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Recently hair analysis has been taken great interest because it provides a wider window of drug detection. Once drug incorporated into the hair, it moves along hair shaft at a rate of approximately 1cm/month as the average rate of hair growth.
In this study, the relationship between the distribution of methamphetamine (MA) in hair and drug history was investigated. The scalp hair samples of five MA abusers (6~12cm in length) were obtained for sectional analysis. Hair strand was cut into 2 or 3cm sections from the root side, and drug concentrations of each segment were evaluated by GC/MS. For quantitative determinations, the following ions were used: m/z 140 (AM), 144 (AM-d_5), 154 (MA), and 158 (MA-d_5).
The concentrations of MA and AM in hair segment were exhibited variable patterns according to their drug consumption histories. In case 4, MA consumption in the last 2 months could be proved because the last-grown segment (0~2) was positive and the previously grown segments (2~4 and 4~7) were negative. These results suggest that sectional analysis of hair is useful in determining past drug histories in the field of forensic science. However, it also has to be taken into account that the growth rate of hair can vary between 0.8 and 1.4 cm/month and that the telogen partition of the hair can increase to 20%.

[PA4-16] [04/18/2002 (Thr) 14:00 - 17:00 / Hall E]

Metallothionein-III Inhibits hydroxyl radical-induced DNA damage and scavenges superoxide radicals

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Metallothionein (MT)-III is a member of a brain specific MT family, in contrast to MT-I and MT-II that are found in most tissues and are implicated in metal ion homeostasis and antioxidant. To investigate the defensive role of MT-III in terms of hydroxyl radical-induced DNA damage, we used purified human MT-III. DNA damage was detected by single strand breaks of plasmid DNA and deoxyribose degradation. In this study, we show that MT-III is able to protect against the DNA damage induced by ferric ion-nitrilotriacetic acid and H2O2, and that this protective effect is inhibited by the alkylation of the sulfhydryl groups of MT-III by treatment with EDTA and N-ethylmaleimide. MT-III was also able to efficiently remove the superoxide anion, which was generated from the xanthine/xanthine oxidase system. These results strongly suggest that MT-III is involved in the protection of reactive oxygen species-induced DNA damage, probably via direct interaction with reactive oxygen species, and that MT-III acts as a neuroprotective agent.

[PA4-17] [04/18/2002 (Thr) 14:00 - 17:00 / Hall E]

Role of Increases of Glutamine Synthetase in Primary Culture of Mixed Gilal Cells (MGC) and Purified Astrocytes (AST) on Methylmercury Toxicity

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Methylmercury (MeHg) is a highly neurotoxic compound producing neuronal death that is partially mediated by glutamate. Although MeHg produces the neuronal death and malfunction, MeHg toxicity in glial cells is not clear. Glutamine synthetase (GS), known as a glial-specific enzyme, catalyzes the synthesis of glutamine from glutamate and ammonia and is associated with ischemic injury and several neurological diseases. Dysregulation of glutamate, an excitatory neurotransmitter, may cause excitotoxicity. Objective of this experiment is to investigat whether MeHg exposure has adverse effects on GS and whether glutamate plays a role in MeHg-induced toxicity of the MGC and AST. To MGC and AST cultured from the cerebral cortex of one day-old rats, MeHg (0, 5 and 10 μM) was exposed for 6 days from 5 days in vitro. MeHg exposure produced dose-dependent increases of GS activity in MGC and AST. Cell viability, total cell

number, and protein content were significantly decreased in these cell models. Counted cell number, cell viability and protein content are significantly higher in AST than in MGC, which were exposed to MeHg (5 or 10 μM) for 6 days. Western blot and immunocytochemistry also showed qualitative increases of GS protein in these cells. Apparent morphological alteration of the glial cells was observed at 5 and 10 μM MeHg-exposed groups. To investigate the effect of glutamate on MeHg toxicity, MeHg (10 μM) and glutamate (0.5 μM) were co-treated to the MGC or AST for 6 days. Exposure of glutamate (0.5 μM) to AST or MGC has no effect on GS activity. However, MeHg (10 μM) exposed cells or cells co-treated with MeHg and glutamate showed significant increases of the GS activity and GS protein. Counted cell number, cell viability and protein content were dose-dependently decreased in MeHg exposed- or co-treatment groups, and were significantly higher in AST than MGC. AST was more resistant to decrease of cell number, cell viability and protein content and % increase of GS activity in AST was significantly higher than in MGC. This data provide evidence that increase of GS activity may have a protective role in MeHg toxicity in glial cells.

[PA4-18] [04/18/2002 (Thr) 14:00 - 17:00 / Hall E]

Effect of TCDD on the expression of rat hepatic cytochrome P450 2A1: Assessment of the effect in vivo and in a hepatocyte culture system

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This study aimed to determine the effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin(TCDD, dioxin) in P450 (CYP) 2A1 expression, using in vivo and in cultured hepatocyte system, in comparison with traditional TCDD-mediated induction of CYP 1A1. Hepatic microsomal testosterone 7a-hydroxylase activity as a marker of CYP2A1 was increase in both male and female rats. As judged by the change in testosterone metabolic activity catalyzed by liver microsome, oral administration of TCDD into rats increased the CYP 2A1 time- and dose-dependently. In cultured hepatocytes, CYP2A1 protein induction by TCDD was matched with changing in CYP2A1 activity. Northern blot analysis confirmed extensive increase of CYP2A1 mRNA induced by TCDD. In addition, resveratrol, specific inhibitor of CYP1A1, had the greatest inhibitory effect (approximately 60%) in CYP2A1 mRNA, caused by the AhR ligand TCDD in a concentration-dependent manner.
These results suggest that the potentiation of CYP2A1 induction by TCDD is regulated at the level of transcription of the CYP2A1 gene, presumably via binding to XRE core sequence and the expression of CYP2A1 is induced by addition of TCDD, which was in agreement with CYP1A1 expression by AhR-TCDD complexes. Despite the fact that CYP1A1 induction is used widely as a measure of environmental TCDD exposure, the data presented in this study suggest that induction of CYP2A1 enzymes is another indicator of exposure to TCDD.

[PA4-19] [04/18/2002 (Thr) 14:00 - 17:00 / Hall E]

In utero exposure of permethrin alters sexual maturation of male and female rat

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Permethrin is one of the pyrethroid insecticides, which are synthetic derivatives of natural pyrethrins contained in the flowers of phyrethrum. Permethrin is a widely used agent for indoor and outdoor pest control due to its high insecticidal potency and low mammalian toxicity. However, any chemical with hormonal activity like estrogen could affect reproductive function including sexual maturation. Our previous study indicated that permthrin showed estrogenic activity. Therefore, we examined whether permethrin changes the sexual maturation of male and female rat. Subcutaneous treatment with permethrin(10 ㎎/㎏) 6 to 18 of gestational day(GD) led to significant delay in vaginal opening of female offspring, and also delay in vaginal opening was observed with intraperitoneal injection (200 ㎎/㎏) 6 to 18 of GD. Male rats exposed to permethrin had significant decreases in anogenital distances (AGDs) on postnatal day (PND) 3, 15 and