Cancer is multifaceted disease that presents many challenges to clinicians and cancer researchers searching for more effective ways to combat its often devastating effects. Among the central challenges of this disease, are the identification of markers for improved diagnosis and classification of tumors, and the definition of targets for more effective therapeutic measures. The objective of this study is to identify potential biomarkers for the early detection of gastric cancer in serum. Sera from normal volunteers and patients with gastric cancer were examined by two-dimensional electrophoresis. In this display proteomics technique the serum proteins are first separated by isoelectric point followed by polyacrylamide gel electrophoresis. Of the several consistent changes observed in the cancer sera, the most striking was a large increase in a protein level of a molecular mass of ~45 kDa. To identify this protein, database accessible via the internet, such as the SWISS-2DPAGE database and HSC-2DPAGE was utilized. The protein was identified as haptoglobin, which was further confirmed by matrix-assisted laser desorption/ionization-time-of-flight (MALDI-TOF) analysis of the spot and Western blotting analysis with the anti-haptoglobin antibody. Of interest, haptoglobin has been previously suggested to be elevated in ovarian cancer patients. More detailed studies are underway to examine its relevance to the cancer and to validate its practical application as a biomarker for early detection of gastric cancer.

[PA4-19] [10/18/2002 (Fri) 09:30 - 12:30 / Hall C]

COX-inhibitors down-regulate TCDD-induced cyp1a1 activity in C57BL/6 mouse and Hepa- I cells.

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In order to understand the mechanism of action of TCDD, we have examined the effect of COX-inhibitors on cyp1a1 activity. We observed the effect of COX-inhibitor on EROD activity in C57BL/6 mouse in vovo. And we also evaluated the effect of COX-inhibitors on cyp1a1 mRNA, mouse cyp1a1 promoter activity and EROD activity in Hepa cell.
When Aspirin were pretreated with 3MC in vivo, the EROD activity that was stimulated by 3MC was inhibited. And Pretreatment of Aspirin, Celecoxib, Nimesulide and other several Cox-inhibitors in vitro, inhibited the TCDD stimulated EROD activity and Luciferase acitivity. In case of cyp1a1 mRNA level, Nimesulide and SB100 were able to decrease cyp1a1 mRNA that was stimulated by TCDD, but other tested COX-inhibitors were not decrease. We don't know this different result exactly.
For the action of Cox-inhibitors on the Cyp1a1, it seems to be important to do pretreatment of these chemicals as apposed to TCDD. In this study, thus, we have suggested that COX-inhibitors such as aspirin, celecoxib, Nimesulide and other several Cox-inhibitors decrease the TCDD induced Cyp1a1.

[PA4-20] [10/18/2002 (Fri) 09:30 - 12:30 / Hall C]

Effects of pyrethroid compounds on alkaline phosphatase activity in estrogen receptor positive human breast cancer cells

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Pyrethroids are one of the most commonly used insecticides in worldwide, but it remains unclear whether pyrethroid compounds possess endocrine disrupting activity or not. T47D cells, an estrogen receptor positive human breast cancer cell line, is known to induce alkaline phosphatase (AlkP) only in response to progestins. Because the action of estrogen may be changed by the action of progestins (Kraus et al, 1995), it is important to examine the potential to produce progestin-mediated effects for determining endocrine disrupting activity of chemicals (DiLorenzo et al, 1991). In this study we investigated the progestagenic/ antiprogestagenic effects of pyrethroid compounds using AlkP activity assay and expression of progesterone receptor in T47D cells. After a 48 hr exposure period, progesterone significantly increased AlkP activity in a dose-dependent manner, and maximum activity was observed at the level of 10^{-8}M. However pyrethroid compounds (bioallethrin, cypermethrin, deltamethrin, fenvalerate, permethrin, sumithrin, and tetramethrin) showed no increase in AlkP activity at any concentration. Among seven pyrethroid compounds fenvalerate and permethrin significantly decreased the progesterone-induced AlkP activity, but only at a relatively high concentration (10^{-5}M). The present study suggests that some pyrethroid compounds (fenvalerate and permethrin) have weak endocrine disrupting effects

via progesterone related mechanism.
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[PA4-21] [10/18/2002 (Fri) 09:30 - 12:30 / Hall C]

Estrogenic Activities of Pyrethroid Compounds in MCF-7 BUS cells

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Pyrethroids are extensively used as insecticide in agriculture and home. Several studies have reported that pyrethroids are relatively safe to humans and wildlife. However, some studies have suggested that pyrethroids possess estrogen-like activity. Thus, the purpose of this study was to investigate the effects of pyrethroid compounds on cell proliferation, and expression of ERs and pS2 using estrogen receptor positive human breast cancer cell line (MCF-7 BUS cells). Seven pyrethroids (bioallethrin, cypermethrin, deltamethrin, fenvalerate, permethrin, sumithrin, and tetramethrin) were tested with 17β-estradiol as a positive control. Among the pyrethroid compounds tested, only sumithrin increased the MCF-7 BUS cell proliferation in a dose-dependent manner, maximum induction of cell proliferation was observed at dose of 10^{-5}M. In ER expression, 17β-estradiol (10^{-10}M) decreased the level of cytosolic ERα and ERβ protein expression compared with the vehicle control, and sumithrin significantly decreased the expression of ERα and ERβ protein at high concentrations, $10^{-7} \sim 10^{-5}$M, in a dose-dependent manner. Similarly to 17β-estradiol, sumithrin dose-dependently increased pS2 mRNA expression. The other six test compounds used in the present study did not show any estrogenic effect at all concentrations (from 10^{-11} to 10^{-5}M). These findings suggest that sumithrin could be considered to induce weak estrogenic activity via ER related pathways.
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[PA4-22] [10/18/2002 (Fri) 09:30 - 12:30 / Hall C]

Down-regulation of inducible nitric oxide synthase and tumor necrosis factor-a expression by Bisphenol A via nuclear factor-kB inactivation in macrophages

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Bisphenol A [BPA, 2,2-bis(4-hydroxyphenyl)propane] is reported to have estrogenic activity; however, its influence on cytokine production or immune system function remains unclear. In this study, we investigated the effects of BPA on the production of nitric oxide (NO) and tumor necrosis factor-a (TNF-a), and on the level of inducible nitric oxide synthase (iNOS) and TNF-a gene expression in mouse macrophages. BPA alone did not affect NO or TNF-a production. In contrast, BPA inhibited lipopolysaccharide (LPS)-induced NO and TNF-a production, and the levels of iNOS and TNF-a mRNA in a dose-dependent manner. Treatment with ICI 182.780, an estrogen-receptor antagonist, inhibited the suppressive effects of BPA. Transient expression and electrophoretic mobility shift assays with NF-kB binding sites revealed that BPA reduced the levels of the LPS-induced NF-kB transcription factor complex. These results demonstrate that BPA may affect the regulation of the immune system function by reducing NO and TNF-a production via the inhibition of NF-kB transactivation mediated through the estradiol receptor.

[PA4-23] [10/18/2002 (Fri) 09:30 - 12:30 / Hall C]

Aluminium increase Iron uptake into Glial cells

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