macrophages obtained from mice exposed to BPA at high dose. Expression intensities of B7-1 and B7-2 on macrophages obtained from mice exposed to BPA at high dose were decreased. In LPS-stimulated macrophages obtained from BPA-untreated mice, NO and TNF-α production were dose-dependently decreased to 53.1% and 23.3% of control with 100μM BPA in vitro, respectively. These results demonstrate that BPA may be related to macrophage activation.

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

STUDY OF BISPHENOL A EFECTS ON THE MONKEY DRUG METABOLISNG ENZYMES VIA RT-PCR

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In order to understand the mechnism of the regulation of drug metabolizing enzyme gene expression, we have studied the induction of CYP and GST enzymes in monkey that is treated with Bisphenol A, 3-methylcholanthrene (3MC) and dibutylphthalate(DBP). The mRNA levels were measured by RT-PCR and enzymatic activity was measured via EROD. in brain, liver, and intestine by RT-PCR. In the case of adult monkey, the 3MC treatment induced CYP 1A1 mRNA in brain by 3.5-fold, and CYP 1A1 mRNA in intestine by 2.5-fold, CYP 1A1 mRNA in the liver by 7-fold respectively. And mRNA levels of GST α, μ, π were also induced by 1.5-fold, 2.3-fold, 3-fold respectively. In the case of fetus monkey, the basal levels of fetus CYP 1A1 mRNA and GSTs mRNAs were very low in comparion to adult monkey and as the age of monkey increased, the basal levels of CYP 1A1 mRNA and GSTs mRNAs were also increased. Bisphenol A and DBP treatment showed minimal induction of CYP1A1 mRNA in brain and liver and also induced GST mRNA by 1.5- to 2.5-fold in brain and intestine. [This study was supported from the HMP-98-B-3-0015]

[PA4-21] [04/20/2001 (Fri) 10:30 - 11:30 / Hall 4]

Telomerase activity is up-regulated with imperfect palindromic estrogen-response element (ERE) in human telomerase reverse transcriptase subunit (hTERT) promoter by the treatment with endosulfan

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Endosulan is a member of the organochlorine class of pesticides. Endocrine disruptors in the environment such as endosulfan may be adversely affecting the health of human and wildlife. We examined the effects of endosulfan on telomerase activity. Telomerase activity in estrogen receptor-positive MCF-7 cells was up-regulated by the treatment with endosulfan. This activation accompanied up-regulation of the telomerase catalytic subunit, hTERT mRNA. Transient expression assays using CAT reporter plasmids containing various fragments of hTERT promoter showed that this imperfect palindromic estrogen-responsive element is responsible for transcriptional activation by ligand-activated ER. These findings may help elucidate the mechanisms of endocrine disruptors.

[PA4-22] [04/20/2001 (Fri) 10:30 - 11:30 / Hall 4]

In vitro approach to investigating the free radical generation of endocrine disruptor

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We investigated Free radical generation of endocrine disruptor,
Bisphenol A and Alkyl esters of phthalic acid using lipid peroxidation, enzyme assay, MTT assay. Bisphenol A generated free radical, increased, lipid peroxidation, damaged antioxidant system and SK-MEL-28 Cell Line viability was dose-dependently increased. Also alkyl ester of phthalic acid generated free radical but slightly. The generation of free radical induced by endocrine disruptor was inhibited by antioxidant and free radical scavenger. The result of the study are demonstration on free radical induced by endocrine disruptor and this result may be useful for evaluating toxic effects of endocrin disruptor

[PA4-23] [04/20/2001 (Fri) 10:30 - 11:30 / Hall 4]

THE ROLES OF ATP AND CALCIUM IN MORPHOLOGY CHANGES AND CYTOTOXICITY INDUCED BY BENZOQUINONE IN PLATELETS

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To understand mechanism of benzoquinone-induced cytotoxicity, the roles of ATP and calcium in platelet toxicity and morphology changes was investigated. Using scanning electron microscopy, morphological changes to platelets following 1,4-benzoquinone exposure consisted of membrane blebbing at 5 min which was significantly different from shape changes (pseudopod formation) observed in response to physiological agonists. Benzoquinone-induced platelet membrane bleb formation was associated with rapid depletion of intracellular ATP and independent of presence of extracellular calcium. Benzoquinone-induced platelet lysis (LDH leakage) observed between 20-30 mins was dependent on extracellular calcium and associated with increased cytosolic calcium. Benzoquinone-induced cytotoxicity was inhibited by calmodulin antagonists, suggesting that calmodulin could play a major role in 1,4-benzoquinone toxicity via protease activation. These results suggested that the progression of events for quinone-induced cytotoxicity in platelets to be as follows: quinones deplete intracellular ATP; formation of blebs occurs; calcium homeostasis is disrupted, resulting activation of calmodulin-dependent proteases; irreversible cytotoxicity occurs.

[PA4-24] [04/20/2001 (Fri) 10:30 - 11:30 / Hall 4]

Suppression of cytochrome P450 1A1 in Mouse hepatoma Hepa-1c1c7 cells by o.p'-DDT

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Organo chlorine pesticides have received the most attention because of their persistence in the environment, ability to concentrate up the food chain, continued detection in the food supply and breast milk, and ability to be stored in the adipose tissue of animals and humans. In the present study we investigated the effect of op-DDT on TCDD-inducible Cytochrome (P450 1A1) gene expression in mouse hepatoma cell line Hepa-1c1c7 cells. Cultured mouse hepatoma Hepa-1c1c7 cells were treated with either o.p'-DDT or/and 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) or in combination to assess the role of o.p'-DDT in the process of P450 1A1 induction. TCDD-induced P450 1A1-specific 7-ethoxyresorufin O-deethylase (EROD) activity was markedly reduced in the concomitant treatment