[PB4-3] [04/21/2000 (Fri) 10:30 - 11:30 / [1st Fl, Bldg 3]]

Regulatory effect of chondroitin sulfates derived from human placenta on mitogen-induced activation of murine splenocytes.

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The glycosaminoglycans (GAG) are the major constituents of placenta connective tissue. The analysis of the proteoglycan extracted from placenta confirmed the presence of chondroitin sulfate which consist of various proportions of both 4-sulfated and 6-sulfated disaccharide repeats. To investigate the activity of placenta chondroitin sulfates regulating the function of immune-related cells, we examined their effects on responsiveness of splenocytes to mitogens such as ConA and LPS. Chondroitin sulfate fractions eluted with 0.2M and 2.0M, but not 0.5M, NaCl suppressed the proliferation of splenocytes in a dose-dependent manner. When the cultures were co-incubated with T-cell mitogen, Con A, both 0.2M- and 2.0M-eluted chondroitin sulfate fractions also markedly suppressed the proliferation of splenocytes, indicating that the chondroitin sulfate fractions play a role in down-regulation of T-cell activation. In contrast, in an experiment that B-cell mitogen, LPS, was added to the cultures, these chondroitin sulfates (0.2M- and 2.0M-eluted fractions) showed just a slight effect on LPS-stimulated splenocytes. Interestingly, 0.5M-eluted chondroitin sulfate fraction had no effect on the proliferation of both ConA- and LPS-stimulated. Taken together, it suggests that human placenta contains chondroitin sulfates which are effective for regulation of immune-related cells, and those proteoglycans from human placenta with 0.2M as well as 2.0M NaCl are responsible for the immuno-regulatory effect, especially down-regulation of ConA-stimulated T-lymphocytes. This paper reports the presence of chondroitin sulfate from the human placenta and its suppression activity of the function of immune-related cells.

[PB4-4] [04/21/2000 (Fri) 10:30 - 11:30 / [1st Fl, Bldg 3]]

Bovine lactoferrin down-regulate T-cell function during SEB-induced septicemia

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It is well-known that breast milk is thought to be a beneficial source to provide the breast-fed host with host defense systems against pathogenesis of infections. Among many molecules contained in milk, lactoferrin (LF), an iron-binding glycoprotein (M.W. 80kDa) secreted from neutrophils and epithelial cells in the mammary gland, has been shown to possess a variety of biological functions such as antibacterial activity and regulation of immune responses. In a series of our study on biological activities of milk proteins, we first found that bovine lactoferrin (LF-B) have antitumor activity to inhibit experimental metastasis of murine tumor cells. Here we show immuno-regulatory effect of LF-B on CD3- mediated activation of splenic T cells in mice.
In the experimental model to activate T cells, splenic T cells obtained from Balb/c mice were treated with anti-CD3 monoclonal antibody for 24 hr, and the level of various cytokines such as IL-2, IL-4, IL-6 and IFN-Y in the supernatant of the cultures was measured by specific ELISA kits. Pre-treatment with LF-B before T cell activation by anti-CD3 antibody markedly suppressed the production of cytokines, and inhibited DNA synthesis. Furthermore, T cells pre-incubated with LF-B followed by anti-CD3 antibody treatment showed significantly decreased expression of CD25 (IL-2Rα). The suppressive effect of LF-B on T cell activation was not restored by addition of T cell activating factors like IL-2 and IFN-Y. Analysis of signal pathway related to the suppressive effect of LF-B revealed that LF-B resulted in down-regulation of tyrosine- dependent phosphorylation of PLC-Y1 during CD3-mediated activation of T cells. Finally we found that LF-B inhibited cytolytic T

lymphocyte (CTL) activity against allogenic tumor cells in vivo.

[PB4-5] [04/21/2000 (Fri) 10:30 - 11:30 / [1st Fl, Bldg 3]]

Induction of secretory and cellular activities by pneumococcal teichoicated fragments in macrophages

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Bacterial components and their derivatives have been reported to mediate various immunomodulating activities and to activate immune cells including macrophage. In this study, the secretory and cellular macrophage response to teichoicated fragments from pneumococcal cell wall subcomponent were examined. Tumoricidal activity was measured by MTT assay and secretory molecules were assessed by biological assay. After stimulation of macrophages with teichoicated fragments (100㎍/ml) for 18hrs, secretion of TNF-α, nitrite and hydrogen peroxide were significantly increased as compared to medium-treated control. In addition, tumorcidal activity of teichoicated fragments-treated macrophages was enhanced, whereas production of IL-1 and IL-6, and phagocytic activity were not induced. These data suggest that teichoicated fragments is a potent inducer of macrophage secretory and cellular activities.

[PB4-6] [04/21/2000 (Fri) 10:30 - 11:30 / [1st Fl, Bldg 3]]

A muramyl dipeptide derivative [MDP-Lys(L18)] enhances antitumor immunity raised by an inactivated tumor vaccine.

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We examine the immunostimulating activity of MDP-Lys(L18), a lipophilic derivative of muramyl dipeptide (MDP) which is a biological subunit of bacteria cell wall, to augment antitumor immunity induced by X-irradiated tumor cells against highly metastatic B16-BL6 melanoma cells. Mice immunized intradermally (i.d.) with the mixture of X-irradiated B16-BL6 cells and MDP-Lys(L18) [Vac+MDP-Lys(L18)] followed by intravenous (i.v.) inoculation of 104 viable tumor cells 7 days after immunization, showed significant inhibition of experimental lung metastasis of B16-BL6 melanoma cells. The most effective immunization for the prophylactic inhibition of tumor metastasis was obtained from the mixture of 100 μg of MDP-Lys(L18) and 104 X-irradiatied tumor vaccine. Furthermore, immunization of mice with Vac+MDP-Lys(L18) 3 days after tumor challenge resulted in significant inhibition of lung metastasis of B16-BL6 melanoma cells in experimental lung metastasis model. Similarly the administration of Vac+ MDP-Lys(L18) 1 or 7 days after tumor amputation markedly inhibited tumor metastasis of B16-BL6 in a spontaneous lung metastasis model. When Vac+ MDP-Lys(L18) was i.d. administered 3 days after subcutaneous (s.c.) inoculation of tumor cells (5X105/site) on the back, mice treated with Vac+MDP-Lys(L18) showed significantly inhibited tumor growth of B16-BL6 cells on day 20. These results suggest that MDP-Lys(L18) is able to enhance antitumor activity induced by X-irradiated tumor vaccine to reduce lung metastasis of tumor cells, and is a potent immunomodulating agent which may be applied prophylactically as well as therapeutically to treatment of cancer metastasis.

[PC1-1] [04/21/2000 (Fri) 14:50 - 15:50 / [1st Fl, Bldg 3]]

Metabolism of acyclovir, ganciclovir and penciclovir in infected cells with