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In the present study, we intended to investigate whether polycationic peptides including poly-L-lysine (PLL) and poly-L-arginine(PLA) specifically inhibit the mucin release from cultured airway goblet cells and how long they exert the inhibitory action. Confluent primary hamster tracheal surface epithelial (HTSE) cells were metabolically radiolabeled with 3H-glucosamine for 24 hr and chased for 30 min in the presence of varying concentrations of either poly-L-arginine (PLA) or poly-L-lysine (PLL) to assess the effects on 3H-mucin release, on the total elution profile of the treated culture medium and on the total mucin content following 24hrs after the treatment of polycationic peptides during 30 min. The results were as follows : (1) PLL 78,000, PLL 9,600 and PLA 8,900 inhibited mucin release in a dose-dependent manner , (2) These polycationic peptides did not inhibit the release of the other releasable glycoproteins with less molecular weights than mucin's , (3) These polycationic peptides decreased the total mucin content following 24hrs after 30 min treatment. We conclude that these polycationic peptides 'specifically' inhibit mucin release from airway goblet cells and they showed the durability in the inhibitory action. This finding suggests that these polycationic peptides might be used as a specific airway mucin-regulating agent.

[PA1-4] [10/18/2001 (Thr) 14:00 - 17:00 / Hall D]

Reversal of multidrug resistance by pyrrolo[3,2-c] quinoline derivatives in cancer cells

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Multidrug resistance (MDR) is a major problem in cancer chemotherapy. The best-characterized mechanism of MDR is mediated by P-glycoprotein (Pgp), a member of the ATP-binding cassette transporter family of proteins. Pgp is expressed in up to 50% of human tumors and is a negative prognostic indicator for chemotherapy outcome in some cancers. Inhibition of this drug efflux pump by pharmacological agents has been shown to reverse resistance and resensitized resistant cells to antitumor agents in vitro and in animal tumor models. A wide variety of compounds such as calcium channel blockers, immunosuppressants, calmodulin antagonists, antihypertensive agent, steroids and antiparasitic agents have been shown to reverse MDR in vitro. However, the activity of these compounds is low, and various side effects have been observed drug in clinical trials. Thus, it is necessary to develop more active and less toxic agents which are capable of reversing MDR of tumor cells. In an effort to investigate new MDR reversal agents, we found that some pyrrolo[3,2-c] quinoline derivatives shown remarkable MDR reversal activity. They increased the cytotoxicity of paclitaxel, a well-known Pgp substrate, to Pgp-expressing cancer cells, but not to Pgp-negative cancer cells.

[PA1-5] [10/18/2001 (Thr) 14:00 - 17:00 / Hall D]

Susceptibility of Helicobacter pylori to newly synthesized antiulcer candidates

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Helicobacter pylori is a microaerophilic spiral bacterium and infection by the organism may cause gastritis in the human stomach.Futhermore, it is considered to be involved in the pathogenesis of peptic ulcers and the development of gastric carcinoma. In this study, we assessed the inhibitory activities of

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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