Department of Pharmacology, Chung Ang University

It has been reported that extremely low frequency magnetic field (ELF MF) is related to alteration of nitric oxide synthase (NOS) activity in vitro. To confirm this result, we studied effects of MF on nitric oxide (NO) pathway in central nerve system (CNS) in vivo. Rats were exposed to sham or 20 G MF (60Hz) for 5 days. In drug experiment, NNA, NOS inhibitor, was administered (10mg/kg, i.p.) once a day during MF exposure. We measured NOS activity, c-GMP level in brain, and pain threshold before and after sham or MF exposure, and NNA. MF exposure increased NOx and c-GMP level in striatum, hippocampus and thalamus, in which this elevation of NOx and c-GMP by MF was blocked by NNA treatment. There was no change of NOx or c-GMP by MF in cortex and cerebellum. Response to thermal stimuli, reported to change according to NO level in brain, was decreased by MF and recovered to normal state by NNA treatment during MF exposure. From these results, we suggest that MF exposure activates NOS pathway in brain, which implicates that MF may alter the brain functions such as behaviors, mood and memory.

Poster Presentations - Field B4. Immunology

[PB4-1] [10/18/2001 (Thr) 14:00 - 17:00 / Hall D]

Mechanism of Allicin-induced apoptosis in Human Gastric Epithelial Cell Lines

Park SY°, Rhee DK , Pyo S

College of Phamacy, Sungkyunkwan University

Garlic (*Allium sativum*) may be one food that contributes constituents that significantly affect human health. Garlic compounds have been shown to inhibit growth of tumors and to modulate the activity of carcinogenesis. Allicin (diallyl sulfide, DAS) is a main component of garlic. Since the mechanism of allicin in tumor growth inhibition remains unclear, we examined whether allicin affects each of the apoptotic parameters measured, i.e., viability, cell cycle arrest and sub-G1 content, morphological change, caspase-3 and -8 activation , and DNA fragmentation. The *in vitro* effect of allicin (5㎍/㎖, 10㎍/㎖, and 20㎍/㎖) on the growth of gastric epithelial cells (Kato III$^{p53(-)}$) was evaluated, and allicin had the inhibitory effect of tumors cells growth in a dose dependent manner. Our data also showed that the inhibitory effect of allicin on proliferation of tumor cells was associated with cell cycle arrest from S to G2M phase transition and with induction of apoptosis. The apoptosis of tumor cells was confirmed by DNA ladder formation and morphological change. However, activation of caspase-3 and -8 was not observed during allicin-induced cell death. In addition, morphological changes and sub-G1 contents was not inhibited by peptide caspase inhibitor(Z-VAD-FMK). These data suggest that allicin-induced cell death is caspases independent and p53 independent.

[PB4-2] [10/18/2001 (Thr) 14:00 - 17:00 / Hall D]

Study on immunomodulatory effect of a prescription including Agaricus blazei murrill

Lee JooRyung, Woo HeeJong+ Kim SungHoon

Department of Oncology, Graduate school of East-West medicine, Kyung Hee University, Yonin, Korea, +Department of Immunology, College of Veterinary Medicine, Seoul National University Suwon, Korea

Agaricus blazei murrill was reported to have immunostimulating and antitumor activities just like other mushrooms. Thus, we formulated a prescription including Agaricus blazei murrill(PAM) as a major

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 speen 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-a(TNF-a) 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, Daejon, 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 1×10^5 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 exherted 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 ㎎/㎏), stimulated the BALB/c mouse splenic lymphocytes to form lymphoblasts (SI = 5.75 at 100 ㎍/㎖), and upregulated the expression of CD25 molecules (IL-2 receptor α-chain). All these results strongly support that PVP exherts 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-γ induction by TNF-α in mixed murine peritoneal macrophage-Tumor cell cultures

Kwak Jangdong°, 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-α) 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-α on the production of IFN-γ in resident , LPS-pretreated and cancer cell-contacted murine macropahges were evaluated by ELISA assay. Macrophages were treated with various dose (1, 5, 25 ng/㎖) of TNF-α for 24, 48 and 72hous. TNF-α was able to induce the production of IFN-γ with time in LPS pretreated and cancer cell-contacted macrophages, whereas IFN-γ was not detected in resident macrophages. These results were also confirmed by RT-PCR. To examine whether TNF-α induce IFN-γ synthesis in interactions of macrophages with tumor cells in vivo, 2×10^5 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/㎖) TNF-α for 24, 48 and 72hours. Treatment with TNF-α induced the