

demonstrate that IFN- $\gamma$  enhances apoptosis in malnutrition-induced macrophages, suggesting that apoptotic regulatory mechanism of IFN- $\gamma$  in malnutrition-induced macrophage is different from complete medium condition.

[PB4-25] [ 2003-10-10 09:00 - 13:00 / Grand Ballroom Pre-function ]

**Gamma-irradiation induced expression of ICAM-1 on human neuroblastoma cells is mediated by the activation of p38 MAP kinase.**

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Since radiotherapy has been suspected to promote tumor metastasis and the presence of increase levels of adhesion molecules have implications for metastasis, we decided to investigate whether gamma-irradiation alters the expression of intercellular adhesion molecule-1 (ICAM-1) on neuroblastoma cells and the activities of relevant intracellular signaling molecules. In the present study, the relative of ICAM-1 expression under gamma-irradiated neuroblastoma cells were assessed by Western blot analysis. Our data indicated that gamma-irradiated neuroblastoma cells significantly increased the ICAM-1 protein level in a dose dependent manner. Also, we showed that treatment of neuroblastoma cells with gamma-irradiation resulted in increase NO release. The effect of gamma-irradiation on activation of NF- $\kappa$ B transcription factor was determined by Western Blotting and our data showed that NF- $\kappa$ B is not involved by gamma-irradiation. We further investigated the effect of PKC, p38 and MEK inhibitors on radiation-induced expression of ICAM-1 by Western Blotting and demonstrated that ICAM-1 expression was partially blocked by p38 inhibitor. We also estimated the NO production in these inhibitors-treated groups and showed that p38 inhibitor significantly increased the NO production in gamma-irradiated cells. These results suggest that NF- $\kappa$ B transcription factor is not involved in gamma-irradiated ICAM-1 expression and the NO production and ICAM-1 expression by gamma-irradiation may be mediated through p38 kinase pathway in neuroblastoma cells.

[PB4-26] [ 2003-10-10 09:00 - 13:00 / Grand Ballroom Pre-function ]

**Release of the Pro-inflammatory Cytokines and Facilitation of Immune Response in LPS-induced Activation of Macrophage by Crude Cordycepin Containing Adenosine (CCCA) from Cordyceps militaris**

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The in vitro effects of extracted fractions of *C. militaris* on the secretion of cytokines in murine macrophage cell line, RAW 264.7 were studied. F1 (crude cordycepin containing adenosine), F2 (ethanol precipitation), F3 (ethanol soluble supernatant) and F4 (fraction of through SK-1B) significantly stimulated the production of cytokine and nitric oxide (NO) on murine macrophage cell line RAW264.7. We examined how the ethanol extract of *C. militaris* regulates production of interleukine 1-beta(IL-1 $\beta$ ), tumor necrosis factor-alpha (TNF- $\alpha$ ), and NO in vitro. F1 (5  $\mu$ g/ml) and F4 (5  $\mu$ g/ml) inhibit these inflammatory mediators in lipopolysaccharide (LPS)-stimulated murine macrophage cell line RAW264.7 by suppressing protein expression of IL-1 $\beta$ , TNF- $\alpha$ , inducible nitric oxide synthase, and cyclooxygenase-2. Moreover, the extract suppresses the nuclear transcription factor (NF- $\kappa$ B)-kappa B activation in LPS-stimulated RAW264.7 cells. However, the production of the macrophage cytokines, IL-1 and TNF- $\alpha$ , by RAW 264.7 treated with F3 was examined from 20 up to 40  $\mu$ g/ml with dose dependent manner. NO production was also increased when cells were exposed to combination of LPS and F3 from 1.2 up to 40  $\mu$ g/ml. These results indicate that the *C. militaris* ethanol extract suppresses inflammation through suppression of NF- $\kappa$ B-dependent inflammatory protein expression, suggesting that the *C. militaris* extract may be beneficial for treatment of endotoxin shock or sepsis.