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Traditionally, cancer chemotherapy have focused on cytotoxic intervention at the level of DNA replication. While cytotoxic agents have shown limited efficacy against rapidly growing tumor cells, they cause serious toxic and side effects due to attack against both normal and neoplastic cells without distinction. Since the role of oncogenic ras protein in human tumors have been dicovered, medicinal chemists have paid their attention to the ras activation catalyzed by farnesyltransferase in the hope of developing cancer cell-specific agent without toxicity on normal cells. YH3939 inhibited farnesylation of H-ras and K-ras4B by purified human farnesyltransferase with IC50 values of less than 1.0 nM. Enzyme kinetic studies of YH3939 have demonstrated that it is competitive with respect to ras protein. YH3939 showed potent inhibition on anchorage dependent and independent soft agar growth of human tumor cells which express mutant K-ras. Furthermore, the processing of oncogenic ras in K-ras4B transformed fibroblast and A549 human lung tumor cell lines was disrupted by YH3939. This accounts for the ability of YH3939 to inhibit tumor cell growth and to abolish the malignancy of cancer cells by blocking oncogenic Ras activity. Therefore, our findings indicate that YH3939 is a potent inhibitor of Ras processing with robust anti-tumor properties.
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[PA1-6] [04/18/2002 (Thr) 14:00 - 17:00 / Hall E]

Antioxidative Effect of In Rat Hippocampal Slice, Compound SY-013, A New Stilbene Derivative.

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Resveratol (trans-3,4',5-trihydroxystilbene) is naturally occuring phytoalexin found in grapes. This ingredient was found to act as a antioxidant agent, anticancer agent and cardiovascular disease drug. Recently, It is feasible to study possible neuroprotective effect of resveratrol against neural injury through chronic administration of the compound to experimental animals. But, Virgili et al reported that resveratrol have not significant degree of neuroprotection because of resveratrol structure being high polar. Our study was designed to search for alternative materials like resveratrol derivatives, which having non polar, high bioactivities. SY-013 (Compound I), which is resverarol derivatives, with a lower polarity than resveratrol for Compound I was synthesized by single step process. To evaluated which Compound I could exert the protective effects on ischemic-induced neuronal damage, Compound I were treated to the reaction medium from the hipocampal slice in ischemic condition. Also It was studied for whether it is directly associated radical scavenge activity.
Our results suggest the compound I has exerted to prevent loss of ATP under ischemic condition in the hippocampal slice. And It suppressed the increase on the radical producing in PC12 cell line.

[PA1-7] [04/18/2002 (Thr) 14:00 - 17:00 / Hall E]

OST-3964, A Human Cathepsin K Inhibitor, Inhibits Bone Resorption In Vitro

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Cathepsin K is a cystein protease that plays an essential role in osteoclast-mediated degradation of organic matrix of bone. This enzyme promises the future therapy for the excessive bone resorption such as