and bulbocavernous muscle (LABC), and cowper's glands (CpG) weights were significantly increased. Flutamide inhibited the testosterone-induced re-growth of accessory sex glands (SV, VP and Cp) and organs (GP and LABC) with dose-dependent manner. A rodent 20-day thyroid/pubertal male assay was performed utilizing immature age-matched intact male rats (33 days of age). All rats (10 rats/group) were treated with testosterone (1.0 mg/kg/day, by s.c.) and flutamide (1, 5, and 25 mg/kg/day, by oral) from PND 33 to PND 53, respectively. Testosterone increased significantly the SV and VP weights, with some effect on GP, LABC, and Cp. When flutamide was administered to immature male rats, the accessory sex organs (SV, VP, GP, LABC, and CpG) growth and development was blocked in dose-dependent manner. However, testes weights were significantly increased following flutamide administration (5 and 25 mg/kg/day). In conclusion, 20-day thyroid/pubertal male assay showed similar sensitivity to Hershberger assay for the screening of androgenic/antiandrogenic compounds.

[PA4-24] [10/19/2000 (Thr) 10:00 - 11:00 / [Hall B]]

3MC and DPB effects on the expression of drug metabolising enzymes via RT-PCR.

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In order to understand the mechanism of the regulation of drug metabolizing enzyme gene expression, we have studies the induction of CYP1A1 and GSTα, μ, π enzymes in monkey that is treated with 3-methylcholanthrene (3MC) and dibutylphthalate (DBP). The mRNA levels were measured by RT-PCR and enzymatic activity was measured via EROD in brain, intestine and liver. And the copy number of CYP1A1 per 3/20㎍ was measured by competitive PCR. In the case of adult monkey, treatment with 3MC induced CYP1A1 mRNA in brain by 2-fold, in intestine by 11-fold and in liver by 10-fold respectively. And the treatment with DBP induced CYP1A1 mRNA. GST μ was not induced by the treatment with 3MC and DBP. GSTα was not induced by the treatment with 3MC and DBP in liver and brain, but it was induced in intestine (1.5-fold). GSTπ was slightly induced by the treatment with 3MC and DBP in brain, intestine and liver. In the case of fetus monkey, the basal levels of fetus CYP1A1 mRNA and GSTs mRNA were low in comparison to adult monkey and as the age of monkey increased, the basal levels of CYP1A1 mRNA and GSTs mRNA were also increased. The treatment with 3MC induced CYP1A1 mRNA in brain and liver, but it didn't significantly induce CYP1A1 mRNA in intestine. GSTμ and GSTα was not induced by the treatment with 3MC and DBP. GST π was slightly induced by the treatment with 3MC and DBP. The copy number of CYP1A1 per RT product of 3/20㎍ total RNA was about 1×10^6 in the 3MC-treated liver, 5×10^4 in control liver, 5×10^3 in 3MC-treated intestine and 1×10^3 in 3MC-treated brain.

[PA4-25] [10/19/2000 (Thr) 10:00 - 11:00 / [Hall B]]

De novo Synthesis Pathway of Ceramide Causes Hypoxia -induced Apoptosis of SH-SY5Y Human Neuroblastoma Cells

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Ceramide has been implicated to be a second messenger in the cell signaling pathway involved in a variety of cellular responses ranging from cell differentiation, cell cycle arrest, cellular senescence, apoptosis to cell survival and cell proliferation in a number of cells. However, there is little information of a role of ceramide in apoptosis in hypoxic injury known to induce necrotic cell death. Ceramide generation was measured in SH-SY5Y cells metabolically labeled with [3H]serine after exposure to chemical hypoxia induced by cobalt chloride. Chemical hypoxia resulted in a