cytochrome C reduction, the expression of cyclooxygenase (COX) in A172 human glioblastoma cells, a cellular model of neuronal system. Chloroquine induced apoptosis of the cells in a time- and concentration-dependent manner. Treatment with chloroquine significantly suppressed lipid peroxidation in the cells. In addition, chloroquine significantly enhanced the expression of COX-2 assed by western blot analysis.

[PB1-3] [04/21/2000 (Fri) 10:30 - 11:30 / [1st Fl, Bldg 3]]

Expression of HIF-1 inducible genes in the aged rat brain

Kang MJ°(1), Yu MA(2), Kim KW(2), Yu BP(2), Woo JS(3), Chung HY(1,2)

1Colleage of Pharmacy, Research Indtitute of Genetic Engineering, and 3Colleage of Medicine, Pusan National University, Pusan 609-735, Korea

Hypoxia-reperfusion generates reactive oxygen species (ROS). Some ROS have been suggested to play important roles as a second messenger in normal and diseases conditions. Recent findings on hypoxia established the induction of a DNA binding protein synthesis called hypoxia inducible factor-1 (HIF-1), which promotes transcription of multiple genes. HIF-1 plays a major role in adaptive responses essential to hypoxia as the case in angiogenesis to maintain O2 homeostasis. HIF-1 has also been shown to activate transcription of genes encoding inducible nitric oxide synthase (iNOS) and heme oxygenase 1 (HO-1) which are important for the regulation of cerebral blood flow by synthesizing NO and CO, respectively. At present, it is no information on the HIF-1 inducible genes expression and DNA binding activity in aged tissues. We investigated expression of HIF-1 inducible genes in brain isolated from Fischer 344 rats at 6, 12, 18, and 24 months of age. We quantified the age-related changes in four genes, vascular endothelial growth factor (VEGF), HO-1, iNOS, and HIF-1? in rat whole brain. Quantitation of DNA binding activity was carried out by EMSA. Results showed that the protein levels of VEGF, HO-1, iNOS, and HIF-1? were increased with age. These changes are attributed to the age-related increase in HIF-1 DNA binding activity. Significances of our findings are the hypoxic induction of HIF-1 inducible genes may be critical factors in the maintenance of cerebral O2 homeostasis and angiogenesis during aging. Our results warrant further investigation on molecular mechanisms underpinning cerebral blood circulation under hypoxic conditions occurring during aging.

[PB1-4] [04/21/2000 (Fri) 10:30 - 11:30 / [1st Fl, Bldg 3]]

Effect of phospholipase A2 inhibitor on ATP-induced histamine release in rat peritoneal mast cells

Lee YH, Cho JH, Park JH, Lee SJ, Jang YU, Kim CJ, Sim SS

College of Pharmacy, Chung-Ang University

To investigate whether phospholipase A2 pathway is involved in histamine release of rat peritoneal mast cells, we measured ATP-induced histamine release in the presence of various enzyme inhibitors that involved in eicosanoid pathway, such as phospholipase A2, cyclooxygenase and lipoxygenase. ATP dose-dependently increased histamine release at a concentration of up to 100 μM but gradually decreased at concentrations of more than 100 μM. P2-purinergic receptor antagonists significantly inhibited ATP-induced histamine release but adenosine (P1-purinergic) receptor antagonists did not. Also adenosine did not cause histamine release from rat peritoneal mast cells. Phospholipase A2 inhibitors, manoalide and OPC, significantly inhibited ATP-induced histamine release. Cyclooxygenase inhibitors, ibuprofen and indomethacin, significantly inhibited ATP-induced histamine release and lipoxygenase inhibitors, baicalein and caffeic acid, also significantly inhibited. From the above results, it is suggested that ATP-induced histamine release is mediated via purinergic receptor, in which all enzymes of phospholipase A2, cyclooxygenase and lipoxygenase are involved.