Poster Presentations - Field A1. Pharmacology

[PA1-1] [10/18/2001 (Thr) 14:00 - 17:00 / Hall D]

Synthesis and Antiviral activity of Azido or Amino Substituted Acyclic Nucleosides

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HCMV(Human cytomegalovirus) is lethal virus, which causes blindness to AIDS patients. Genciclovir is a nucleoside analogue and has been a drug of choice for HCMV although it exhibited many problems such as low solubility. Since then, a number of compounds have been synthesized and evaluated for anti-HCMV activity in order to find new anti-HCMV drugs to overcome side effects of genciclovir. Based on the structure of genciclovir, novel acyclic nucleoside analogues to introduce N3 or NH2 on the acyclic moiety were synthesized via acid-catalyzed 1,4-addition as a key step. Synthesis and antiviral activity of our novel nucleoside analogues will be presented in detail.

[PA1-2] [10/18/2001 (Thr) 14:00 - 17:00 / Hall D]

Effect of Dopamine Agonists and Antagonists in the Immunological Aspect

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Dopamine receptor-related diseases such as Parkinson's disease or Schizophrenia require a long-term treatment with dopamine drugs, and it has been suggested that their immune functions are seriously altered. In this study, we tested whether dopamine drugs have any effect on the degranulation of mast cell (RBL-2H3) and nitric oxide production from macrophage cells (RAW 264.7), which presumably represent key aspects of the allergic and inflammatory reactions respectively. Among dopamine agonists (Dopamine, Bromocriptine, 7-OH-DPAT) and antagonists (Sulpiride, U99194A) tested, bromocriptine and 7-OH-DPAT showed potent inhibition of IgE receptor-mediated mast cell degranualtion (IC50 value, 10μM). On the other hand, LPS-induced nitric oxide induction from RAW 264.7 cell was markedly reduced by Bromocriptine and Dopamine (IC50 value, 10μM). In case of nitric oxide production, Bromocriptine inhibited the NOS expression in a dose- and time-dependent manner. Several signaling components of IgE receptor such as Syk, PLC γ2, MAPK, and M2 type pyruvate kinase were tested. However, the biochemical targets of dopamine drugs for the inhibition of mast cell degranultion were not clear. These results show that long-term uses of dopamine drugs could bring in immunological problems as well.
Dopamine drugs seem to inhibit the nitric oxide production from macrophages by directly inhibiting NOS expression, and prevent mast cell degranulation through mechanisms not identified yet.

[PA1-3] [10/18/2001 (Thr) 14:00 - 17:00 / Hall D]

Specificity and durability in the inhibition of mucin release from airway goblet cells by polycationic peptides

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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