of TCDD and o.p'-DDT in a dose dependent manner. TCDD-induced P450 1A1 mRNA level was also markedly suppressed in the concomitant treatment of TCDD and op'-DDT. Transient transfection assay using dioxin-response element (DRE)-linked luciferase revealed that o.p'-DDT reduced transformation of the aryl hydrocarbons (Ah) receptor to a form capable of specifically binding to the DRE sequence in the promoter of the P450 1A1. These results suggest the down regulation of the P450 1A1 gene expression by op'-DDT in Hepa-1c1c7 cells might be antagonism of the DRE binding potential of nuclear Ah receptor [This work was supported by KFDA Grant and RCPM from KOSEF].

[PA4-25] [04/20/2001 (Fri) 10:30 - 11:30 / Hall 4]

Species variation of neuropathy target esterase and its application to the neurotoxicity evaluation of pesticides

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Neuropathy target esterase (NTE) is an integral membrane protein in vertebrate neurons and plays an important role in neural development. Inhibition of more than 75% in NTE activity is associated with organophosphate-induced delayed polyneuropathy that is characterized by paralysis of the lower limbs and degeneration of long axons in the central and peripheral nervous systems. NTE activity was compared in three different species of hens, rats and mice and was applied to the neurotoxic evaluation of pesticides. NTE activity was determined by measurement of phenyl valerate esterase activity that is resistant to inhibition by paraoxon and sensitive to inhibition by mipafox. Tissue homogenates prepared from dissected brain regions in the three species were preincubated with inhibitors prior to phenyl valerate addition. Hydrolysis was stopped by protein denaturation and the production of the phenol content was spectrophotometrically determined. NTE activity was the highest in the cerebellum (2.10 ± 0.05 μmole/min/g tissue) in hens among three species, and was in significant decreasing order of whole brain (the entire brain regions except for the cerebellum and brainstem)> brainstem> spinal cord. In rats, NTE activity is lower than that in hens. Mice was the lowest in the activity among three species. This NTE activity was applied to pesticides that are not reported to NTE activity for neurotoxic evaluation.

[PA4-26] [04/20/2001 (Fri) 10:30 - 11:30 / Hall 4]

Environmental Estrogen effects on the TCDD stimulated CYP1A1 expression

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Environmental estrogens are studied recently in order to understand the health effects of them and the mechanism of action. CYP1A1 has been well known to be regulated by PAHs such as 3MC and TCDD. There are some possibility of crosstalk between TCDD and estrogen in terms of CYP1A1 expression. We have studied the two-way crosstalk between the arylhydrocarbon receptor (AhR) and estrogen receptor (ER) signaling pathways.
In our previous data, 17β-estradiol (E2) significantly inhibited TCDD-induced CYP1A1 gene expression and this inhibitory effect was partially recovered by concomitant treatment of tamoxifen. Like E2, 4-nonylphenol (NP), octylphenol (OP) and bisphenol A (BPA), known as 'Endocrine Disruptors', showed the estrogenic activities. In this study, we examined the effects of these chemicals on TCDD-induced CYP1A1 gene expression and CYP1A1 enzyme activity. And we investigated if their effects were mediated by ER signaling pathway. [This study has been supported by G7 from ME and HMP-98-B-3-0013]