Pharmacology lab, College of Pharmacy, Chonnam National University, Kwang-Ju, 500-757 Korea

Aggregation of the high affinity IgE receptor on mast cells results in many biochemical, events leading to the release of histamine, serotonin, prostaglandins arachidonic acid metabolites, and cytokines. Previously we have shown that M2 pyruvate kinase interacts with the gamma chain of IgE receptor on the ITAM (immunoreceptor tyrosine-based activation motif) region. We also have shown that the enzymatic activity of pyruvate kinase is inhibited upon cross-linking of IgE receptors through the phosphorylation on the tyrosine residues. In this study, we permanently transfected RBL-2H3 cells with M1 pyruvate kinase to test whether the IgE receptor-mediated inhibition of M2 pyruvate kinase is essential for the degranulation of mast cells. When cells were transfected with M1 pyruvate kinase, that is, the IgE receptor-mediated inhibition of pyruvate kinase (M2) was overshadowed, the degranulation of mast cells were significantly inhibited, suggesting that IgE receptor-meidated inhibiton of M2 pyruvate kinase is important for the degranulation of mast cells. Src inhibitor (PP2), but not Syk inhibitor (piceatannol), abolished the IgE receptor-mediated tyrosine phosphorylation of M2 pyruvate kinase and enzyme activity changes, showing that M2 pyruvate kinase is under the control of Src.

[PA1-62] [10/18/2002 (Fri) 09:30 - 12:30 / Hall C]

Heterotrimeric G protein γ12 Subunit is Region-Specifically Expressed in Rat Brain

Myung Chang-Seon°, Yoon KyungBum, Song YongJin, Shin JongWon

관동대학교 의과대학 약리학교실

The G protein γ12 subunit (Gγ12) is widely-expressed and, given the extensive role of the βγ subunit (Gβγ) in cell signaling, is a uniquely known substrate for protein kinase C, indicating phosphorylation as a potential regulatory mechanism. The mRNAs for numerous subtypes of putative Gγs have been identified in mammalian tissues, but little is known about their expression in brain, so that the systemic survey of the localization of mRNAs encoding twelve of Gγs in brain is needed to be performed. This study presents the localization of mRNAs encoding Gγ12 by quantitative RT-PCR and Northern or in situ hybridization in 8 different regions of rat brain: (1) frontal cortex area, (2) cerebral cortex area, (3) striatum, (4) hippocampus area, (5) thalamus, (6) brain stem, (7) cerebellum area, (8) hypothalamus-amygdala-septum-preoptic area. Striking region-specific patterns of expression were observed. The results show that Gγ12 expressed very well in frontal cortex and brain stem and comparatively not in other regions. Therefore, although Gγ12 has full activity for many effectors including phospholipase C and adenyly cylcase, Gγ12 is region-specifically expressed in brain and there may be its own specialized role for Gβγ containing this subunit in cell signaling.

[PA1-63] [10/18/2002 (Fri) 09:30 - 12:30 / Hall C]

Histamine Releasing Factor (HRF) Evokes [3H]Dopamine Release by a Ca^{2+} - independent Pathway in Pheochromocytoma Cells

Seo Ji-Hui°, Kim Hwa-Jung

College of Pharmacy, Ewha Womans University, Seoul, Korea

The recombinant histamine-releasing factor (rHRF) has been reported to induce a secretion of histamine and cytokines from inflammation-related cell types such as basophils and eosinophils, and to function as a growth factor in immune B cells. Recently, decreased expression level of HRF protein was observed in brain of patients with Alzheimer disease and Downs syndrome, suggesting a possible significant role in neurological systems. The novel functional role of HRF in dopamine release from

neuronal cells was investigated in this study. PC12 cells were incubated in the medium loaded with [3H]dopamine (0.5μCi/ml) for 3 h at 37℃ and then were incubated in Krebs-Ringer-HEPES buffer containing test drugs and HRF for 20min. The amount of dopamine release was determined by measuring radioactivity of media samples. Intracellular calcium ($[Ca^{2+}]i$) were determined by monitoring fura-2 fluorescence by the dual wavelength method. rHRF evoked dopamine release in a concentration- and a time-dependent manner, and also increased $[Ca^{2+}]i$ in a Ca^{2+}-containing buffer. rHRF did not produced a increase of $[Ca^{2+}]i$ in the absence of extracellular Ca^{2+}, however, interestingly, rHRF evoked dopamine release in the Ca^{2+}-free buffer, both dopamine release and $[Ca^{2+}]i$ increased by KCl and bradykinin were blocked in a Ca^{2+}-free buffer. Both dopamine release and $[Ca^{2+}]i$ increased by rHRF was not affected by a treatment of nifedipine (5 uM), a L-type Ca^{2+} channel blocker, whereas dopamine release and $[Ca^{2+}]i$ evoked by KCl was inhibited. HRF-stimulated dopamine release was also not inhibited by a MAP kinase inhibitor, , or a calcium-dependent cPLA2 inhibitor. Only a selective inhibitor of calcium-independent iPLA2 produced an inhibitory effect on rHRF-induced dopamine release. These results suggest that rHRF-induced increase in dopamine release is controlled by the Ca2-independent process, and a Ca^{2+}-independent PLA2 pathway is involved in a HRF-induced dopamine release.

[PA1-64] [10/18/2002 (Fri) 09:30 - 12:30 / Hall C]

Pre-conditioning attenuated the MPP^+-induced cytotoxicity

Lee Seung-Jin°, Yang Sang-In, Jang Choon-Gon, Lee Seok-Yong

Lab. of Pharmacology, College of Pharmacy, Sungkyunkwan University

MPP^+ is known to be a neurotoxic substance that induces the degeneration of dopaminergic neurons and Parkinson-like syndrome. Incubation with MPP^+ induced the expression of heme oxygenase-1 (HO-1) in PC-12 cells and HO-1 revealed a protective effect against MPP^+-induced cytotoxicity. In this study, we tested the effect of pre-conditioning on the MPP^+-induced cytotoxicity. The PC-12 cells were incubated with MPP^+ for 3 hrs, and then after 12 hrs the cells were exposed to several concentration of MPP^+. Pre-incubation (pre-conditioning) with MPP^+ significantly attenuated the cytotoxic effects of MPP^+ and induction of heme oxygenase may be involved in this protective effect.

[PA1-65] [10/18/2002 (Fri) 09:30 - 12:30 / Hall C]

Action of lysophosphatidylcholine in U937 human monocytes

Yun Mi-Ran°, Im Dong-Soon

Laboratory of Pharmacology, College of Pharmacy, Pusan National University

Atherosclerosis is a main cause of cardiovascular diseases (that is angina, hypertension, cardiac infarction) and stroke. High level of low-density lipoproteins (LDL) in blood has been implicated as an important factor of atherosclerosis progression. Recently researches in endothelial cells unveiled the roles of lysophosphatidylcholine (LPC), a constituent of oxidized LDL in atherosclerosis. However, action of LPC in monocytes has not been studied. We challenged a set of LPC in U937 human monocytes and found that LPC stimulated cell growth and mobilized Ca^{2+}. The Ca^{2+} response was not blocked by pertussis toxin, an inhibitor of $G_{i/o}$ proteins or U73122, a phospholipase C inhibitor. Furthermore, The response was totally blocked by EGTA addition in extracellular media, suggesting