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

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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

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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]]