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A adenovirus-mediated $p16^{INK4a}$(Ad5CMV-p16) tumor suppressor gene transfer to the non-small cell lung cancer cells resulted in significant inhibition of cancer cell growth (Anticancer Res., 1998, 18:3257-3261). For the safety evaluation of adenovirus-mediated gene transfer, we investigated gene expression after transduction of Ad5CMV-p16 gene in the p16 null A549, H460 non-small cell lung cancer cells. We compared the differential gene expressions in Ad5CMV-p16-treated cells with control cells by using the cDNA chip which carries 2400 genes related with signal transduction, cell cycle, and oncogenes. To detect any unexpected protein overexpression by transfection of Ad5CMV-p16 to the target cells, we also conducted 2D-electrophoresis. In this study, we found that several genes were up or down regulated by 2 fold or more. These results suggested that we have to consider the potential effects of the other gene expressions besides therapeutic gene on the host cells as a safety concerns.

[PA4-18] [04/20/2001 (Fri) 10:30 - 11:30 / Hall 4]

Monitoring Studies on Endocrine Disruptors(Cd, Pb, Hg) in Humans

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There has been a long-standing concern in the estimation of human exposure to endocrine disruptors particulary heavy metals like as Cd, Pb and Hg. If the placenta of pregnant woman can't work to block endocrine disruptors like as heavy metals, they can be transfered to the fetus and newborn baby. So it is very important to quantify the degree of exposure in biological samples of pregnant women.
This research was intended to study the monitoring of heavy metals(Cd, Pb, Hg) as endocrine disruptors in Korean pregnant women's biological samples like as blood, cord blood, placenta and colostrum.
This showed that the concentration of Cd is 1.26±0.59㎍/L, that of Pb is 33.56±14.58㎍/L, that of Hg is 6.05±18.14㎍/L in blood, the concentration of Cd is 0.38±0.32㎍/L, that of Pb is 25.73±15.40㎍/L, that of Hg is 3.95±2.24㎍/L in cord blood, the concentration of Cd is 73.85±63.35㎍/L, that of Pb is 22.01±9.95㎍/L, that of Hg is 31.62±20.20㎍/L in dried placenta, the concentration of Cd is 1.52± 2.13㎍/L, that of Pb is 7.65±15.49㎍/L, that of Hg is 21.09±13.80㎍/L in colostrum.

[PA4-19] [04/20/2001 (Fri) 10:30 - 11:30 / Hall 4]

Bispenol A-induced alternation of peritoneal macrophage activation in mice

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Bisphenol A(BPA), endocrine disruptor, is monomer used in manufacturing epoxy resins or polycarbonates, and can be occupationally or environmentally exposed to human. To investigate of immunomodulating effect on macrophage activation, female ICR mice were administered to BPA(p.o., 100mg/kg/day or 1000mg/kg/day for 30 days). Nitric oxide(NO) production was increased to 60.2% and tumor necrosis factor(TNF)-α production was decreased to 25.8% of control in LPS-stimulated

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