production by gastric (NCI-N87) adenocarcinoma cells. The NO production by gastric adenocarcinoma cell lines was increased by IFN-γtreatment, which was inhibited by pretreatment of 5-FUra. Pretreatment of 5-FUra showed much higher reduction of NO production than by L-NAME, L-NMMA, well known NOS inhibitors. 5-FUra reduced the mRNA production of inducible NOS in carcinoma cells. Gel retardation result showed that 5-FUra decreased the NF-kB binding into iNOS promoter. Taken together, these data suggest that 5-FUra inhibits NO production in colon and stomach adenocarcinoma cells by inactivating NF-kB.

[PA1-6] [04/21/2000 (Fri) 10:30 - 11:30 / [1st Fl, Bldg 3]]

YH3096 causes G2/M enrichment and induces Anoikis in human tumor cells harboring K-ras mutation

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The ability of Ras oncoproteins to cause malignant transformation requires their post-translational modification by prenyl group. Prenylation allows the ras oncoprotein to localize to the plasma membrane where it plays a pivotal role in growth factor signalling and malignancy. For this reason, inhibition of Ras prenylation is being pursued as a way of developing anticancer drug. YH3096 inhibits anchorage dependent and independent growth of human tumor cells which express mutated K-ras. Furthermore, the prenylation of oncogenic ras in A549 human lung cancer cell lines was disrupted by YH3096. This leads to cell cycle arrest in G2/M phase as well as anokis, induction of detachment-mediated apoptosis. This accounts for the ability of YH3096 to inhibit tumor cell growth and to abolish the malignancy of cancer cells. Therefore, it is concluded that YH3096 is a potent inhibitor of Ras processing leading to mitotic arrest and loss of ras-driven malignancy. This study was supported by a grant of the Korea Health 21 R & D project, Ministry of Health & Welfare, Republic of Korea (HMP-98-D-7-0010).

[PA1-7] [04/21/2000 (Fri) 10:30 - 11:30 / [1st Fl, Bldg 3]]

Hypoglycemic Effect and Mutagenicity of JG-381

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JG-381, a racemic form of oxirane-2-carboxylate derivative, was examined for mutagenicity using various tests : the reverse mutation test on bacteria, chromosomal aberration test on cultured mammalian cells and micronucleus test on mice. Also the oral hypoglycemic effect of JG-381 was evaluated by measuring of plasma glucose in both normal and streptozotocin-induced diabetic rats. In the reverse mutation test on bacteria using Salmonella typhimurium strain TA98, TA100, TA102, TA1535, TA1537 with or without a metabolic activation system (S9 mix), JG-381 significantly increased reverse colonies in all test strains compared with the control. In the chromosomal aberration test using cultured Chinese Hamster Lung (CHL) cells, JG-381 increased the number of aberrant cells in the presence of S9 mix. In the micronucleus test, micronucleated polychromatic erythrocytes in the JG-381-treated mice were not significantly different from those of the vehicle-treated mice. These results indicate that JG-381 has mutagenic potential under this conditions. In normal rats single oral administration of JG-381 significantly lowered the level of plasma glucose in a glucose tolerance test. In contrast, in diabetic rats vivo four weeks treatment of JG-381 did not affect the level of plasma glucose.