in BAE (bovine aortic endothelial) cells. Anti-proliferative effects were examined by morphological changes and MTT assay after exposure to different time (0-3 hr) and concentration (3-7 μM) of HNE. As results, we observed apoptotic bodies with propidium iodide staining and detected induction of apoptosis by HNE with flow cytometry assay and DNA fragmentation on both conditions. We also studied apoptosis related events with Western blotting. BAE cells exposed to HNE for 0 and 3 hr resulted in increased poly(ADP-rebose) polymerase cleavage, up-regulation of Bax, and p53 proteins. Even though there was no decrease of Bcl-2 level, we observed the change of Bax/Bcl-2 ratio at a certain experimental condition. In addition, HNE caused G2 phase cell cycle arrest as flow cytometry assay. These data suggest that HNE contribute apoptosis and cell cycle arrest in BAE cells. We are under the study of cell cycle modulation effects by HNE on the levels of cyclins D and E and cdks, PCNA, pRb expression change and ATP depletion.

[PA1-10] [10/18/2002 (Fri) 09:30 - 12:30 / Hall C]

Inhibitory effects of resveratrol analogs on lipopolysaccharide-induced cyclooxygenase-2 activity in RAW264.7 cells

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It has been known that resveratrol, a phytoalexin present in grapes mainly, has antioxidant, anti-inflammatory, and cancer chemopreventive activity. One mechanism of its anti-inflammation and cancer prevention is considered to modulate cyclooxygense-2 (COX-2) activity. Since COX-2 plays an important role in inflammation and carcinogenesis, the potential COX-2 inhibitors have been considered as anti-inflammatory or cancer chemopreventive agents. In order to discover novel chemopreventive agents, we synthesized about thirty analogs of resveratrol and evaluated their COX-2 inhibitory activity with the production of prostaglandin E_2 (PGE_2) in RAW264.7 cells. As a result, several compounds showed more potent inhibitory activity than resveratrol. Especially, [3-(4-methoxyphenyl)-vinyl]thiophene (Compound 1) and [3-(4-methoxyphenyl)-vinyl]furan (Compound 2) were potential inhibitors. Further studies are under way to investigate their mechanism of action whether affecting COX-2 expression and transcriptional regulation or not. This study suggests that these compounds might be potential candidates for developing anti-inflammatory or cancer chemopreventive agents.

[PA1-11] [10/18/2002 (Fri) 09:30 - 12:30 / Hall C]

The Antiproliferative Effects of Bile Acids and Their Derivatives on HepG2 Human Hepatocellular Carcinoma Cells

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We studied on the antiproliferative effects of bile acids and their derivatives on HepG2 human hepatocellular carcinoma cells. Ursodeoxycholic acid (UDCA) and its synthetic derivative HS-1030, and chenodeoxycholic acid (CDCA) and its synthetic derivatives, HS-1199 and HS?200, were used. We focused on the regulation of cell cycle and induction of apoptosis by these bile acid derivatives. Although UDCA and CDCA exhibited no significant effect on the viability of the cells utilized at the concentration ranges tested, their synthetic derivatives decreased their viability in a concentration dependent manner as determined by MTT assay. Flow cytometric analysis demonstrated that the

UDCA and HS-1030 increased sub-G1 population. HS-1199 and HS-1200 also increased G1 phase population. In DNA fragmentation assay, the cells were harvested at 24 and 48 hr after the synthetic of bile acids. As results, UDCA, CDCA, HS-1030, HS-1183 and HS-1199 shows DNA ladders but not HS-1200. *Western blotting performed using poly(ADP-ribose) polymerase*, Bax, p53, p27, caspase-3, and cyclin E, cyclin B and -actin. In Western blots, UDCA, CDCA, HS-1030, HS-1183 lead to apoptosis. And HS-1200 shows GI cell cycle arrest manners, interestingly only HS-1200 increased Bax level.

[PA1-12] [10/18/2002 (Fri) 09:30 - 12:30 / Hall C]

Effect of Synthetic Bile Acid Derivatives on the Cell Cycle Modulation of HT-29 Human Colon Cancer Cells

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We studied the effects of 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, on the human colon adenocarcinoma cell line, HT-29 (p53 mutant type). The effects on cell viability and growth were assessed by MTT assay and cell growth study. While UDCA and CDCA exhibited no significant effect, their novel derivatives inhibited the proliferation of HT-29 cell line in a concentration- and time-dependent manners. Especially, HS-1199 and HS-1200 showed the most significant anti-proliferative effects on HT-29 cell line. According to propidium iodide staining and flow cytometry analysis, this effect may be a result from S cell cycle arrest. Furthermore, we observed the level of cyclin-dependent kinase inhibitor p21 was increased after the treatment of HS-1183, HS-1199, and HS-1200. The 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.

[PA1-13] [10/18/2002 (Fri) 09:30 - 12:30 / Hall C]

Effects of cationic polyamines under 10 kD range of molecular weight on basic and induced mucin release from airway goblet cells

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In this study, we tried to investigate whether polymerized basic amino acid e.g. poly-L-lysine(PLL) which has the molecular weight under 10 kD significantly affects the physiological and stimulated mucin release from cultured hamster tracheal surface epithelial cells. Confluent primary hamster tracheal surface epithelial(HTSE) cells were metabolically radiolabeled with 3H-glucosamine for 24 hr and chased for 30 min in the presence of either PLLs or adenosine triphosphate(ATP) and PLL to assess the effects on basic or ATP-stimulated 3H-mucin release. Possible cytotoxicities of PLLs were assessed by measuring lactate dehydrogenase(LDH) release from HTSE cells during treatment. The results were as follows : (1) PLLs significantly inhibited basic mucin release from cultured HTSE cells in a dose-dependent manner from the range of 46mer(M.W. 9,600) to 14mer ; (2) PLL 46mer significantly inhibited the stimulated mucin release by ATP from cultured HTSE cells ; (3) there was no significant release of LDH from cultured HTSE cells during treatment. We conclude that PLLs inhibit