[PA4-35] [04/17/2003 (Thr) 14:00 - 17:00 / Hall P]

Cadmium altered zinc homeostasis in the Neuronal Cell

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In this study, we investigated the effect of cadmium on genes expression related to zinc homeostasis in HT22 hippocampal neuron cell line by RT-PCR and western blotting technics. In the time-course effect, cadmium up-regulated the relative levels of MT-I and MT-II to㉥b-actin at 4 hr after treatment. These effects were consistent with MT-I/II protein contents by western blot analysis. But MT-III, a specific MT isoform in brain, was not affected by cadmium. In the dose-dependent effect, cadmium (0,5 - 2.0 ㎍M) up-regulated MT-I and MT-II levels by a dose-dependent manner. Cadmium dose-dependently down-regulated zinc transporter (ZnT-1), which serves as zinc efflux transporter. Our results suggest that cadmium can exert neurotoxicities (including degenerative neuron disease) via alteration of zinc metabolism in CNS.

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Effects of Dially Sulfide on Thioacetamide-induced Hepatotoxicity

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Effects of diallyl sulfide (DAS), a component of garlic, on thioacetamide-induced hepatotoxicity were investigated in male ICR mice. When mice treated subcutaneously with 100, 200 and 400 mg/kg of DAS in corn oil for three consecutive days, the activity of cytochrome P450 (P450) 2E1-selective p-nitrophenol hydroxylase was dose-dependently suppressed. In addition, the activities of P450 2B-selective benzyloxyresorufin O-debenzylase and pentoxyresorufin O-depentylase were dose-dependently induced by the treatment with DAS. To investigate a possible role of metabolic activation by P450 enzymes in thioacetamide-induced hepatotoxicity, mice were pre-treated with 400 mg/kg of DAS for 3 days, followed by a single intraperitoneal treatment with 100 and 200 mg/kg of thioacetamide in saline for 24 hr. The activities of serum alanine aminotranferase and aspartate aminotransferase greatly increased by thioacetamide were recovered in DAS-pretreated animals. Taken together, our present results indicated that thioacetamide might be activated to its hepatotoxic metabolite(s) by P450 2E1, not by P450 2B, in male ICR mice.

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[PA4-37] [04/17/2003 (Thr) 14:00 - 17:00 / Hall P]

The Influence of Bisphenol A on the Thyroid Hormone System in vivo

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It is well-known that bisphenol A(BPA), an industrial raw material for polycarbonate and epoxy resins, shows estrogenic activity. Recent research from our laboratory has shown that BPA disrupts interaction between thyroid hormone and its receptor in a non-competitive manner, and alters the thyroid-hormone dependent expression of growth hormone(GH) and prolactin(PRL). In this study, we investigated the influence of BPA on the thyroid hormone system in vivo model to establish a screening method for endocrine disruptors. BPA (1mg/kg/day; 2mg/kg/day) were administered to Sprague-Dawley rats in drinking water during the pregnancy and lactation. We determined the maternal plsma levels of total T4 before the day of administration and on days 7, 14, 20 of gestation and day 7 of lactation, and neonatal plasma levels of total T4 on postnatal days of 4, 7, 14, and body weight on postnatal days of 4, 5, 7, 12, 14. In addition that, immunohistochemical study was performed to determine the levels of thyroid hormone receptor protein β1 and β2(TR-β1, β2) in cerebral cortex of neonates on postnatal days of 5, 7, 14. Plasma concentrations of total T4 in dams and those of total T4 in neonates were not altered by maternal treatment with BPA. Strong signals of thyroid receptor were seen in the neonatal brain exposed to BPA or PTU perinatally compared to normal pups', which indicates that TR-β1 and TR-β2 were overexpressed by BPA exposure and hypothyroidism. These results suggest that the perinatal exposure to BPA can disturb the thyroid hormone system resulting in overexpression of thyroid hormone receptor in the cerebral cortex of the neonates.

[PA4-38] [04/17/2003 (Thr) 14:00 - 17:00 / Hall P]

Effects of Polycyclic Aromatic Hydrocarbons on Liver and Lung Cytochrome P450s in Male ICR Mice

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Certain polycyclic aromatic hydrocarbons (PAHs) have been reported to induce cytochrome P450 (P450) 1A1 and 1A2. In the present studies, the effects of six well-known PAHs on the activities of hepatic and pulmonary P450 enzymes were investigated in male ICR mice. When mice were treated intraperitoneally with 3, 10 and 30 mg/kg of individual PAHs for 3 consecutive days, the activities of ethoxyresorufin- and methoxyresorufin-O-dealkylases were significantly and differentially induced in liver and lung. Moreover, other P450 isozyme-associated monooxygenase activities were also induced significantly in liver and lung with characteristic induction profiles. Our present results suggest that individual PAHs might have inductive effects on P450 isozymes, and that the characteristic inductive effects of individual PAHs on certain P450 isozymes would be developed as a marker for determining exposure to certain PAHs. (Supported by the Echotechnopia21 Program, Ministry of Environment).

[PA4-39] [04/17/2003 (Thr) 14:00 - 17:00 / Hall P]

Effects of Age, Brain-regional Selectivity, and Ovariectomy on Sexual Dimorphism of Organophosphate Pesticide Terbufos

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