[PB4-12] [10/17/2002 (Thr) 13:30 - 16:30 / Hall C]

Immune responses to synthetic peptides of RSV F protein

Kim JungKwon[oa], Lee HoanJong[b], Kim Hong-Jin[a]

[a]College of Pharmacy, Chung-Ang University, Seoul, 156-756, Korea;[b]Dept. of Pediatrics, College of medicine, Seoul National University, 110-744, Korea

The fusion (F) protein of respiratory syncytial virus(RSV) is an important antigen in including cross-protective immunity with neutralizing activity. Two peptides homologous to amino acid 205-225(F/205-225) and 255-278 (F/255-278) of the F glycoprotein of RSV containing B cell and T cell epitope were synthesized and then conjugated with KLH. To evaluate the immunological activities of the two conjugated vaccines, the vaccines were administrated into BALB/c mice for times by the intranasal(i.n) route in the presence of cholera toxin B(CTB) as a mucosal adjuvant. Each the peptides specific serum IgG responses and saliva IgA were detected after a second immunization, and a third immumization, respectively. Combined immunization of F/205-225 and F/255-278 also had the similar immunological response in the IgG and IgA levels with that of F/205-225 or F/255-278 alone. These results indicate that the two peptide-conjugate vaccines could be candidates for the development of RSV vaccines.

[PB4-13] [10/17/2002 (Thr) 13:30 - 16:30 / Hall C]

Anti-/pro-apoptotic regulatory potentials of LPS/IFN-γ in the mulnutrition induced macrophage

Cho SeongJun[o], Rhee DongKwon, Pyo SuhkNeung

College of Pharmacy, Sungkyunkwan University, Suwon, 440-746, Kyunggi-Do, South Korea

Macrophage activated by LPS/IFN-γ play a important role in imflammation, innate immunity and tumor immunity. The recent report has indicated that LPS treated bone marrow macrophages were induced apoptosis, but IFN-γ protects from apoptosis induced by several stimuli in complete medium condition (Jordi et al., Immunity, Vol.11, 103-113, 1999). Since relationship between LPS or IFN-γ and apoptosis in malnutirition (conditional medium condition;without amino acid, serum) is unknown, we investigated the anti- or pro-apoptotic potentials of LPS or IFN-γ to the malnutirition induced macrophage. Peritoneal macrophages were isolated from mouse, purified macrophages were treated with LPS or IFN-γ in complete medium condition. After treatment, cells were further incubated in conditional medium condition to induce apoptosis. Apoptotic cells were determined by MTT assay, Annexin V assay, PI staining and DNA fragmentation assay. Apoptotic cells of LPS treated macrophage were increased as compared with those of untreated macrophage. However, treatment of cells with IFN-γ resulted in the enhancement of apoptosis. These data demonstrate that LPS or IFN-γ regulates apoptosis of macrophage by different mechanism in malnutrition. Moreover, these results suggest that apoptotic pathway of LPS or IFN-γ treated macrophage is regulated differently in manutrition and complete medium condition.

[PB4-14] [10/17/2002 (Thr) 13:30 - 16:30 / Hall C]

The Production of IFN-γ by 3LL/TNF-α-Activated Macrophages Requires p38, JAK-2 Signalling and is Enhanced by New Protein Synthesis.

[1]Park DaeSup[o], [1]Cho SeongJun, [1]Baeg HyeKyoung, [2]Baek SoYoung, [2]Lee HyunAh, [1]Pyo SuhkNeung.

[1]College of Pharmacy, Sungkyunkwan University, SUWON, SOUTH KOREA;[2]The Cancer Center, Samsung Medical Center, SEOUL, SOUTH KOREA

Macrophages have been known to play an essential role in tumor angiogenesis and produce a number of growth stimulators and inhibitors. Thus macrophages appear to influence every stage of angiogenesis.
In this report, TNF-α was able to induce the production of IFN-γ in cancer cell-contacted macrophage. TNF-α alone released relatively little IFN-γ whereas live tumor cells (3L L) alone releasd IFN-γ markedly from macrophage. However, TNF-α and 3LL together enhanced IFN-γ release synergistically. The effects of TNF-α on

the production of IFN-γ in tumor environments were evaluated by ELISA and confirmed by RT-PCR.
Using specific inhibitors, we investigated the mechanisms underlying synergistic enhancement of IFN-γ expression in murine macrophage by TNF-α and 3LL. Since TNF-α is sufficient to activate nuclear factor κB (NF-κB) and several mitogen-activated protein kinase (MAPK) pathway, the inhibitor SN50, which specifically blocked NF-κB pathway and the inhibitor SB203580, which specifically inhibited enzymatic activity of cellular p38 MAP Kinase were utilized. Inhibition of p38 MAP Kinase activation abolished 3LL and TNF-α stimulated IFN-γ production for 20 hr treatment, but inhibition of NF-κB did not. In addition, inhibition of JAK-2 activity with the specific inhibitor AG-490 prevented the expression of IFN-γ mRNA for 20 hr treatment. Furthermore, the ability of TNF-α and 3LL to enhance IFN-γ production appears to require new TNF-α stimulated gene expression, because it is blocked by the reversible protein synthesis inhibitor cycloheximide.
Our data suggest that enhancement of IFN-γ production by TNF-α is mediated p38 in early time, and JAK-2 in late time, and TNF-α stimulated IFN-γ production in tumor environment requires new protein synthesis.

[PB4-15] [10/17/2002 (Thr) 13:30 - 16:30 / Hall C]

Functional Importance of TRAF6-Binding Motif in IL-1 Mediated Signal Transduction

Yim Mijung[O]

College of Pharmacy, Sookmyung Women's University

Crystal structure of TRAF6 in complex with TRAF6-binding sites from CD40 was previously determined. The structure revealed a distinct TRAF6-binding groove of CD40, the key structural determinant of interaction. The structural information leads to a proposed TRAF6-binding motif. This allows the identification of TRAF6-binding sequences in the hIRAK protein, whose functional requirement in IL-1 mediated signal transduction is further demonstrated using site-directed mutagenesis. The mutational effects of hIRAK on the down-stream NF-κB signaling shows the importance of the TRAF6 interface for signaling by IL-1.

[PB4-16] [10/17/2002 (Thr) 13:30 - 16:30 / Hall C]

Modulation of the activity of ex vivo cultured leukemic-DC by L-ascorbic acid (LAA)

Lee Hyunah[O], Baek SoYoung, Lee HongGi, Kim KiHyun, Park ChanHyung

The Cancer Center, Div. Hematology/Oncology, Samsung Medical Center, Sungkyunkwan University of Medicine, Seoul, Korea

L-ascorbic acid (LAA) was shown to modulate the in vitro growth of leukemic-colony forming cells from patients with acute myelogeneous leukemia (AML). Dendritic cells (DCs) were successfully cultured from the leukemic blasts by us and others. The effects of LAA on the ex vivo cultured leukemic-DC were studied. Plastic adherent cells from the leukemic blasts were cultured with GM-CSF and IL-4 (each 103 U/ml) with or without LAA (300 uM) for 7 days and harvested. Surface marker phenotyping indicated the cultured leukemic-DCs were HLA-DR+++, CD1a++, and CD80+ (98.86%, 23.46% and 13.35%, respectively). LAA reduced the proportion of HLA-DR+ (48.60%) and CD1a+ cells (11.84%). LAA lowered the leukemic-DC stimulated proliferation of cord blood cells (849.47% vs. 2685.16% of responder only) and CTL activity against HL-60 (38.9% vs. 71.7% cytotoxicity at E:T ratio 50:1). These data together with the reduction of leukemic-DC production of IL-12 by LAA suggest that the LAA may suppress the leukemic-DC activation.

Poster Presentations - Field C1. Biochemistry

[PC1-1] [10/17/2002 (Thr) 13:30 - 16:30 / Hall C]