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Recent industrial society has human widely exposed to PAHs that are comming from the incomplete combustion of organic material as widerspread environmetal contaminants. Biological activities of PAHs are not known although PAHs are considered as carcinogens. The mechanism of action of PAHs has been studied extensively, however it is not clear how PAHs turn on CYP1A1 in human breast cancer. Our labolatory have been studied the effect of PAHs in the human breast cancer cell MCF-7. In this study, we examined the ZR-75-1 human breast cancer cells as a new system to evaluate bioactivity of PAHs and to compare the PAH action with that of MCF-7 cells. ZR-75-1 human breast cancer cell line is response to estrogen and progesteron. We have been able to estabilish long term culture system of this cells then used for the study to the effect of 13 different PAHs and environmental samples. We demonstrate that PAHs induced the CYP1A1 promoter and 7-ethoxyresolufin O-deethylase(EROD) activity in a concentration-dependant manner. RT-PCR analysis indicated that PAHs significantly up-regulate the level of CYP1A1 mRNA. Some of PAHs showed stronger stimulatory effect on CYP1 gene expression than TCDD. Apparently, ZR-75-1 cells have Aryl hydrocarbon receptors, therefore it would be good experimental tool to study the cross-talk between PAHs and steroid actions.

[PA4-32] [04/17/2003 (Thr) 14:00 - 17:00 / Hall P]

Environmental endocrine disruptors and endometriosis

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Endometriosis is classically defined as the growth of endometrial glands and stroma at extra-uterine sites. Although it is a common gynecological problem accompanied by chronic pelvic pain, infertility, and adhesion formation, the etiology of this disease is unknown. Endometriosis pathogenesis may involve endocrine and immune dysregulation since uterine endometrial growth is regulated by sex hormone in concert with bioactive mediators produced by uterine immune and endocrine cells. thus, exposure to environmental toxicants disrupting endocrine and immune responses potentially affect the development and progression of endometriosis.
In this study, we attempted to identify the possible association between dioxin like compounds (such as TCDD, PCDDs, PCDFs, and PCBs) and the occurrence and severity of endometriosis using CALUX (Chemically Activated LUciferase eXpression) bioassay method. We analyzed the serum levels of dioxin like compounds in the endometriosis patients (n=46) and control patients with similar symptoms (n=14). Among them, adipose tissues of 10 cases were analyzed by high resolution GC/MS for validation of CALUX bioassay. The CALUX TEQs significantly correlated with the total TEQs determine by GC/MS (r2 = 0.96). So we demonstrated that CALUX bioassay is a rapid, sensitive and quantitative assay for biomonitoring of dioxin like compounds from small volume of blood. This study showed statistically significant association between exposure to dioxin like compounds and the occurrence of endometriosis ($p < 0.003$). The mean TEQ of control patient was 0.144 ㎍ TEQ/L and the mean TEQ of endometriosis patient was 0.321 ㎍ TEQ/L. After adjusting confounding factor, we found that the higher stage of the endometriosis, the higher level of CALUX TEQ. The TEQs of endometriosis I, II, III, and IV was 0.213 ㎍ TEQ/L, 0.284 ㎍ TEQ/L, 0.352 ㎍ TEQ/L, and 0.450 ㎍ TEQ/L, respectively.

[PA4-33] [04/17/2003 (Thr) 14:00 - 17:00 / Hall P]

The Inhibitory Effect of Zinc on the Cadmium-Induced Apoptosis in Human Breast

Cancer Cells

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Zinc is known to have an inhibitory effect on apoptosis and an antioxidative effect scavenging reactive oxygen species (ROS) under oxidative stress. We studied the influence of zinc on cadmium-induced apoptosis especially associated with ROS in MCF-7 human breast carcinoma cell line. For the determination of appropriate experimental concentration and time, we executed MTT [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide] assay and DNA fragmentation assay. MCF-7 cells exposed to various concentration of cadmium for 24h showed 50% cell viability at approximately 100mM. And the amount of DNA fragment significantly increased at 12h. To observe apoptosis features, we performed DNA fragmentation assay on 1.5% agarose gel, nuclei staining using DAPI (4',6-diamidino-2-phenylindole) and detection of caspase-9 protein expression by western blot. When we treated cadmium in MCF-7 cells, we observed significant nucleosomal DNA fragmentation, caspase-9 induction and an increase of apoptotic body at 12h. Positively, zinc inhibited DNA fragmentation, caspase-9 activation on cadmium-induced apoptosis. Also, we observed that cadmium (100mM, 12h) elevated peroxides level, which is thought as an apoptosis-inducing factor, and depleted antioxidative enzymes (SOD, CAT). As zinc came up to our expectations, it had ROS scavenging effect and could recover depletion of antioxidative enzymes. Cells co-treated with 100uM zinc and cadmium showed higher superoxide (SOD) level than control at 12h. Also, catalase (CAT) level was simlar to control level at 12h. These results suggest that zinc could inhibit cadmium-induced apoptosis triggered by ROS.

[PA4-34] [04/17/2003 (Thr) 14:00 - 17:00 / Hall P]

TERT mRNA expression is up-regulated in MCF-7 cells and mouse mammary gland organ culture (MMOC) system by endosulfan treatment

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Endosulfan is one of the organochlorine pesticides, well-known endocrine disruptors (EDs). Many EDs show the estrogenic effect. Estrogen is a group of hormones that play an important role in mammary gland function and implicated in mammary carcinogenesis. In the present study, using mouse mammary gland organ culture (MMOC) system, we studied the effects of endosulfan on nodule like alveolar lesion (NLAL) formation in the mouse mammary gland development. Additionally, we found that the telomerase catalytic subunit, TERT mRNA expression levels were increased in endosulfan-treated mammary glands in a dose-dependent manner. As it was reported that the telomerase could be activated by estrogen, we examined the effects of endosulfan on telomerase activity and found that telomerase activity in estrogen receptor-positive MCF-7 cells was up-regulated by endosulfan treatment. Moreover, this activation was accompanied by the up-regulation of TERT mRNA expression. Also, a transient expression assay using CAT reporter plasmids, which contain various fragments of TERT promoter, showed that this imperfect palindromic estrogen-responsive element is responsible for transcriptional activation by endosulfan. These results may help elucidate the endocrine disrupting mechanism of endosulfan.