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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