

component and five other herbs. On the basis of overall data of constituent herbs, effects of aqueous extract from PAE was evaluated on immunomodulatory activity. Spleenocytes was isolated from mice treated with PAE of 2 mg, 10 mg and 50 mg per mouse. PAE significantly proliferated spleen cells to 2.5-3.4 fold as compared with control data. PAE also induced Th1 type cytokines such as IL-2 and r-IFN, while it didn't induce Th-2 type cytokine(IL-4). PAE increased tumor necrosis factor- $\alpha$ (TNF- $\alpha$ ) production in RAW cells in a dose-dependent manner and cytostatic activity in L929, macrophage-sensitive cells. These results suggest that PAE has immunomodulatory activity.

[PB4-3] [ 10/18/2001 (Thr) 14:00 - 17:00 / Hall D ]

### Antitumor immunomodulatory activity of Protein-Polysaccharide fraction prepared from Korean wild mushroom *Psathyrella velutina*

Lee Ji-Seon, Chung Kyeong-Soo

College of Pharmacy, Chung-Nam National University, Daejeon, 305-764, Korea

A protein-polysaccharide fraction of a Korean wild mushroom *Psathyrella velutina* was prepared and its antitumor immunomodulatory activity was investigated. When the protein-polysaccharide fraction PVP (= *Psathyrella velutina* protein-polysaccharide) was administered once daily for seven days from days 1 to day 7 into male ICR mice which were implanted with  $1 \times 10^5$  cells of sarcoma 180 tumor cells into the peritoneum on day 4, it inhibited the growth of sarcoma 180 cells by 92.8 %. In XTT assay, PVP also exerted in vitro anti-proliferation activity on U-937, a human monoblastoid cell line, as well as sarcoma 180 cells. PVP showed marked stimulatory activity on the immune system in that it induced the accumulation of PEC (the stimulation index (SI) = 4.90 at 100 mg/kg), stimulated the BALB/c mouse splenic lymphocytes to form lymphoblasts (SI = 5.75 at 100  $\mu$ g/ml), and upregulated the expression of CD25 molecules (IL-2 receptor  $\alpha$ -chain). All these results strongly support that PVP exerts its antitumor activity through stimulation of the immune system as well as direct anti-proliferative activity on the tumor cells.

[PB4-4] [ 10/18/2001 (Thr) 14:00 - 17:00 / Hall D ]

### IFN- $\gamma$ induction by TNF- $\alpha$ in mixed murine peritoneal macrophage-Tumor cell cultures

Kwak Jangdong<sup>o</sup>, Cho Seongjun, Baek Soyoung, Lee Hyunah, Pyo Suhkneung

College of Pharmacy, Sungkyunkwan University, Suwon, Korea, The Cancer center, Samsung Medical Center, Seoul, Korea

Tumor angiogenesis is believed to be induced due to increased production of angiogenic factors (such as TNF- $\alpha$ ) and decreased production of angiogenic inhibitors (such as IFN) by cancer cells, vascular endothelial cells, and other stromal cell types. Of stroma constituents, macrophages have an essential role in tumor angiogenesis and produce a number of growth stimulators and inhibitors. Thus macrophages are expected to influence every stage of angiogenesis. The effects of TNF- $\alpha$  on the production of IFN- $\gamma$  in resident, LPS-pretreated and cancer cell-contacted murine macrophages were evaluated by ELISA assay. Macrophages were treated with various dose (1, 5, 25 ng/ml) of TNF- $\alpha$  for 24, 48 and 72 hours. TNF- $\alpha$  was able to induce the production of IFN- $\gamma$  with time in LPS pretreated and cancer cell-contacted macrophages, whereas IFN- $\gamma$  was not detected in resident macrophages. These results were also confirmed by RT-PCR. To examine whether TNF- $\alpha$  induce IFN- $\gamma$  synthesis in interactions of macrophages with tumor cells in vivo,  $2 \times 10^5$  syngenic tumor cells (3LL or B16F10) were injected i.p. On day 11, macrophages that were purified from peritoneal exudate cells were treated with various dose of (1, 5, 25 ng/ml) TNF- $\alpha$  for 24, 48 and 72 hours. Treatment with TNF- $\alpha$  induced the

production of IFN- $\gamma$  in macrophages. Taken together, these results suggest TNF- $\alpha$  treatment induces the production of IFN- $\gamma$  in murine macrophages from tumor environment.

[PB4-5] [ 10/18/2001 (Thr) 14:00 - 17:00 / Hall D ]

### Immune effects of pedunculagin on Dendritic cell.

Kim HanJun, Oh WonSik, Lee Dolk<sup>o</sup>

Department of Pharmacology, College of Pharmacy, Chung Ang University, Seoul, Korea

Dendritic cells are known as the most potent antigen presenting cell(APC). Currently, many studies on an activation of dendritic cells are actively ongoing because dendritic cells are known to be well against the infected cells by cancers or viruses. In line with this, the study was focused on the activation of dendritic cells by using pedunculagin, which is hydrolytic ellagitannin. In vitro, the total RNAs were extracted from murine dendritic cell at 4, 8, 12, 24hr after the application of 1, 10, 100 $\mu$ g/ml of pedunculagin with no other stimulators. However, it is considered there has been no great deal in expressing IL-10 mRNA, telling that pedunculagins are not that much related to the expression of IL-10 mRNA. This result shows that pedunculagin does not generate the action of suppression against INF or macrophage by IL-10 in dendritic cell of mouse.

[PB4-6] [ 10/18/2001 (Thr) 14:00 - 17:00 / Hall D ]

### The role of TNF- $\alpha$ in tissue-dependent production of IFN- $\gamma$ by LPS from macrophages.

Baek Soyoung<sup>o</sup>, Kwak Jang-Dong<sup>1</sup>, Pyo Shuk-Neung<sup>1</sup>, Lee Hyunah

The cancer center, Samsung Medical Center, The college of Pharmacy, Sungkyunkwan University, Seoul Korea

Macrophages have an crucial roles in tumor angiogenesis by producing cytokines and growth factors. Lipopolysaccharides(LPS) is known to stimulate the macrophages to produce an angiogenic cytokines like TNF- $\alpha$  or IFN- $\gamma$ , an anti-angiogenic factor. In this study, we examined the differential effect of LPS on residential macrophages from the spleen and peritoneal cavity to produce the angiogenesis-related cytokines. LPS (100ng/ml) activated the residential splenic macrophages to produce IFN- $\gamma$  (1968 pg/ml, 484% of control) and TNF- $\alpha$  (429 pg/ml, 339% of control). On the other hand, peritoneal macrophages did not respond to LPS to produce cytokines (under detection limit by ELISA). To mimic the macrophages in tumor environment, Mac 1+ cells were purified by magnetic beads from the peritoneal cavity of C57BL/6 mice injected with syngeneic B16F10 melanoma cells for 11 days. Cells from the tumor environment were activated by LPS to produce IFN- $\gamma$  (26 pg/ml). Anti-TNF- $\alpha$  antibody increased the IFN- $\gamma$  production (46 pg/ml, 178% of LPS alone). Data suggested that LPS may modulate the macrophages to produce angiogenesis-related cytokines in tissue-dependent manner. And the production of IFN- $\gamma$  and TNF- $\alpha$  from the macrophages in tumor environment may imply the control of angiogenic switch. This study was supported by Korea Science and Engineering foundation, 2000.

[PB4-7] [ 10/18/2001 (Thr) 14:00 - 17:00 / Hall D ]

### Immune activating effects of pedunculagin