Tyrosine kinase inhibitors reverse lawsone methyl ether stimulation of renal dipeptidase release but not of alkaline phosphatase release.

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Lawsone methyl ether (LME, 2-methoxy-1,4-naphthoquinone) is a natural compound found in balsaminaceae. In this study the effect of LME on the release of renal dipeptidase (RDPase) and alkaline phosphatase (APase) known as glycosylphosphatidylinositol (GPI) anchored proteins was examined from the renal proximal tubules. Compared with control, LME (0.5mM) increased RDPase release (218%) and APase release (135%). The increase of RDPase release by LME showed concentration-dependent effect but the release pattern of APase did not. It was also confirmed by time-dependent manner. Signaling via several GPI anchored proteins is known to be mediated mostly via cytoplasmic molecules such as protein tyrosine kinases or trimeric G-protein. Therefore we investigated that the influence of LME might involve intracellular phosphorylation using genistein and herbimycin A, tyrosine kinase inhibitors. Genistein and herbimycin A treatment completely abolished the stimulatory effect of LME on RDPase release. On the contrary, both of tyrosine kinase inhibitors elevated the release of alkaline phosphatase in comparison with the group of LME control. Different pathways are likely to regulate the effect of LME on the RDPase and APase release. LME stimulation of RDPase, but not APase, may involve tyrosine phosphorylation signaling.

[PC1-29] [10/17/2002 (Thr) 13:30 - 16:30 / Hall C]

The Lipidperoxidative effect of Houttuynia cordata Thunb & Saururus chinensis

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Houttuynia cordata Thunb is a traditional medicine which has been used as antidote and antiphlogistic agent. Saururus chinensis is a perennial herb which cultivated as medicinal and decorative use, the aerial part of which have been used for the treatment of edema, jaundice and gonorrhoea in Korean folk medicine.
The lipid peroxidation inhibition effects of Houttuynia cordata Thunb, Saururus chinensis Leaf, H. cordata, S. chinensis Root and H. cordata, S. chinensis Fermentation were investigated in the levels of liver tissue total homogenates and serum of SD-rats intoxicated with carbon tetrachloride(CCl4). The rats were intraperitoneally given Houttuynia cordata Thunb and Saururus chinensis at dose of 100mg/kg daily for two weeks. Aspartate aminotransferase(AST), Alanine aminotransferase(ALT), Total cholesterol, HDL, LDL-cholesterol, Total lipid, Triglyceride were determined in serum. MDA levels were determined in the liver. The results showed that Houttuynia cordata Thunb and Saururus chinensis inhibited lipid peroxidation.

[PC1-30] [10/17/2002 (Thr) 13:30 - 16:30 / Hall C]

Curcumin Inhibits Phorbol Ester-induced Expression of Cyclooxygenase-2 In Vivo through Suppression of Extracelluar Signal-regulated Kinase (ERK)1/2 and NF-κB in Mouse Skin

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Curcumin derived from turmeric (*Curcuma longa* L., Zingiberaceae) has been shown to possess marked chemopreventive activities, but the underlying molecular mechanisms remain unclear. In the present work, curcumin was found to inhibit 12-*O*-tetradecanoylphorbol-13-acetate (TPA)-induced expression of cyclooxygenase-2 (COX-2) in female ICR mouse skin as determined by Western and Northern blot analysis as well as immunohistochemical staining. Curcumin treatment attenuated TPA-stimulated epidermal NF-κB activation, which was associated with its blockade of degradation and phosphorylation of the inhibitory protein IκBα and also of subsequent translocation of the p65 subunit to nucleus. Curcumin also inhibited activation of ERK1/2 and p38 MAP kinase in mouse skin. In this study, we further examined the roles of p38 and ERK in TPA-

induced NF-κB activation. The MEK1/2 inhibitor U0126 strongly inhibited NF-κB activation through blockade of Iκ Bα phosphorylation, while p38 inhibitor SB203580 did not much influence TPA-induced NF-κB activation in mouse skin. Taken together, suppression of TPA-induced COX-2 expression by blocking activation of ERK and NF-κB may account for molecular mechanisms by which curcumin exerts anti-tumor promoting effects on mouse skin tumorigenesis.

[PC1-31] [10/17/2002 (Thr) 13:30 ~ 16:30 / Hall C]

Proteome Analysis of Apicidin-Treated Human Cervix Cancer Cells

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Apicidin[cyclo(N-O-methyl-L-tryptophanyl-L-isoleucinyl-D-pipecolinyl-L-2-amino-8-oxodecano y)], a 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 p21WAF1/Cip1 and gelsolin. However, proteome of altered by apicidin are poorly studied. In this study, we used a functional proteomics approach to identify the proteome altered by apicidin in HeLa cells at 24hr post-treatment. To identify the proteome altered by apicidin, we used two-dimensional electrophoresis and MALDI-TOF mass spectrometry; We were able to resolve more than 1000 protein spots each in both treated and untreated HeLa cells. We found here that cyclophilin I was decreased by *apicidin treatment. Cyclophilin I have been shown to process peptidyl-prolyl cis-trans isomerase activity*, which is thought to contribute to the proposed role of cyclophilin I as mediator of protein folding and as chaperones. Also Hsp27 has shown to be modified by apicidin treatment, e.g. phosphorylation or acetylation. This modification might be attributable to the morphological change by apicidin, because Hsp27 phosphorylation has been considered to be closely involved in actin-cytoskeleton rearrangement. These results suggest that apicidin may affect the function of molecular chaperones, and the elucidation of possible role of these proteins is our current subject.

[PC1-32] [10/17/2002 (Thr) 13:30 ~ 16:30 / Hall C]

Differential involovement of JNK in apicidin-induced apoptosis.

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We previously reported that apicidin induces apoptosis through selective induction of Fas/Fas ligand, resulting in the release of cytochrome C from mitochondria to the cytosol and subsequent activation of caspase-9 and ?. However, we observed that apicidin did not induce the apoptosis in a specific cell line, such as HeLa, which was characterized by nuclear DNA fragmentation. On the basis of these facts, we tested whether JNK activation is involved in cell death induced by apicidin. JNK signaling pathway might be required for the apicidin induction of apoptosis in Jurkat cells but not HeLa cells, because specific inhibition of JNK with SD600125 and dominant negative JNK significantly inhibited PARP cleavage in Jurkat cell, but not HeLa cell. Furthermore, we observed the difference in constantly expressed level of Hsp70, which acts as an anti-apoptotic chaperone through the inhibition of JNK activity via physical interaction, suggesting that this difference might be contributable to the decision between apoptosis and survival in response to apicidin. Therefore, we will attempt to elucidate the possible role of Hsp70 using a specific down regulation with antisense oligonucleotide against Hsp70 in HeLa cell and overexpression of Hsp70 in Jurkat cell, respectively

[PC1-33] [10/17/2002 (Thr) 13:30 ~ 16:30 / Hall C]

Apicidin Induction of cyclin E might be mediated by Sp1 Transcription Factor

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