Augmentation of Macrophage Antitumor Activities and Nitric Oxide Production by Oregonin

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Oregonin, a diarylheptanoid derivative from Alnus hirsuta Turcz, Betulaceae was evaluated on its antitumor activity. Oregonin is a novel immunomodulator augmenting macrophage activity, which associated with the anti-tumor functions. To investigate the cytotoxicity of oregonin on tumor cells, MTT assays and NO production tests have performed to examine the influence of oregonin on macrophage in detail. The tumoricidal activity was evaluated by the cell viability through the method of MTT assay. The measurement of cytotoxicity in the oregonin-treated group both in vitro and in vivo showed a significant difference from that of control group. In vivo, oregonin significantly increased NO production, dose-dependently. In addition, in vitro, thioglycolate-induced inflammatory macrophages increased NO production, dose-dependently after the incubation. These results may indicate that oregonin reacts similarly to both the inflammatory and non-inflammatory macrophages.

[PB4-5] [04/18/2002 (Thr) 14:00 - 17:00 / Hall E]

Enhancement of NK Cytotoxicity, Antimetastasis and Elongation Effect of Survival Time in B16-F10 Melanoma Cells by Oregonin

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Oregonin, a diarylheptanoid derivative purified from Alnus hirsuta Turcz, Betulaceae, was investigated to see about its antitumor activity. Oregonin is a novel immunomodulator, which augments the activation of natural killer cell that leads a powerful anti-tumor activity. To evaluste the cytotoxicity of oregonin against tumor cells, we examined the effectiveness of NK cell. During the course of study, we learnt that oregonin could increase the cytotoxicity of NK cell, and this was confirmed by MTT assay. In addition, the survival time of C57BL/6 mice were measured by inoculating B16-F10 melanoma cells via intra muscular (i.m.). Oregonin treatment after 10 hours of inoculation showed a significant extension of survival time by 51.32% comparing to control group at 10mg/kg dose. Moreover, oregonin significantly reduced the case of pulmonary metastasis being developed from B16-F10 melanoma cells. These findings suggest that oregonin may be classified as a new and novel immunomodulator due to its potential anti-tumor activity.

[PB4-6] [04/18/2002 (Thr) 14:00 - 17:00 / Hall E]

Truncation of N-terminal amino acid residues of leukotactin-1 increases agonistic potency on CCR1 and CCR3

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Leukotactin-1 (Lkn-1) is a human CC chemokine that binds to both CC chemokine receptor (CCR)1 and CCR3. Structurally, Lkn-1 is distinct from other human CC chemokines in that it has long amino acid residues preceding the first cysteine at the NH2-terminus, and contains an extra two cysteines. NH2-terminal amino acids of Lkn-1 were deleted serially and the effects of each deletion were investigated. In CCR1 expressing cells, serial deletion up to 20 amino acids (Δ20) did not change the calcium flux-inducing activity significantly. Deletion of 24 amino acids (Δ24), however, increased the agonistic potency approximately 100-fold. Deletion of 27 or 28 amino acids also increased the agonistic potency to the same level shown by Δ24. Deletion of one more amino acid (Δ29), however, abolished the agonistic activity almost completely showing that at least 3 amino acid residues preceding the first cysteine at the NH2-terminus are essential for the biological activity of Lkn-1. Loss of agonistic activity was due to impaired binding to CCR1. In CCR3 expressing cells, Δ24 was the only form of Lkn-1 which revealed increased agonistic potency. Our results indicate that postttranslational modification is a potential mechanism for the regulation of biological activitiy of Lkn-1.