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

Differential Role of MAP Kinases in Antioxidant Response Element-mediated rGSTA2 Induction by t-BHQ

Kang KW°, Cho MK and Kim SG

College of Pharmacy, Seoul National University

The protective adaptive response to electrophiles and reactive oxygen species (ROS) is mediated with the activation of antioxidant response element (ARE) and subsequent induction of phase II detoxifying enzymes. The current study was designed to identify the mitogen-activated protein (MAP) kinase signaling pathways responsible for the induction of rGSTA2 by tert-butylhydroquinone (t-BHQ) and to study the role of phosphatidylinositol 3-kinase (PI3-kinase). c-Jun N-terminal kinase (JNK), extracellular signal-regulated kinase (ERK) and p38 MAP kinase all were activated in H4IIE hepatoma cell by t-BHQ treatment. The nuclear ARE complex was activated 1-6 h after t-BHQ treatment, as assessed by electrophoretic mobility shift assay. The rGSTA2 mRNA level was elevated by t-BHQ at 6-24 h, which led to the enzyme induction. Both nuclear ARE activation and increase in rGSTA2 mRNA was abolished by wortmannin or LY294002, PI3-kinase inhibitors. Curcumin a JNK inhibitor, completely inhibited both ARE activation and an increase in rGSTA2 mRNA. Conversely, either PD98059 or SB203580 enhanced the t-BHQ-induced increases in rGSTA2 mRNA and protein levels. These data provided evidence that JNK, p38 kinase and ERK differentially regulate the ARE-mediated rGSTA2 induction by t-BHQ and that PI3-kinase plays a crucial role in the expression of rGSTA2.

[PA1-2] [04/21/2000 (Fri) 10:30 - 11:30 / [1st Fl, Bldg 3]]

Fluorogenic HCV NS3 Protease Assay

Shim JY°, Jung YH, Lee BY

Yuhan Research Center, Yuhan Corporation, #27-3, Tangjeong-Dong, Kunpo, Kyunggi-Do 435-715, Korea

Hepatitis C Virus (HCV) is the etiologic agent of both parenterally transmitted and community acquired non-A, non-B hepatitis. One of the approaches to anti-HCV drug is the design and synthesis of specific small molecule compounds inhibiting the proteolytic processing of the HCV polyprotein. This proteolytic processing is catalyzed by a chymotrypsin-like serine protease, which is located in the N-terminal region of non-structural protein 3 (NS3). Over 2000 protease inhibitors were evaluated for their inhibitory activity on HCV NS3 protease through a fluorogenic assay based upon resonance energy transfer using recombinant NS3 protease. The cDNA of HCV NS3 (1-180) protease was cloned into expression vector. The fusion protein with the N-terminal six histidine was over-expressed in *Escherichia coli*. Through a high throughput screening program, YH3893 was identified as a potent inhibitor on NS3 protease having the competitive mode of action with respect to the substrate, NS5A/5B. This study was supported by a grant (CH1-3-12) from MOST.

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

in vitro Activities of Macrolides, Lincosamide, and Streptogramin B against Gram-positive bacteria

Lim JA, Yun HJ ,Cho HS ,Min YH ,Choi EC