Pharmacol 63:607-616) showed that transcription factor AP-1 is important signal factor involved in PC12 cell differentiation, we further determined AP-1 and other transcription factor NF-κB activation during cell differentiation. Concomitant with cell differentiation, AP-1 and NF-κB was activated at lower dose (0.5-5 U/ml) of EPO in a dose dependent manner. In addition, in the presence of anti-EPO antibody, the effect of EPO was partial blocked. These data show that EPO induced neuronal cell differentiation, and transcriptional factor AP-1 and NF-κB may be involved in neuronal cell differentiation.

[PC3-16] [2003-10-10 09:00 - 13:00 / Grand Ballroom Pre-function]

The Effect of Anticarcinogenic Activity of Rhodiola Sachalinesis Extract

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This study was performed to determine the anticarcinogenic activity of the Rhodiola Sachalinesis Extract (RS) on several microorganisms and human cancer cell lines. Among the various solvent fractions of RS, the ethylether partition layer (RSMEE) showed the strongest antimicrobial activity, ethylacetate partition layer (RSMEA) resulted in good antimicrobial activity. We also determined the effect of RS extract and fractions on cytotoxicity, and chemopreventive effect on human cancer cells. The experiment was conducted to determine cytotoxicity of RS partiton layers on HepG2, HeLa, HT-29 and MCF-7 cells by MTT assay. Among the various partition layers of RS, RSMEE were showed the strongest cytotoxic effects on all cancer cell lines. The Quinone reductase induced activities of HepG2 cell, the ethylether partition layer (RSMEE) was 3.21 times more effective compared to the control value of 1.0. This value was significantly higher than that of previous results using the other materials. Therefore, vased on these studies, RS may be developed into a potentially usful antimicrobial and anticarcinogenic agents.

[PC3-17] [2003-10-10 09:00 - 13:00 / Grand Ballroom Pre-function]

Activation of MKK6 induces invasive and migrative phenotypes in MCF10A human breast epithelial cells

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Ras expression has been suggested as a marker for tumor aggressiveness of breast cancer, including the degrees of invasion and tumor recurrence. We previously showed that p38 MAPK is a key signaling molecule differentially regulated by H-ras and N-ras, leading to H-ras-specific cell invasive and migrative phenotypes in human breast epithelial cells (Cancer Res.: 63, 5454-5461, 2003). In this study, we further investigated the role of p38 MAPK pathway in the induction of metastatic potential in MCF10A cells as a "gain of function" study. We established stable transfectants of MCF10A expressing constitutively activated mutant of MAP kinase kinase (MKK)-6, the direct upstream activator of p38 MAPK. We show the induction of invasion and cell migration with specific upregulation of MMP-2 in these cells, demonstrating the role of p38 MAPK pathway in the metastatic potential in MCF10A cells. [Supported by a grant (R04-2003-000-10063-0) from the Basic Research Program of the Korea Science & Engineering Foundation]

[PC3-18] [2003-10-10 09:00 - 13:00 / Grand Ballroom Pre-function]

Characterization of Erythropoietin Producing Cell Lines after Introduction of Urea Cycle Enzymes, Carbamoly Phosphate Synthetase and Ornithine Transcarbamoylase

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An efficient Erythropoietin (EPO)-expression system in mammalian cells is required for massive production for therapeutic use. Ammonium ion is a major problem in the production of valuable recombinant proteins in cultured animal cells. Therefore, it is of importance to devise a system by which a high productivity of human therapeutic recombinant protein can be maintained or enhanced under low ammonium concentration. To reduce the ammonium ion accumulated in EPO producing Chinese Hamster Ovary (CHO) cells, IBE, we introduced the first two genes of the urea cycle, carbamoyl phosphate synthetase (CPSI) and ornithine transcarbamoylase (OTC), into IBE using a stable transfection method. Transfectants expressing CPSI and OTC, were selected and confirmed by RT-PCR. The CO5 cell line, IBE expressing CPSI and OTC had 12.6%, 21.6%, and 24% higher cell growth and 15%, 26%, and 33% lower ammonia concentrations in the media per cell than the parental cell line, IBE, at the time of the cells reaching a high density, when the media were changed at 1-, 2-, and 3-day intervals, respectively. In addition, CO5 cells showed 2-2.5 times higher productivity of EPO than IBE cells. Comparisons of the glycosylation of EPO purified from both cell lines, IBE and CO5 revealed that EPO produced from CO5 cells contained a more acidic proportion of isoforms with approximately 15% higher sialic acid contents per EPO than that produced from IBE cells in spite of the higher EPO production in CO5 cells. These results suggest that the improvement of higher ammonia removal activity in CHO cells from the introduction of the first two enzymes of the urea cycle led to enhance recombinant human EPO productivity with higher cell viability as well as increased sialylation of EPO due to the reduction of the ammonia concentrations in culture media.

[PD1-1] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

Molecular modeling study of indeno[1,2-c]isoquinolines and 3-arylisoquinolines using CoMFA

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• The potent antitumor activities of 3-arylisoquinolines promoted us to explore the structure-activity relationship of these compounds. A series of 3-arylisoquinoline derivatives were evaluated for antitumor cytotoxicity against human lung tumor cell (A 549). For the next stage, we decided to prepare the constrained form of 3-arylisoquinolines as indeno[1,2-c]isoquinolines. As a result, diverse spectrum against human tumor cell lines was obtained. In order to study structure-activity relationship (SAR) of these compounds the comparative molecular field analysis (CoMFA) was carried out. CoMFA has been a useful technique in defining important 3-dimentional (3-D) properties and postulated pharmacophore model. In order to carry out conformational search of these compounds, we used the X-ray crystallographic structure of 7,8-dimethoxy-3-phenyliosquinolin-(2H)-one as well as a grid search. Finally, we could get good Cross-Validated R2 (Q2) values with pharmacophore models. A facile synthesis of indeno[1,2-c]isoquinolines with a 3D-QSAR study will be presented.

[PD1-2] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

Formal synthesis of core unit of apicularen A and its synthetic derivatives

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Over the past few years, a variety of macrocyclic salicylate natural products have been isolated from both terrestrial and marine sources based on their ability to induce a particular phenotype in mammalian cells. Extracts of the myxobacterium Chondromyces showed high cytotoxicity against cultivated mammalian cells and bio-guided fractionation revealed the cytotoxicity was due to one main metabolite identified as the novel macrolide apicularen A. Beginning to understand the molecular basis for these distinct activities will require structure-function correlation studies and the development of synthetic chemistry in this area. Apicularen A possesses a structure characterized by a salicylic acid residue, a macrolide ring bridged by an oxygen atom in such a way as to