vitro.

[PA1-9] [04/20/2001 (Fri) 10:30 - 11:30 / Hall 4]

M2 type Pyruvate Kinase as Novel screening system for anti-allergic agents

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For the efficient screening of anti-allergic agents, the assay method should be simple and faithfully reflect the in vivo system that we are eventually interested in. Recently, by yeast two-hybrid screening we have shown that M2 type pyruvate kinase interacts with the high affinity IgE receptor (FcεRI), and strongly regulated when FcεRI is cross-linked by antigen. Pyruvate kinase is tyrosine phosphorylated, thereby the affinity for the substrate is decreased. We also have shown that several signaling components are involved in the signaling pathway connecting FcεRI and pyruvate kianse. Pyruvate kianse seems to be the final common path where various signaling components involved in FcεRI signaling merge. Therefore, it is likely that pyruvate kinase faithfully reflects the whole FcεRI signaling cascade, compared with other signaling components that are partly involved in the signaling cascade. We have tested effects of several compounds, on pyruvate kinase, including resveratrol and tanshinones that we have reported to have anti-allergic effects, and as we expected, strong correlation was observed between the modulation of pyruvate kinase and anti-allergic actions of compounds we tested. Our results suggest that this simple and easy enzyme assay could be used as an efficient screening system for the new anti-allergic drugs.

[PA1-10] [04/20/2001 (Fri) 10:30 - 11:30 / Hall 4]

Inhibition of Growth Factor-induced MAP kinase and Akt Activation in Rat Aortic Vascular Smooth Muscle Cells by NQ304, a 1,4-Naphthoquinone Derivative

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We recently reported that 2-chloro-3-(4-hexylphenyl)-amino-1,4-naphthoquinone(NQ304), a naphthoquinone derivative, had potent inhibitory effects on the platelet aggregation in vitro and thrombosis in vivo. Furthermore, we reported the antiplatelet mechanism of NQ304 by the reduction of the thromboxane A2 formation, inhibition of adenosine triphosphate release and intracellular calcium mobilization. In this study, we examined the possible antiproliferative effect of NQ304 on rat aortic vascular smooth muscle cells (VSMCs). NQ304(1-10 μM) significantly inhibited the serum(10% fetal bovine serum)- and PDGF-BB(50ng/ml)- induced proliferation in a dose-dependent manner on rat aortic VSMCs. Furthermore, flow-cytometeric analysis showed that NQ304 arrested the G0/G1 and S phase of cell cycle progression. We also examined the intracellular signaling effect of NQ304 on the serum- and PDGF-BB- induced activation of mitogen-activated protein kinase(ERK1/2) and Akt by western blotting in cultured rat VSMCs. Pretreatment of rat VSMCs with NQ304 resulted in a significant inhibition of the serum- and PDGF-BB- induced activation of ERK1/2 and Akt. These results suggest that the antiproliferative effects of NQ304 may be exerted by the inhibition of the serum- and PDGF-BB induced ERK 1/2 and Akt, which can contribute to prevent atherosclerosis by inhibiting VSMCs proliferation.

[PA1-11] [04/20/2001 (Fri) 10:30 - 11:30 / Hall 4]