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

expressions, and NO and ONOO- productions. In order to demonstrate whether ROS are involved in HNE-induced apoptosis, N-acetylcysteine (NAC), ROS scavenger, was used in this study. The results indicated that the apoptosis-inducing HNE was inhibited by NAC. Therefore, the oxidant activity might be involved in HNE-induced apoptosis. These data suggest that HNE contributes to induce apoptosis on YPEN-1 cells.

[PC3-5] [04/18/2003 (Fri) 09:30 - 12:30 / Hall P]

Ircinin-1 from the Sponge *Sarcotragus* sp. Induces of Apoptosis in SK-MEL-2 Human Skin Cancer Cells

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The marine sponge of the genus *Petrosia* sp. is known to contain unique metabolites such as furanoterpenoids. These furanoterpenoids have been reported to possess various bioactivities. We have shown previously that ircinin-1 induced cell cycle arrest and apoptosis in SK-MEL-2 human skin cancer cells dose- and time-dependently. In this study, we demonstrated that ircinin-1-induced apoptosis is accompanied by cleavage of poly(ADP-ribose) polymerase protein and PLC-γ1 degradation and release of cytochrome *c* from mitochondria to cytosol. This was associated with the cleavage/activation of caspase-3 and caspase-9 proteins. Even though the inhibitor of apoptosis protein (IAPs) was expressed in ircinin-1-untreated or -treated SK-MEL-2 cells, only cIAP-1, but not XIAP or cIAP-2, was cleaved during ircinin-1-induced apoptosis at Western blot and RT-PCR studies. These findings suggest that the ircinin-1-induced apoptosis was conducted by the mechanism that interferes with activity of caspase-3 and the downregulation of IAPs.

[PC3-6] [04/18/2003 (Fri) 09:30 - 12:30 / Hall P]

Comparison on the effects of Cytotoxicity and Quinone Reductase Inducing Activity from Porphyra tenera and Enteromorpha linz

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The seaweed, as source of bio-active substances as well as food, has received much attention in recent years. This study was carried out to determine the cytotoxic and chemopreventive effects of Porphyra tenera (PT) and Enteromorpha linza (EL). The PT and EL extracts from methanol were fractionated to five different types, which are hexane, ethylether, ethylacetate, butanol and water. Cytotoxicity of PT and EL extracts was determined by MTT assay using HepG2, C6, MCF-7 and HT29 cell lines. Among the various fractions, hexane(PTMH) and aqueous(PTMA) fractions of PT were showed significant cytotoxic effects on the all cancer cell lines which we used. From the results of quinone reductase (QR)-inducing activities using HepG2 cells, expecially hexane fractions at a dose of 100 ug/mL in PT was 4.6 times more effective compared to the control of 1.0. In general, the effect of cytotoxicity and QR to the five different types of EL showed less effective than the fractions of PT. Therefore, based on these studies, the PTMH and PTMA may be developed into potentially useful bio-active materials for