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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