newly synthesized naphthyridine derivatives against several clinical isolates of H.pylori. MICs were determined by a routine agar dilution technique with blood agar base #2, supplemented with 10% fetal bovine serum. The results showed that the strains were susceptible to our compounds as well as omeprazole. Some of the compounds were about 3 to 5 times more potent than omeprazole. These reuslts suggest that our new compounds have potent inhibitory activities against H. pyloriand might be useful for the clinical eradication of H. pylori.

[PA1-6] [10/18/2001 (Thr) 14:00 - 17:00 / Hall D]

Tetrandrine Stimulates the Apoptosis of Rat Hepatic Stellate Cells

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One of the therapeutic goal for hepatic fibrosis is to eliminate the activated hepatic stellate cells by apoptosis, as hepatic stellate cells play a central role in hepatic fibrosis. In this study, we investigated apoptosis stimulation by tetrandrine in activated rat hepatic stellate cells.
Transformed rat hepatic stellate cells (T-HSC/Cl-6) and rat hepatocytes were treated with tetrandrine. Treatment with tetrandrine in T-HSC/Cl-6 cells resulted in morphologic alterations, induction of low molecular weight DNA fragmentation, activation of caspase-3 and caspase-8, subsequent proteolytic *cleavage of poly(ADP-ribose) polymerase in a concentration-dependent manner, at concentrations that* had no effect on the viability of rat hepatocytes. But tetrandrine had no effect either on mitochondrial membrane depolarization or the release of cytochrome c from mitochondria into the cytosol.
In conclusion, results above demonstrate that tetrandrine stimulates apoptosis via caspase-3 and caspase-8 activation in T-HSC/Cl-6 cells at concentrations that have no toxicity on hepatocytes. And this might be one of the antifibrotic mechanims of of tetrandrine in vivo.

[PA1-7] [10/18/2001 (Thr) 14:00 - 17:00 / Hall D]

Dimethylsulfoxide Inhibits the Degranulation of Mast Cells by Interfering the Signaling Pathway of FcεRI, M2 type Pyruvate Kinase

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We examined the effects of DMSO, a universal solvent for various chemicals, for the signaling pathways of high affinity IgE receptor (FcεRI). DMSO significantly inhibited FcεRI-mediated degranulation of RBL-2H3 cells. In order to find out specific signaling components affected by DMSO, cells were treated with DMSO and the FcεRI-mediated tyrosine phosphorylations of Syk, PLC-γ1, PLC-γ2, ERK, and pyruvate *kinase were examined. DMSO at 0.5% specifically inhibited FcεRI-mediated tyrosine phosphorylation of* M2 type pyruvate kinase, which we recently reported as a new signal component of FcεRI. These results show that DMSO could interfere with the signaling of FcεRI when used above certain concentration by *interfering with the modulation of M2 type pyruvate kinse through FcεRI.*

[PA1-8] [10/18/2001 (Thr) 14:00 - 17:00 / Hall D]

Vasorelaxant effect of BMS-180448, a novel ATP sensitive K+ channel opener, in rat aorta

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The purpose of this study was to determine the mechanism of vasorelaxant effect of BMS-180448, a novel ATP sensitive K^+ channel opener, in rat aorta. BMS-180448 showed a concentration-dependent reduction of phenylephrine (0.3μM)-induced contraction in the endothelium-intact and in the endothelium-denuded rat aortic rings (IC_{50}:1±0.01μM, 1.09±0.06μM). Pretreatment of N-nitro-L-arginine methyl ester (L-NAME) had no effect on the response of BMS-180448, suggesting that the vasorelaxant effect of BMS-180448 is endothelium-independent and not mediated through nitric oxide pathway. BMS-180448 produced the complete relaxations in $PGF_{2\alpha}$ (10μM)- and U46619 (0.1μM)-contracted rat aorta (IC_{50}< 0.1μM), whereas, it had no effects on rat aortic rings contracted by KCl and phenylephrine. These data show that BMS-180448 act as an antagonist at the thrombaxane A_2/prostaglandin H_2 receptor to produce vascular relaxation. These inhibitory effects of BMS-180448 were reversible and did not affect the resting tension. In addition, BMS-180448 inhibited Ca^{2+} induced contraction of rat aortic rings depolarized by 30 mM KCl. In conclusion, these findings suggest that BMS-180448 inhibited the contraction of rat aortic rings, concentration-dependently and endothelium-independently. This vasorelaxant effect is mainly associated with the thrombaxane A_2/prostaglandin H_2 receptor blocking activity, and may also act by the inhibition of Ca^{2+} mobilization.

[PA1-9] [10/18/2001 (Thr) 14:00 - 17:00 / Hall D]

Differential Regulation of Phospholipase Cγ Isoforms Through FcεRI, High Affinity IgE Receptor

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The signaling components of high affinity IgE receptor (FcεRI) were searched by yeast-hybrid screening of the cDNA library constructed from RBL-2H3 cells. The cytoplasmic part of the FeεRI-βchain was found to specifically interact with PLC-γ2, and further comparatives studies were conducted focusing on the differential regulation of two PLC-γ isoforms through FcεRI. PLC-γ2 but not PLC-γ1 interacted with FeεRI in RBL-2H3 cells, however, both enzymes were phosphorylated through FeεRI on tyrosine and serine residues. The tyrosine phosphorylation of PLC-γ1 but not that of PLC-γ2 was abolished by wortmannin, a PI-3 kinase inhibitor. Go 6983, an atypical PKC subtype-specific inhibitor, potentiated the tyrosine phosphorylations of both PLC-γ isoforms, suggesting that atypical PKCs have inhibitory effects on PLC-γ enzymes. In contrast, Go 6976, a typical PKC subtype-specific inhibitor, or over night treatment of RBL-2H3 cells with 1 μM PMA, a manuever to deplete typical PKC inhibited the tyrosine phosphorylation of PLC-γ1 but not that of PLC-γ2. These results show that PLC-γ1 would increase cellular IP3 and PKC in a PI-3 kinase-sensitive manner. Typical PKCs have positive regulatory effects on PLC-γ1 but atypical PKCs have inhibitory effects. In contrast, PLC-γ2 directly interacts with FcεRI and mediate the signaling of FcεRI in an atypical PKC-sensitive manner.

[PA1-10] [10/18/2001 (Thr) 14:00 - 17:00 / Hall D]

Inhibition of nitric oxide production and inducible nitric oxide synthase gene expression by THI 52, a new synthetic naphthyl-benzylisoquinoline alkaloid