[PC1-1] [04/18/2002 (Thr) 14:00 - 17:00 / Hall E]

DA-125, a new antitumor agent, inhibits topoismerase II as topoisomerase poison and DNA intercalator

Lee MinJun°, Kim MiRa, Seo JinWook, Shin ChaGyun

Department of Biotechnology, Chung-Ang University, Ansung 456-756, Korea

Inhibitory mechanism of DNA replication by a new antitumor agent, DA-125, was studied by evaluating formation of DNA-topoisomerase complex in the simian virus 40 (SV40) replicating system. DA-125 induced a dose-dependent formation of DNA-topoisomerase complex, indicating that DA-125 has topoisomerase poison properties. In the experiments used with two different chemicals simultaneously, adriamycin, a known DNA intercalator, blocked formation of DNA-topoisomerase complex induced by etoposide (VP16), a known topoismerase II poison, in a dose-dependent manner. On the contrary, DA-125 inhibited formation of DNA-topoismerase complex induced by VP16 to a maximum level of the complex caused by DA-125 alone, suggesting that DA-125 has strong DNA intercalator properties. However, DA-125 and adriamycin did not inhibit formation of DNA-topoisomerase complex caused by camptothecin, a known topoisomerase poison. On the basis of these observations, therefore, it is suggested that DA-125 inhibits topoisomerase II as topoisomerase II poison and DNA intercalator.

[PC1-2] [04/18/2002 (Thr) 14:00 - 17:00 / Hall E]

Subunit assembly of laminin variants in bovine aortic endothelial cells

Jeon Hoon°, Choi GoYa, You HeeTae, Cui Xun

College of Pharmacy,Woosuk University

Bovine aortic endothelial cells(BAEC) produce two variant forms of laminin with a subunit composition of AB1B2 and A'B1B2. Anlyses of the intracellular assembly of these subunits revealed that the B1B2 dimer formed first, and that A or A'joined to form the AB1B2 or A'B1B2 trimer. Angiostatic steroids shifted the relative size of the A and A' monomer pool in BAEC, and competition between the A and A' subunits in joining the B1B2 dimer produced AB1B2 and A'B1B2 in different ratios. This result suggests that subunit replacement is the general mechanism for producing laminin variants by various cells for tissue morphogenesis. When laminin subunits in BAEC were cross-linked with dithio-bis-succinimidylpropionate (DSP) and immunoprecipitated with anti-laminin antiserum, monomeric A,A',B1 and B2 monomers and the B1B2 dimer migrated as extremely large molecules in sodium dodecyl sulfate gel electrophoresis under nonreducing conditions. When the crosslinking disulfide bonds were cleaved under reducing conditions, they migrated as the usual subunits. This result suggests that molecular chaperones were involved in the process of the assembly and replacement of laminin subunits.

[PC1-3] [04/18/2002 (Thr) 14:00 - 17:00 / Hall E]

Effect of NQ304, an Antithrombotic Agent, on the Arachidonic Acid Metabolism in Rabbit Platelet Aggregation

Son DongJu°, Park YoungHyun, Yoo HwanSoo*, Yun YeoPyo*

College of Natural Sciences, Soonchunhyang University, Asan, Korea * College of Pharmacy, Chungbuk National University, Cheongju, Korea

In the previous study, we have reported that 2-chloro-3-(4-hexylphenyl)-amino-1,4-naphthoquinone (NQ304), a vitamin K derivative, had potent inhibitory effects on human platelet aggregation *in vitro* and *ex vivo*, and on animal pulmonary thrombosis. In the present study, the effect of NQ304, an antithrombotic agent, on platelet aggregation and arachidonic acid (AA) metabolism was investigated using by rabbit washed platelets. Measurements of AA liberation and generation of thromboxane B_2 (TXB_2) and prostaglandin D_2 (PGD_2), through cyclooxygenase pathway, or 12-hydroxyeicosatetraenoic acid (12-HETE), through lipoxygenase pathway, from [^{3}H]AA were evaluated by radio-chromatographic analysis with washed rabbit platelets *in vitro*. Collagen-, AA, or U46619-stimulated platelet aggregation were inhibited dose-dependently by NQ304. The IC_{50} values of NQ304 on collagen-, AA- and U46619-induced rabbit platelet aggregation were calculated to be 3.9, 1.2 and 4.3 μM, respectively. Furthermore, NQ304 potently suppressed the AA liberation from [^{3}H]AA-labeled rabbit platelets exposed to collagen, indicating that it may affect phospholipase A_2 (PLA_2) activation on collagen-induced AA liberation from membrane phospholipids. However, NQ304 didn't suppress the TXB_2 generation induced by addition of [^{3}H]AA in intact rabbit platelets, whereas PGD_2 and 12-HETE generation were enhanced by NQ304. These results suggest that NQ304 may affect PLA_2 activation and which stimulate PGD_2 or 12-HETE generation from AA, thus eliciting the inhibition of platelet aggregation.

[PC1-4] [04/18/2002 (Thr) 14:00 - 17:00 / Hall E]

Upregulation of NF-kappaB Expression by Alkylating Carcinogens in Human Transfectant Keratinocytes

Moon Ki-Young°, Lee YoungJong, Kim Seung-Kyoon, Choi Young-Kuk, Kim JungEun, Kim YeongShik[1]

Department of Clinical Pathology, Bioindustry and Technology Research Institute, Kwangju Health College, Kwangju, 506-701 and [1]Natural Products Research Institute, Seoul National University, Seoul 110-460, Korea kmoon@www.kjhc.ac.kr

Effect of alkylating carcinogens, e.g., *N*-nitroso-*N*-methylurea, *N*-nitroso-*N*-ethylurea, ethyl iodide and benzyl bromide on the activation of NF-kappaB was evaluated in human transfectant HaCaT and SCC-13 cells in order to investigate the possible correlation of NF-kappaB expression with chemical carcinogenesis. Human HaCaT and SCC-13 cells transfected with pNF-kappaB-SEAP-NPT plasmid were used to determine the NF-kappaB expression induced by alkylating agents. These transfectants release the secretory alkaline phosphatase (SEAP) as a transcription reporter in response to the NF-kappaB activity and contain the neomycin phosphotransferase (NPT) gene conferring resistance to the geneticin. Alkylating carcinogens significantly upregulated the NF-kappaB activations in a time-dependent manner until 72h at concentrations of 0.5 ~ 5 μ , M in both keratinocytes cell lines. This results suggest that carcinogenic activities of alkylating chemicals may be associated with their ability to increase NF-kappaB activation at the genetic molecular basis and NF-kappaB activation in response to chemical carcinogens may provides some of the molecular levels of regulatory activities of carcinogenic chemicals in human skin cells on carcinogenecity.

[PC1-5] [04/18/2002 (Thr) 14:00 - 17:00 / Hall E]

Anti-inflammation activity of the organoseleniums : inhibition of iNOS and COX-2 protein level.

Shin KyungMin°, Park ByungGyu, Jang JungAn, Kim RyungGyu, Shen LiuLan, Lee KyungTae, Jeong JinHyun

College of Pharmacy, Kyung Hee University, Seoul 130-701, Korea

Nitric Oxide (NO) has been known as multifunctional mediator produced by iNOS in inflammatory process and acting on various cells, and PGs are also called inflammatory mediator, produced by COX-2 in inflammatory tissues. In this point of view modulation of iNOS and COX-2 expression level represent a new treatment of inflammtory and autoimmune disease.
The present study examined effect of di- 3-hydroxyphenyl diselenide, di-4- hydroxyphenyl diselenide, and