[6]-Gingerol, a major pungent ingredient of ginger (Zingiber officinale Roscoe, Zingiberaceae) has a wide array of pharmacologic effects. Our previous studies have demonstrated that [6]-gingerol inhibits mouse skin tumor promotion and anchorage-independent growth of cultured mouse epidermal cells stimulated with epidermal growth factor. In this study, we have investigated the molecular mechanisms underlying anti-tumor promoting effects of [6]- gingerol on mouse skin carcinogenesis. Cyclooxygenase-2 (COX-2), a key enzyme in the prostaglandin biosynthesis, has been recognized as a molecular target for many chemopreventive as well as anti-inflammatory agents. The murine COX-2 promoter harbours several transcriptional elements, particularly those involved in regulating inflammatory processes. One of the essential transcription factors responsible for COX-2 induction is NF-κB. Topical application of phorbol ester-induced COX-2 expression in both mouse skin in vivo and non-trnasfromed murine keratinocytes (Pam212) in culutre. [6]-Gingerol treatment prior to topical application of phorbol ester inhibited the COX-2 expression through suppression of NF-κB activation in mouse skin. [6]-Gingerol, through possible down-regulation of p38 MAPK, abrogated the DNA binding activity and transcriptonal activity of NF-κB by blocking phosphorylation of p65/RelA at the Ser 536 residue. These findings suggest that [6]-gingerol exerts an anti-tumor promotional activity through inhibition of the p38 MAPK-NF-κB signaling cascade in mouse skin.

[PC1-23] [2003-10-10 09:00 - 13:00 / Grand Ballroom Pre-function]

Apicidin-induced gelsolin expression via Sp1 sites is mediated by PKC signaling

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Gelsolin, a actin binding protein, has been demonstrated to be involved in controlling cell morphology, motility, signaling, and apoptosis. It's expression is frequently downregulated in cervix cancer and several types of different human cancers indicating the role of gesolin in suppression of tumorigenicity. Apicidin, a novel histone deacetylase inhibitor, has been shown to cause growth arrest and morphological change of cancer cells, resulting from the alternation of protein expression, such as $p21^{WAF1/Cip1}$ and gelsolin. However, the molecular mechanism of apicidin induction of gelsolin remains to be elucidated. In this study, we investigated the molecular mechanism of gelsolin expression by apicidin. Treatment of HeLa cells with mithramycin, which has been demonstrated to inhibit the binding of Sp1 family transcription factors to genes containing G+C-rich promoters, led to the downregulation of gelsolin expression by apicidin indicating that Sp1 family transcription factors might mediate apicidin induction of gelsolin. In addition, inhibitor study using different types of well known specific kinase inhibitors revealed that apicidin induction of gelsolin expression was inhibited by PKC inhibitor calphostin C but not by other kinase inhibitors. similarly, PKCe dominant-negative mutant also decreased the level of gelsolin protein induced by apicidin. In summary, Sp1 transcription factors is responsible for apicidin induction of gelsolin and this transcriptional activation might be mediated by protein kinase C.

[PC1-24] [2003-10-10 09:00 - 13:00 / Grand Ballroom Pre-function]

Characterization of Acharan Sulfate Binding Proteins in Murine Lewis Lung Carcinoma Cell

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We have focused on various biological activities of acharan sulfate (AS) isolated from the giant African snail Achatina fulica. In a previous study, AS showed antiangiogenic and immunomodulating activity. We also investigated antitumor activity of AS. In vitro AS had no cytotoxicity within 0 to 200 ug/ml in tumor cells such as Lewis lung carcinoma(LLC) , KM1214 (human colon cancer cell) and Caki-1 (human kidney cancer cell) by both MTT and SRB assay. In vivo AS was used to treat C57BL/6 mice bearing LLC by subscutaneous injection. On day 21st, tumor tissues were removed and weighed. The tumor growth was inhibited by 37% at

the dose of 30 mg/kg, compared with the control. To confirm the localization of AS in tumor tissues, paraffin sections were prepared after 4% formaldehyde fixation. The fixed tissues were stained by alcian blue-periodic acid-Schiff's reagent. After subscutaneous injection, we found that AS was mainly localized on the outer membrane of tissues. Based on the fact, we performed an in vitro binding assay between AS and LLC by varying the incubation time and concentrations. The binding to cells was markedly increased when 50 ug/ml of the sample was incubated at for 5 h. Then, LLC surface proteins were biotinylated to identify the binding proteins to acharan sulfate. The biotinylated cells were lysed and collections were fractionated on AS affinity column with a stepwise salt gradient (0, 0.1, 0.3, 0.5, 0.7, 1.0, and 2 M). Each fraction was analyzed by SDS-PAGE and Western blotting. The blots were stained with a horseradish peroxidase(HRP)-conjugated streptoavidin and o-phenylenediamine. We focused on the proteins eluted at 0.7M and 1M NaCl, of which the molecular weights are approximately 92,000 and 118,000 Da, respectively. We speculate that AS binds tumor cell surface proteins that are related to the inhibition of tumor growth.

[PC1-25] [2003-10-10 09:00 - 13:00 / Grand Ballroom Pre-function]

Polyunsaturated fatty acids regulate APP metabolism.

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Polyunsaturated fatty acids (PUFAs) play many important physiological roles on cellular process through the regulations of intracellular signaling. Recent clinical studies suggest that PUFAs such as n-3 fatty acids (docosahexaenoic acid, 22:6 and a-lnolenic acid, 18:3) may reduce the risk of incident Alzheimer's disease (AD). And also the reports regarding the decrease of n-3 fatty acids in AD brain support the correlation between PUFAs and AD. AD is a neurodegenerative disorder with pathological hallmarks of amyloid plaques and neurofibrillary tangles. It is recognized that β-amyloid is closely associated with the etiology of AD. β-Amyloid and its co-metabolite APPβ are produced from amyloid precursor protein (APP) by the actions of β- and γ- secretase (amyloidogenic pathway). In addition, APP is also metabolized to p3 and APPα by the actions of α- and γ-secretase (non-amyloidogenic pathway). Here we tested whether different PUFAs (docosahexaenoic, palmitoleic, oleic, linoleic, linolenic, erucic, arachidonic, elaidic, nervonic and petroselinin acid) affect on APP metabolism using APP and β- secretase overexpressing HEK293 cells. The levels of sAPPα, sAPPβ, holo APP and β-secretase were measured and compared with each other.

[PC1-26] [2003-10-10 09:00 - 13:00 / Grand Ballroom Pre-function]

Tyrosinase Inhibitory Prenylated Flavonoids from Sophora flavescens

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For the purpose of the development of a skin-whitening agent, Sophora flavescens was evaluated for tyrosinase inhibitory activity and its active principles were identified followed activity-guided isolation. The ethanol extract and dichloromethane fraction from S. flavescens showed significant inhibition of mushroom tyrosinase. From the dichloromethane fraction, three known prenylated flavonoids, sophoraflavanone G, kuraridin, and kurarinone, were isolated. Compared with kojic acid (IC_{50}=20.5 μM), these compounds possessed more potent tyrosinase inhibitory activity. The IC_{50} values were 6.6, 0.6, and 6.2 μM for sophoraflavanone G, kuraridin, and kurarinone, respectively.

[PC1-27] [2003-10-10 09:00 - 13:00 / Grand Ballroom Pre-function]

Aromatic diamine JSH-21 inhibits LPS-induced NO production by targeting NF-kB