

acid treated hepatic microsomes, as determined by immunoblot analysis in a manner consistent with that of the enzyme activity levels. These results suggest that 18beta-glycyrrhetic acid may act as a more specific suppressor for P4502E1 than P4501A1 and P4502B1/2 [This work was supported by Korea Research Foundation Grant ( KRF-2000-041-F00314)].

[PA4-15] [ 04/20/2001 (Fri) 10:30 – 11:30 / Hall 4 ]

### The Inhibitory Effects of *Houttuynia cordata* Extracts against Cadmium induced Cytotoxicity (VII)

Lee JH, Jeong SI, Han DS1, Baek SH<sup>0</sup>

Department of Natural Products, Professional Graduate School of Oriental Medicine, and 1Department of Oral Anatomy, School of Dentistry, Wonkwang University.

This study was carried out to evaluate the cytotoxicity of cadmium on NIH 3T3 fibroblasts and to develop the antidote on NIH 3T3 fibroblasts which was damaged by Cd50 of cadmium. The antitoxic activity of *Houttuynia cordata* extract in NIH 3T3 fibroblasts was evaluated by MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl-2H-tetrazoliumbromide) and SRB (sulforhodamine B protein) assays. The light microscopic study was carried out to observe morphological changes of the treated cells. These results were obtained as follows: The concentration of 10–2 mg/ml of *Houttuynia cordata* extract shows significant antitoxic activity. The number of NIH 3T3 fibroblasts were antitoxic and tend to regenerate. These results suggest that the chloroform extract of *Houttuynia cordata* retains a potential antitoxic activity.

[PA4-16] [ 04/20/2001 (Fri) 10:30 – 11:30 / Hall 4 ]

### Activation of cPLA2 Leading to Increase in Glutathione and Downregulation of iNOS May Make LLCpk1 Cells Resist to TNF- $\alpha$ -induced Cell Death

Chin MR<sup>0</sup>, Chae GY, Kim DK

Dept. of Environmental & Health Chemistry, College of Pharmacy, Chung-Ang University

Group IV cytosolic PLA2 (cPLA2) is known to be involved in hydrogen peroxide-induced cytotoxicity in LLC-pk1 kidney epithelial cells. However, the precise mechanism by which cPLA2 is implicated in TNF- $\alpha$ -induced cell death is not fully elucidated. Here we found that cPLA2-overexpressed LLC-pk1 cells, but not vector-cells, is resistant to TNF- $\alpha$ -induced cell death. Treatment of TNF- $\alpha$  to vector-LLCpk1 cells, but not cPLA2-overexpressed LLC-pk1 cells, provoked a DNA fragmentation and change in nuclear morphology as detected by 4,6-diamidino-2-phenylindole staining. There was a significant increase in the level of glutathione in the cPLA2-overexpressed LLC-pk1 cells. Treatment of TNF- $\alpha$  for 24 h up-regulated the inducible nitric oxide synthase (iNOS) in vector-LLCpk1 cells, but not cPLA2-overexpressed LLC-pk1 cells. In contrast, arachidonic acid (AA), the product of cPLA2, induced more cell death in cPLA2-overexpressed cells than in vector-LLCpk1 cells and the enhancement in cell death in cPLA2-overexpressed cells was not blocked by any inhibitor of cyclooxygenase and lipoxygenase. Our results suggest that the sustained release of AA by action of cPLA2 may make LLCpk1 cells resist to TNF- $\alpha$ -induced cell death through antioxidant defense system and iNOS-related pathway.

[PA4-17] [ 04/20/2001 (Fri) 10:30 – 11:30 / Hall 4 ]

### cDNA Microarray Analysis of the Gene Expression after Ad5CMV-p16INK4a Gene Transfer in the Non-Small Cell Lung Cancer Cells

Park MS<sup>o</sup>, Oh HY, Han ES, Park HS, Eom MO, Jung HK, Kang HI, Kim OH

Department of Toxicology, National Institute of Toxicological Research, Korea Food and Drug Administration, Seoul, Korea.

A adenovirus-mediated p16<sup>INK4a</sup>(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

Kang CS, Choi BK, Park SH, Park SA, Park SS, Choi MS, Kang MH, Hong CH<sup>o</sup>, Han SB<sup>\*</sup>, Jang SJ

Division Of Drug Standardization, Department of Drug Evaluation, KFDA, <sup>\*</sup> Seoul Clinical Laboratory

There has been a long-standing concern in the estimation of human exposure to endocrine disruptors particularly 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 transferred 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  $1.26 \pm 0.59 \mu\text{g/L}$ , that of Pb is  $33.56 \pm 14.58 \mu\text{g/L}$ , that of Hg is  $6.05 \pm 18.14 \mu\text{g/L}$  in blood, the concentration of Cd is  $0.38 \pm 0.32 \mu\text{g/L}$ , that of Pb is  $25.73 \pm 15.40 \mu\text{g/L}$ , that of Hg is  $3.95 \pm 2.24 \mu\text{g/L}$  in cord blood, the concentration of Cd is  $73.85 \pm 63.35 \mu\text{g/L}$ , that of Pb is  $22.01 \pm 9.95 \mu\text{g/L}$ , that of Hg is  $31.62 \pm 20.20 \mu\text{g/L}$  in dried placenta, the concentration of Cd is  $1.52 \pm 2.13 \mu\text{g/L}$ , that of Pb is  $7.65 \pm 15.49 \mu\text{g/L}$ , that of Hg is  $21.09 \pm 13.80 \mu\text{g/L}$  in colostrum.

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

### Bisphenol A-induced alternation of peritoneal macrophage activation in mice

Byn JA<sup>o</sup>, Heo Y<sup>\*</sup>, Pyo MY

College of Pharmacy, Sookmyung Women's University, Seoul, <sup>\*</sup>College of Natural Science, Catholic University of Dagu, Daegu

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)- $\alpha$  production was decreased to 25.8% of control in LPS-stimulated