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Sumithrin is one of the synthetic pyrethroid insecticides, developed classes of insecticides, due to its high activity against insects, and relatively low mammalian toxicity compared to other insecticide classes. Sumithrin is commonly used insecticide for in-door pest control, providing for human exposure. Our uterotrophic assay using immature SD female rats demonstrated that sumithrin acts like an estrogen agonist. Estrogen or antiestrogen clearly influence reproductive development. Therefore, We determined the effects of in utero exposure to sumithrin on postnatal body weight, reproductive development (anogenital distance(AGD), vaginal opening, organ weight) in rat offspring. Pregnant SD rats were intraperitoneally injected with sumithrin (300 ㎎/㎏/day) from gestation day(GD) 6 to 18. Male and female offsprings were examined at postnatal days(PND) 3, 15 and 1, 22, respectively. Rat exposed to sumithrin had a statistically significant increase in body weight on PND21(male) and 22 (female) and brought significant decreas in male AGD on PND 15 and 21. Also, vaginal opening was accelerated significantly ($P < 0.05$). These results indicate that persistent exposure to this compound may contribute to reproductive developmental dysfunction.

[PA4-20] [10/18/2001 (Thr) 14:00 - 17:00 / Hall D]

Identification and Cloning of Multiple Forms of Neutral Sphingomyelinase in Bovine Brain

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Neutral form of sphingomyelinase (N-SMase) is a family of enzymes which hydrolyze sphingomyelin to produce a lipid-derived tumor suppressive second messenger ceramide. N-SMase exists as multiple forms in brain and seems to transmit different signals and to give rise to different pools of ceramide, eliciting cellular responses ranging from apoptosis and cell cycle arrest to cell survival and cell proliferation. In previous study, we have identified at least seven forms of N-SMase activities termed N-SMase α, β, ɣ, δ, ε, ζ, λ in bovine brain based on extraction patterns, column profiles and biochemical properties (*J. Neurochem. 75, 1004-1014, 2000, Jung et al.*). Here we first report the purification of 68 kDa N-SMase λ, a cytosolic form of Mg^{2+}-independent N-SMase. Second, we report cDNA cloning of the 30 kDa forms of SMase α, β, ɣ, δ using a specific antibody against the 30 kDa protein from rat brain λZAP II cDNA library expressing proteins. The resulting three positive clones were identified as an identical gene encoding one of isoforms of a signaling protein playing a crucial role in cell survival and death. Third, we also identified the 60 kDa N-SMase ε as a known stress protein whose role has not been fully defined by MALDI-TOF analysis. We are underway to confirm these proteins as the respective N-SMase enzymes through overexpression of these proteins in eukaryotic cells and immunoprecipitation experiments.

[PA4-21] [10/18/2001 (Thr) 14:00 - 17:00 / Hall D]

Role of Ceramide in Hypoxia-induced Neuronal Cell Death

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Ceramide is an important lipid messenger involved in mediating a variety of cell functions including proliferation, differentiation, growth arrest and apoptosis. This study was undertaken to determine

whether ceramide formation plays a role in hypoxia-induced apoptosis. Ceramide level was measured in SH-SY5Y human neuroblastoma cells by metabolic labeling with [^{3}H]palmitic acid or [^{3}H]serine. Hypoxia resulted in the increase in ceramide production with subsequent evidence of apoptosis in SH-SY5Y cells. Both fumonisin B1 (FB1), a ceramide synthase inhibitor, and L-cycloserine, a serine palmitoyltransferase inhibitor, blocked hypoxia-induced ceramide generation while sphingomyelin levels remained unchanged. L-cycloserine, but not FB1, reduced hypoxia-induced apoptosis. This may be due to a known cytotoxic sphingolipid, sphinganine accumulated by cotreatment of hypoxia and FB1. Hypoxia-induced cell death and ceramide production were significantly potentiated by NOE (N-oleoylethanolamine), an inhibitor of ceramidase, and PDMP (DL-thero-1-phenyl-2-decanoylamino-3-morpholino-1-propanol), an inhibitor of glucosylceramide synthase (GCS). PARP cleavage and caspase 3 activation were accelerated and potentiated by treatment of PDMP but not NOE. This indicated that GCS is more important in hypoxia-induced apoptosis than ceramidase. Hypoxia-induced neuronal cell death was potently inhibited by an inhibitor of caspase, z-VAD-fmk (z-VAD-fluoromethylketone). Our results suggest that hypoxia-induced neuronal cell death may be caused by increase in the *de novo* synthesis of ceramide pathway and the subsequent activation of caspase.

Poster Presentations - Field B1. Physiology

No submitted abstract in the field B1 (Physiology)

Poster Presentations - Field B2. Pathology

[PB2-1] [10/18/2001 (Thr) 14:00 - 17:00 / Hall D]

Anti-proliferative Effects of Godulbaegi Extracts on Human Cancer Cells

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We investigated the anti-proliferative effects of godulbaegi (*Ixeris sonchifolia* H.) root extracts, luteolin (3', 4', 5, 7-Q-glucoside and 3', 4', 5, 7-tetrahydoxyflavone) and apigenin (3', 4', 5, 7-O-gluconic acid) on SK-MEL-2 human melamine cancer cells and HepG2 liver cell line. In MTT assay 3', 4', 5, 7-tetrahydoxyflavone showed the most efficient anti-proliferative effects. According to PI staining and DNA fragmentation assay, we postulated that this effects may be a result from cell cycle arrest, then we examined the changes of protein expression related cell cycle arrest and apoptosis. Western blotting data represented that the expression of p53, cyclin A and cyclin B1 were decreased against the increase of quantity of 3', 4', 5, 7-tetrahydoxyflavone in HepG2 cell line. However, luteolin induced apoptosis in SK-MEL-2 cells. Now we are performing more experiments to clear the potentiality of it's cell cycle arrest and/or apoptosis inducing effects on human cancer cells.

[PB2-2] [10/18/2001 (Thr) 14:00 - 17:00 / Hall D]

Inhibitory Action of Phenylpropanoids on Phospholipase A2 Activity in RAW 246.7 Cells

Kim Chang Jong, Lee Seung June°, Zang Yong Un, Sim Sang Soo