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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In the brain, glial cells serve in the role to sequester metal from the neural microenvironment and therefore play an important role as a cellular deposition site. The central nervous system is highly vulnerable to oxidative stress, and free iron can stimulate oxidative stress by the Fenton reaction. Aluminum may upregulates the transferrin-independent iron uptake system and stimulate oxidative stress. Nramp2, also known as DMT1, is a 12-transmembrane(TM) domain protein responsible for dietary iron uptake as well as metal ions such as iron, lead, manganese, zinc, copper, and cobalt. In regulation of metals levels in the brain, the interaction between metals is as yet unknown. The molecular mechanism of upreglation of iron uptake by aluminum is also unknown. We investigated whether aluminum influence on uptake of lead and iron into astrocytes(SV-FHA cells) and V373 cells. We did also whether DMT1 was influenced by aluminum. SV-FHA cells were cultured in high-glucose DMEM and V373 cells cultured low-glucose DMEM. Cells were treated with Aluminium chloride. Lead uptake were done in incubation condition of pH 5.5 and 7.4, as the previous used method. Iron uptake was done in 20mM HEPES buffer containing serum-free, 6μM NTA, 2mM CaCl2, 2mM MgCl2, 15μM Ascorbic acid, and 1.5μM FeCl3. Lead uptake into astrocytes increased concentration-dependently by aluminum treatment, but uptake into V373 cells decreased. Iron uptake increased time- and concentration-dependently by aluminum treatment, and the effects of aluminum were blocked by citrate. The effects of aluminium on lead and iron uptake were not related with DMT1.

[PA4-24] [10/18/2002 (Fri) 09:30 - 12:30 / Hall C]

The effects of estradiol and its metabolites on the regulation of CYP1A1 expression.

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The effects of estradiol and its metabolites on the regulation of CYP1A1 expression.
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2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD) is the most potent halogenated aromatic hydrocarbon congener that induces expression of several genes including CYP1A1. Exposure to TCDD results in many toxic actions such as carcinogenesis, hepatotoxicity, immune suppression, and reproductive and developmental toxicity. Dramatic differences in dioxin toxicity have been observed between the sexes of some animal species, suggesting hormonal modulation of dioxin action. Many studies have been reported and propose several mechanisms of anti-estrogenic effects of TCDD. In contrast, the effect of estrogen on the regulation of CYP1A1 are not clear at present. There are several reports showing conflicting results. It seems that induction/inhibition of CYP1A1 may be dependent on cell-type and concentration.
The purpose of this study was to investigate the regulation of TCDD-induced CYP1A1 gene expression by estradiol and its metabolites. We examined whether estradiol and its metabolites altered TCDD-mediated induction of CYP1A1 enzyme activity. 17β estradiol and 16α estriol at non cytotoxic concentrations caused a significant concentration dependent decline of TCDD-induced EROD activity. To determine whether reduced EROD activity reflected altered CYP1A1 mRNA expression, we measured CYP1A1 mRNA level by RT-PCR. And to examine whether estradiol and its metabolites have effects on TCDD-induced CYP1A1 gene expression at the transcription level, we also performed transient transfection with an AhR responsive reporter plasmid containing the 5' flanking region of the human CYP1A1 gene to examine whether estradiol and its metabolites have effects on TCDD-induced CYP1A1 gene expression at the transcription level.

[PA4-25] [10/18/2002 (Fri) 09:30 - 12:30 / Hall C]

Role of phospholipid metabolism in Methylmercury-induced Cytotoxicity

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Methylmercury (MeHg; CH3HgCl) is a ubiquitous environmental toxicant that readily bioaccumulates in aquatic foodchains. This toxicant is most highly exposed to humans through the ingestion of contaminated food, and