[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

Eun Dae-wook°, Cho Eun-Jung, Lee Hoi Young, Hong Sungyoul, Han Jeung-Whan, Lee Hyang Woo
Lab. of Biochem. & Mol. Biol., College of Pharmacy, Sungkyunkwan University, College of Medicine, Konyang University, Department of Genetic Engineering, College of Life Sci. & Tech., Sungkyunkwan University

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

Joo Eun Ji°, Hahn Bum Soo, Kim Yeong Shik
Natioral Product Research Institute, Seoul National University and National Institute of Agricultural Biotechnology

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