mastocytoma P815 cells

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The inhibitory effects of tetrahydropapaverine on serotonin biosynthesis in serotonin-producing murine mastocytoma P815 cells were investigated. Tetrahydropapaverine at concentration ranges of 5-20 μM decreased serotonin content in a concentration-dependent manner in P815 cells and showed 42.1 % inhibition of serotonin content at 5.0 μM for 24 hr. The value of 50 % inhibitory concentration, IC_{50}, of tetrahydropapaverine was 6.2 μM. Under these conditions, tryptophan hydroxylase (EC 1.14.16.4, TPH) was inhibited for 24-36 hr after treatment with tetrahydropapaverine in P815 cells (49.1 % inhibition at 7.5 μM). In addition, tetrahydropapaverine inhibited the activity of TPH, prepared from the P815 cells (P815-TPH), with the IC_{50} value of 5.7 μM. Tetrahydropapaverine inhibited un-competitively P815-TPH with the substrate L-tryptophan, and inhibited non-competitively with the cofactor DL-6-methyl-5,6,7,8-tetrahydropteridin. The K_i value of tetrahydropapaverine with L-tryptophan was 10.1 μM. These data indicate that tetrahydropapaverine leads to a decrease in serotonin content by the inhibition of TPH activity in P815 cells.

[PA1-59] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

Anti-inflammatory mechanism of bee vemon in Raw 264.7 cells and Synoviocyte

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Bee venom (BV) has been utilized to relieve pain and to treat inflammatory diseases such as rheumatoid arthritis (RA). However, the molecular mechanism by which BV-induced anti-arthritis effect has been not reported yet. Therefore, in the present study we investigated anti-inflammatory effect of BV in a murine marcrophage cell line Raw 264.7 cell and synoviocyte obtained from RA patients. The present data showed that BV has a preventive effect on lipopolysaccharide (LPS) and sodium nitroprusside (SNP) induced induction of COX-2, cPLA2 and iNOS. BV also reduced the production of NO and PGE_2 dose dependently (0.5-5 ug/ml). BV also inactivated LPS and SNP-induced NF-κB, an important transcription factor regulating expression of COX-2, cPLA2 and iNOS. In addition, BV blocked NF-κB-dependent luciferase activity in Raw264.7 cells and THP-1 cells. Moreover, BV inhibited nuclear translocation of p50 subunit of NF-κB. These results showing that BV induced target disruption of p50 subunit in the activation of NF-κB, thereby inhibition of expression of genes involving in the inflammatory response may be critical in the anti-inflammatory effect of BV.

[PA1-60] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

A long duration of anticoagulant activity of acharan sulfate in vivo

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Introduction: We previously reported that a new glycosaminoglycan, acharan sulfate (AS) from the African giant snail Achatina fulica showed anticoagulation activity in vitro, but it was much less than that of heparin. In the present study, the anticoagulant activity of AS was investigated in vivo. Methods: AS and heparin were administered to rats in various concentrations and anticoagulant activities were measured. Both were also compared in a thrombin-induced Results: Intravenous administration of acharan sulfate prolonged the clotting time (APTT) in mice and rats in a dose-dependent manner. Although the activity was low in rats, it could be maintained over 5h after administration of AS (30 mg/kg). In contrast, the activity of heparin (5 mg/kg) was restored to the normal level after 3 h. In a thrombin-induced lethality model in mice AS (20 mg/kg) protected the lethality by 80 percent, while heparin (20 mg/kg) did not show any protective activity after 3.5 h administration of

drugs. We could also determine the plasma concentration of AS even 5 hours after administration to rats. Conclusion: These results show that the longer duration of AS in blood has a possibility to interact with coagulation factors.

[PA1-61] [2003-10-10 14:30 - 17:30 / Grand Ballroom Pre-function]

gInhibition effect of nitric oxide production and NF-κB nuclear translocation by 2-hydroxycinnamaldehyde in RAW 264.7 cells

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Cinnamaldehyde is the main component of cinnamon bark oil and show several biological activities such as anti-tumor, anti-fungal, anti-mutagenic and anti-inflammatory effects. A couple of studies have investigated how the natural compound exerts its anti-inflammatory effect. In despite of numerous investigations, the biological mechanism of effects belong to cinnamaldehyde remain unclear. We isolated 2-hydroxycinnamaldehyde(HCA) from the bark of Cinnamomun cassia Blume and reported a various of biological activities of HCA. HCA also exert several biological effects as much as that of cinnamalgehyde. In this study, we investigated anti-inflammatory effects of 2-hydroxycinnamaldehydes and putative mechanisms of its action in Raw 264.7 cells. HCA inhibited Nitric Oxide(NO) production in RAW 264.7 cells, which IC_{50} value was 1.3μM. Using gel shift assay, we showed that HCA inhibit activation of the transcription factor NF-κB, a central regulator of NOS and inflammatory response of body. We are also investigating of other molecular mechanism of HCA; Whether HCA can inhibit COX-2 expression, and thereby inhibit prostaglandin E2 production, another important inflammatory mediator through interfering NF-κB activation. We provide evidence that HCA is a potent anti-inflammatory agent and could serve as lead compounds for the development of pharmaceutically used anti-inflammatory remedies.

[PA2-1] [2003-10-10 09:00 - 13:00 / Grand Ballroom Pre-function]

Histone deacetylase inhibitor Trichostatin A enhanced the efficiency of adenovirus mediated gene transfer into non-small cell lung cancer cells

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One of the major limitations in using adenoviral vector for gene therapy is inefficient infection of host cells. The presence of coxsackievirus and adenovirus receptor (CAR) and α-integrin on cell surfaces is required for efficient adenovirus infection. In this study, we investigated the effect of trichostatin A, a histone deacetylase inhibitor, on transfection efficiency after transduction of adenovirus mediated $p16^{INK4a}$ gene transfer. In our previous study, $p16^{INK4a}$ tumor suppressor gene transfer in the non-small cell lung cancer cells (A549 cells) by transduction of recombinant adenovirus (Ad5CMV-p16) resulted in significant inhibition of cancer cell proliferation. We found that A549 cells treated with trichostaitn A prior to adenoviral vector (Ad5CMV-LacZ) infection had an increase in expression of β-galactosidase. $p16^{INK4a}$ gene expression was also increased in A549 cells after combination treatment of trichostatin A and Ad5CMV-p16 by RT-PCR. On the other hand, there was only weak combination effect of trichostatin A and Ad5CMV-p16 in normal lung cell lines (CCD-16, MRC-9). Currently, we are investigating the effect of trichostatin A on CAR expression level. These studies suggest that trichostatin A increases the efficiency of adenoviral transgene expression in cancer cells and this combination therapy may be useful in cancer gene therapy.

[PA2-2] [2003-10-10 09:00 - 13:00 / Grand Ballroom Pre-function]

Biodistribition of [^{125}I]-labeled biotinylated dendrimer derivatives for antibody pretargeting