[PC1-18] [04/18/2003 (Fri) 09:30 - 12:30 / Hall P]

Suppressoin of NF-κB signaling pathways by ergolide in HeLa cells

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In previous study, we investigated the mechanism of suppression of inducible nitric oxide synthase (iNOS) and cyclo-oxygenase-2 (COX-2) by ergolide, sesquiterpene lactone from *Inula Britannica*. In this study, the suppression of iNOS and COX-2 by ergolide might be attributed to selective inhibition of NF-κB signaling pathways. Here, we investigated the suppression mechanism of NF-κB signaling pathways by ergolide in TPA-stimulated HeLa cells. We showed that ergolide inhibited NF-κB promoter activity. This effect was accompanied by the parallel reduction of NF-κB DNA binding activity as well as nuclear translocation of subunit p65 of NF-κ B. In addition, ergolide decreased the degradation of IκB and phosphorylation of IκB in TPA-stimulated HeLa cells. Ergolide also inhibited protein levels of phospho-IKK in TPA stimulated-HeLa cells. These results indicate that the inhibition of NF-κB signaling pathways may be associated with the inhibition of IKK activity. Taken together, the results suggest that suppression of NF-κB signaling pathways is responsible for the anti-inflammatory activity of ergolide through inhibition of IKK activity, which play important roles in inflammatory signaling pathways

[PC1-19] [04/18/2003 (Fri) 09:30 - 12:30 / Hall P]

Why is β-ketoacyl-ACP synthase II (FabF) is toxic in *E. coli* fatty acid biosynthesis ?

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In the type II system, there are two elongation enzymes in *E. coli*, FabB is well-known to its ability to elongate *cis*-3-decenoly-ACP (C10:1) in unsaturated fatty acid synthesis, whereas FabF is important for the thermal regulation of fatty acid composition by its ability to elongate palmitoleic acid to vaccenic acid, based on their genetic mutation anaylsis. Radiochemical enzyme assay was performed using myristoyl-ACP as a substrate, which is known for general substrate of FabB and FabF. The specific activity of FabB (139.7 ± 3.9 pmole/min/mg) was about 10-fold less than that of FabF (2032 ± 39.4 pmole/min/mg). Both FabF and FabB made triacetic acid lactone (TAL) from malonyl-ACP, and FabF was 10-fold more active than FabB. Within the cell, FabF could effectively convert malonyl-ACP to TAL instead of fatty acid biosynthesis. It could be an explanation why FabF is toxic when it is overexpressed. These data demonstrated that FabF can function in unsaturated fatty acid synthesis like FabB, and in the regulation of malonyl-CoA level by conversion malonyl-ACP to TAL.

[PC1-20] [04/18/2003 (Fri) 09:30 - 12:30 / Hall P]

Purification and Partial Characterization of a Lectin with Potent Immunomodulatory Activity from the Mushroom *Fomitella fraxinea*

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A novel lectin has been purified from the fruiting bodies of the mushroom, *Fomitella fraxinea*, which belongs to bracket fungi by a combination of ion-exchange chromatography on DEAE-cellulose and gel filtration chromatography on Sephacryl S-200 HR. The lectin, designated as FFrL, was a homotetrameric protein with a molecular weight of 50 kDa as demonstrated by SDS-PAGE (sodium dodecyl sulfate-polyacrylamide gel electrophoresis) and MALDI-TOF-MS (matrix assisted UV laser desorption/ionization time-of-flight mass spectrometry). When amino acid composition was analyzed, FFrL was found to be rich in acidic amino acids. FFrL agglutinated various cells including the erythrocytes of mouse and rat, the thymocytes of mouse, RAW 264.7 and sarcoma 180 murine cell lines, THP-1 and HeLa human cell lines but did not agglutinate human erythrocytes. D(+) fructose and methyl-D mannopyranoside inhibited hemagglutinating activity of FFrL. The immunomodulatory activity of FFrL was demonstrated by its potent proliferative activity toward murine splenic lymphocytes. The mitogenic activities of FFrL determined by flow cytometric analysis and XTT assay were more potent than those of Con A.

[PC1-21] [04/18/2003 (Fri) 09:30 - 12:30 / Hall P]

Chemopreventive Allylthiopyridazines, K compounds, Inhibit Invasion, Migration and Angiogenesis in SK-Hep-1 Hepatocarcinoma Cells Possibly via MMP-2 Downregulation

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Dietary organosulfur compounds have been shown to inhibit the proliferation of tumor cells. Synthetic sulfur-containing compounds including oltipraz exert chemopreventive and hepatoprotective effects. We previously showed that synthetic allylthiopyridazine derivatives designated as K compounds induced apoptosis in SK-Hep-1 hepatocarcinoma cells (Eur. J. Cancer: 37, 2104-10, 2001). In the present study, we investigated the effects of the K compounds on invasive and migrative properties of SK-Hep-1 cells. Here, we show that 3-methoxy-6-allylthiopyridazine (K6) and 3-propoxy-6-allylthiopyridazine (K17) efficiently inhibit SK-Hep-1 cell invasion and migration. A prominent downregulation of matrix metalloproteinase (MMP)-2 was observed, suggesting that the compounds inhibit invasion and migration possibly through a specific downregulation of MMP-2. Since hepatocellular carcinoma is characterized as a hypervascular tumor, we further investigated the possible inhibitory effect of the K compounds on angiogenesis. The compounds exerted anti-angiogenic activity as evidenced by tube formation of human umbilical vein endothelial cells (HUVECs). Taken in conjunction with the fact that hepatocellular carcinoma is one of the most lethal malignancies and there is no effective preventive measure to date, our findings may be critical to the chemopreventive potential of the compounds for hepatocellular carcinoma.

[PC1-22] [04/18/2003 (Fri) 09:30 - 12:30 / Hall P]

Characterization of 2-hydroxymuconic semialdehyde dehydrogenase from Burkholderia cepacia G4

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