(CHL) cells with IC50 of 12.8 mM. NOCF induced apoptosis of CHL cells, which was demonstrated by morphological changes, DNA fragmentation and flow cytometric analysis. Treatment of CHL cells with NOCF induced significant G2/M cell cycle arrest without any change in the level of p53 protein. Caspase-3, an executioner of apoptosis was also activated by the treatment of CHL cells with NOCF. The concentration of NOCF inducing apoptosis was so low that we speculate about the environmental significance of these pesticides.

[OA-8] [04/20/2001 (Fri) 15:15 - 15:30 / Room 1]

Hypoxia-induced Neuronal Cell Death Is Caused by Increase in the de novo Synthesis of Ceramide Linked to Caspase Activation

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Ceramide is known to be a lipid-derived 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. To examine the role of ceramide in hypoxia-induced neuronal cell death, ceramide generation was measured in SH-SY5Y human neuroblastoma cells metabolically labeled with [3H]palmitic acid or [3H] serine. The chemical hypoxia resulted in a rapid increase in ceramide production with subsequent evidence of cell death in SH-SY5Y cells. The inhibitor of ceramide synthase, fumonisin B1, but not L-cycloserine, a serine palmitoyltransferase inhibitor, reduced the hypoxia-induced enhancement of ceramide. Cobalt chloride also upregulated hypoxia-inducible factor 1a (HIF-1a) known to stimulate the transcription of provoked apoptosis followed by elevation of ceramide levels, but did not induce a concurrent decrease in sphingomyelin. C6-ceramide also induced apoptosis in SH-SY5Y cells in a similar kinetic frame. NOE (N-oleoylethanolamine), an inhibitor of ceramidase, and PDMP (DL-threo-1-phenyl-2-decanoylamino-3-morpholino-1-propanol), an inhibitor of glucosyl ceramide synthase, increased the ceramide level and induced DNA fragmentation in SH-SY5Y cells. Cobalt chloride-induced cell death and ceramide production were significantly potentiated by both NOE and PDMP. A bacterial Sphingomyelinase increased ceramide level, but did not induce cell death. This hypoxia-induced neuronal cell death was potently inhibited by an inhibitor of caspases, 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 subsequent activation of caspase.

Oral Presentations - Field B

[B1. Physiology] [B2. Pathology] [B3. Neuroscience] [B4. Immunology]

[OB-1] [04/20/2001 (Fri) 13:30 - 13:45 / Room 2]

Role of intracellular calcium release in asiatic acid-induced apoptosis in HepG2 human hepatoma cells

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