition, HNE induced intracellular ROS generation and NF-κB expression. Cells exposed to 15 μM HNE for 0.5 ~ 4 hr resulted in increased NF-κB expression. Also, HNE induced COX-2 and iNOS