PLA₂, cPLA₂), all reduced muscarinic receptor-mediated sAPP release, suggesting that all of the three PLA₂ isoforms might be involved in muscarinic receptor-mediated sAPP release. OxoM (a muscarinic receptor agonist)-induced calcium entry was reduced by pretreatment of manoside (an irreversible PLA₂ inhibitor), TEA-PC and BEL, but not AACOCF₃. In addition, we observed that pretreatment of SKF96365 and Gd³⁺ (inhibitors of CCE) inhibited OxoM–induced cPLA₂ activation but showed no significant effect on iPLA₂ activation induced by OxoM. These results indicate that although both calcium-independent iPLA₂ and sPLA₂ isoforms does not regulated by CCE, they participate in the muscarinic receptor-mediated activation of CCE, and then the CCE induced by PLA₂ isoform activation involves in muscarinic receptor-mediated increase in sAPP release. On the other hand, cPLA₂ activation induced by muscarinic receptor activation could regulate muscarinic receptor-mediated CCE followed by sAPP release.

[PB4-1] [ 2003-10-10 09:00 - 13:00 / Grand Ballroom Pre-function ]

Immuno-modulation effects of cefodizime, a cephalosporin, in rat dendritic cells
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According to recent reports, cefodizime (CEF), a third generation cephalosporin has the capability of chemotactic activity of neutrophils and monocytes and may act as the strong immuno-modulator. This study was planned to demonstrate whether CEF has the proposed effect on rat dendritic cells in vitro. Dendritic cells were taken from rat spleen tissue and cultured for a week. The obtained dendritic cells were treated with 10μg/ml, 50μg/ml, 100μg/ml cefodizime and 10IU/ml IFN-γ+1μg/ml LPS. Through the studies, we found that cytokines, such as IL-1β, IL-6, IL-12, were induced by cefodizime in dendritic cells. This result indicated that cefodizime can be used as one of adjuvant therapies in diseases that need an immuno-boosts during a main treatment, i.e. cancer therapy. In conclusion, we recognized that cefodizime may induce the activation macrophage, NK cell, CTL, B cell in collaboration with activated dendritic cells. The present study suggests that cefodizime may extend its major role for antibiotics to multi-potential immuno-modulators.

[PB4-2] [ 2003-10-10 09:00 - 13:00 / Grand Ballroom Pre-function ]

Antitumor activity of Acanthopanax senticosus extract and its possible immunological mechanism
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Antitumor and immunomodulatory activities of an aqueous extract (GF100) of Acanthopanax senticosus was examined. In experimental lung metastasis of colon26-M3.1 carcinoma cells, intravenous (i.v.) administration of GF100 2 days before tumor inoculation significantly inhibited lung metastasis in a dose-dependant manner. The i.v. administration of GF100 also exhibited the therapeutic effect on tumor metastasis of colon26-M3.1 cells, when it was injected 1 day after tumor inoculation. In an in vitro cytotoxicity analysis, GF100 at the concentration up to 1000 μg/ml did not affect the growth of colon26-M3.1 cells. In contrast, GF100 enhanced the responsiveness to a mitogen, concanavalin A (ConA), of splenocytes in a dose-dependent manner. Peritoneal macrophages stimulated with GF100 produced various cytokines such as IL-1β, TNF-α, IL-12 and IFN-γ in an in vitro experiment. The macrophages obtained from the mice which were injected with GF100 (500 μg) 3 days before the assay showed significantly higher tumoricidal activity against tumor cells than that of the untreated macrophages. In addition, the i.v. administration of GF100 significantly augmented NK cytotoxicity to Yac-1 cells. The depletion of NK cells by injection of rabbit anti-asialo GM1 serum completely abolished the inhibitory effect of GF100 on lung metastasis of colon26-M3.1 cells.

[PB4-3] [ 2003-10-10 09:00 - 13:00 / Grand Ballroom Pre-function ]
Dendritic Cell as an effective cancer immuno-cell therapy module I: Anti-tumor effect of cultured DCs in murine leukemia model
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As a potent antigen presenting cells and a powerful inducer of antigen specific immunity including cytotoxic T cell activity, dendritic cells (DCs) are being considered as a promising anti-tumor therapeutic module. Unlike solid tumors, leukemia is the hematologic malignancy involving immune effector cells. The expected usage of DCs in leukemia is the treatment of minimal residual disease (MRD) after the remission or stem cell transplantation. In this study, syngeneic leukemia cells were inoculated intra-venously into the mouse (WEHI-3 into the Balb/c), and the autologous tumor cell lysate pulsed DCs were injected as a therapeutic module twice in two weeks. To mimic the minimal residual disease (MRD), one day before the first DC injection (3-5 X105 DCs/mouse, i.p.), 5X104 WEHI-3 cells inoculated i.v. Three weeks after final DC injection, the tumor formation and the growth were observed as well as the DC-induced systemic anti-tumor immunity with the splenic lymphocyte. Bone marrow origin mouse myeloid-DCs were cultured with GM-CSF and IL-4 for 7 days and pulsed with leukemic cell lysate (50ug/ml protein, for 18hrs). Compared to the saline treated group, DC or pulsed DC injected group did not make the tumor as observed by gross or microscopic section of tissues. Tumor specific T cell proliferations were significantly increased in DC or pulsed-DC injected group as were measured by CFSE-staining. The proportion of IFN-r producing CD8+ cells (flow cytometry) and the IFN-r production (ELISA) were increased significantly in DC treated group. The data indicating the promising anti-leukemic effect of cultured DCs in MRD model by inducing the tumor specific immunity.

[PB4-4] [2003-10-10 09:00 - 13:00 / Grand Ballroom Pre-function]

Immunomodulatory activity of betulinic acid from Lycopus lucidus in murine macrophage RAW 264.7 cells
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Betulinic acid (BA), a pentacyclic triterpene isolated from Lycopus lucidus, has been reported to be a selective inducer of apoptosis in various human tumor cells. It also exhibits anti-inflammatory and immunomodulatory properties. Due to its high level of these activities and lack of toxicity, BA is an attractive and promising compound as a new drug and recently undergoing preclinical development as an immunomodulators. How BA mediates these matters is not known yet. Because of the critical role of the monocytes and tissue macrophages in inflammatory and immune responses, we postulated that BA modulates the activity of its immunomodulatory properties at least two groups of protein mediators of inflammation, Interlukin-1β (IL-1β) and the Tumor necrosis factor-α (TNF-α). In this study we investigated the effect of BA on murine macrophage RAW 264.7 cells to activate macrophage at low concentration (2.5 μg/ml) and induced pro-inflammatory cytokines. The enhanced surface CD40 molecule was expressed on the resting cells at 2.5 μg/ml of BA or LPS/BA. Furthermore, BA enhanced TNF-α induced apoptosis. Overall, our results indicated that BA induced activation of macrophage and pro-inflammatory cytokines. This may provide a molecular basis for the ability of BA to mediate macrophage, suppress inflammation, and modulate the immune response.

[PB4-5] [2003-10-10 09:00 - 13:00 / Grand Ballroom Pre-function]

The Effect of allicin on radiation-induced expression of ICAM-1 and activation of JNK and p38 MAP kinase pathway in human endothelial cells.
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