D2 or D3 receptors with dopamine produced a rapid dose-dependent activation of MAPK. Activation was evident within 5 min, and showed maximum activation in 10 min, then gradually decreased by 30 min. The maximum activation was attained at 10μM of dopamine. However, D2 and D3 dopamine receptors showed some differences in MAPK activation such as ERK subtype specificity and pertussis toxicity sensitivity. Activation of MAPK mediated by both D2 or D3 dopamine receptors was not affected by coexpression of the C-terminus of beta-adrenergic receptor kinase (βARK), which selectively inhibits $G_{\beta\gamma}$-mediated signaling. Furthemore, co-expression of dominant-negative dynamin (K44A), an inhibitor of endocytic vesicle formation, did not affect MAPK activation mediated by both D2 or D3 dopamine receptors, suggesting that MAPK activation is not accompanied by the sequestration of D2 or D3 dopamine receptors.

[PA1-35] [10/19/2000 (Thr) 10:00 - 11:00 / [Hall B]]

DMSO inhibits the degranulation of mast cells by affecting the signaling components of FcεRI

Kuo NY°, Ryu H, Choi HS, Kim KM

Pharmacology Lab, College of Pharmacy, Chonnam National University, Kwang-ju, 500-757 Korea

DMSO, a non-polar solvent, is frequently used to dissolve the chemical compounds or natural products which are insoluble in water. However, DMSO is known to provokes various unwanted activites such as the stimulation of cell proliferation, also in our studies, over certain concentration, DMSO dose-dependently inhibited the antigen-stimulated degranulation of rat mast cells, RBL-2H3 cells. In accordance with this, we examined the effect of DMSO on the tyrosine phosphorylation of syk, PLCγ2, MAPK, and pyruvate kinase, the signal components of FcεRI (high affinity IgE receptor). At the concentration of 0.1 to 0.5%, DMSO did not have any effect on the tyrosine phosphorylation of Syk or PLCγ2. Interstingly, both pyruvate kinase and MAPK were tyrosine phosphorylated at concentration above 0.1 and 0.5%, respectively. Subsequent studies suggested that DMSO inhibits the degranulation of mast cells by modulating the pyruvate kinase activity.

[PA1-36] [10/19/2000 (Thr) 10:00 - 11:00 / [Hall B]]

FcεRI negatively regulates of phospholipase C-γ2 through protein kinase C

Yun EJ°, Kuo NY and Kim KM

Pharmacology Lab, College of Pharmacy, Chonnam National University, Kwang-ju, 500-757 Korea

We have reported that the cytoplasmic part of the FcεRI-β chain interacts with PLC-γ2 and crosslinking of FcεRI causes the phosphorylation of PLC-γ2 both on tyrosine and serine residues. As subsequent studies we tested the roles of protein kinase C on the regulation of PLC-γ2 through FcεRI. When RBL-2H3 cells were treated with Go6983, a PKC subtype-specific inhibitor, the tyrosine phosphorylation of PLC-γ2 was potentiated. Meanwhile, the depletion of PKC by overnight incubation with PMA (0.1 μM) potentiated the tyrosine phosphorylation of PLC-γ2. It is well understood that the activation of PLCγ hydrolyses phosphatidylinositol 4,5-bisphosphate to diacylglycerol and inositol 1,4,5-triphosphate, which activates PKC and causes the release of Ca2+ from intracellular Ca2+ stores. Therefore, our observations suggest that PKC acts as a negative control over PLC-γ2.

[PA1-37] [10/19/2000 (Thr) 10:00 - 11:00 / [Hall B]]

Intracerebroventricular administration of Hemin elicits febrile response

Park HJ°, Lee SH, Park HY, Lee SY

Lab. of Pharmacology, College of Pharmacy, Sungkyunkwan University, Suwon

It is widely accepted that inflammation and exogenous pyrogens evoke fever through the activation of macrophages to release endogenous pyrogenic cytokines (IL-1β, IL-6 and TNF-α) and the ending step in febrile response is the action of a PGE2 on thermoregulatory pathways in the hypothalamus. However, the precise mechanism by which blood-borne cytokines increase PGE2 synthesis in hypothalamus is still unclear. Recently, nitric oxide (NO) was proposed as a possible signal transducer of circulating pyrogen-induced PGE2 synthesis in hypothalamus. In our previous study, i.c.v. administration of exogenous carbon monoxide (CO), which has very similar character with NO in biological activity, markedly increased the body temperature. So, we study the effects of hemin, which is a substrate of CO-producing enzyme (heme oxygenase, HO) and a inducer of HO, on body temperature in this study. Hemin(i.c.v.) markedly increased in body temperature and this response was blocked by ZnPP IX (inhibitor of HO), indomethacin, or cycloheximide (inhibitor of gene transcription). Hemin maximally induced HO-1 in hypothalamus at 3 hrs after administration.
These results suggest that hemin-induced pyresis is partially due to induction of HO-1 and endogenous CO is a possible signal transducer of febrile response in hypothalamus.

[PA1-38] [10/19/2000 (Thr) 10:00 - 11:00 / [Hall B]]

Effects of long-term administration of NOS inhibitor on aortic contractility

Park HY°, Lee SY

Lab. of Pharmacology, College of Pharmacy, Sungkyunkwan University

Nitric oxide (NO) is one of the important modulators that control vascular smooth muscle tone. The chronic inhibition of NO synthase (NOS) elicits the hypertension in rats. However, the mechanism of hypertension induced by chronic inhibition of NOS is not clear. Thus, to clarify the mechanisms of occurance of hypertension, we studied the effects of adrenergic agents on aortic contractility in rats treated with NOS inhibitors for 21 days were examined.
Chronic administration of L-NAME significantly increased in the blood pressure. The pressor effect of norepinephrine and the depressor effect of prazosin were significantly increased in the L-NAME-induced hypertensive rats. Phenylephrine, a α-receptor agonist, AlF_4^-, G-protein stimulator, elicited the more potent contraction in the aorta of the rats treated with L-NAME for 21 days than in the aorta of the untreated rats. The potentiation of contractile action of phenylephrine by treatment with L-NAME for 21 days was significantly reduced in the endothelium-free aorta. However, the contractile action of phenylephrine was still more potent in the endothelium-free aorta of the rats treated with L-NAME for 21 days than in the endothelium-free aorta of the untreated rats. These results suggests that the hypertension by choronic inhibition of NOS is partially due to the changes of the intracellular signal transduction system of aortic smooth muscle.

[PA1-39] [10/19/2000 (Thr) 10:00 - 11:00 / [Hall B]]

Interrelationship between the IL-1β-induced pyresis and heme oxygenase in hypothalamus

Park HJ°, Lee SY