[PA1-6] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

Effects of DW-286a, a fluoroquinolone antibiotic agent, on hERG channel currents expressed in CHO cells

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Prolongation of the QT interval may result in a potentially dangerous arrhythmia. The most commonly proposed mechanism for QT interval prolongation(LQT) by pharmaceuticals is inhibition of the rapid delayed rectifier potassium channel (I_{Kr}). The LQT potency of pharmaceuticals can be effectively evaluated by examining the effect on human ether-a go-go-related gene (hERG) channels expressed in CHO cells, known to be equal to I_{Kr}. We have transfected hERG into CHO cell lines transiently to express high levels of functional hERG channels. Western blot analysis showed one protein band (130 ~ 150 kDa). We used these cells to evaluate LQT potency of DW-286a at 30°C. Recently DW-286a, a fluoroquinolone antibiotic agent with the formula{7-(4-Aminomethyl-3-methoxyimino-4-methylpyrrolidin-1-yl)-1-cyclopropyl-6-fluoro-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxylic acid hydrochloride}, has been developed by Dong-Wha Pharmaceutical INC. (Anyang, Korea) for the treatment of both gram-positive and gram-negative bacterial infections. DW-286a decreased hERG channel currents in a dose-dependent manner with an estimated IC_{50} of 83.59±7.36 mM. But, the blockade of DW-286a on hERG channel was slight as compared with other fluoroquinolone antibiotic agents(ex. IC_{50} of sparfloxacin; about 34 mM)

[PA1-7] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

Studies of the agonist-induced receptor sequestration of dopamine D2 receptor

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The dopamine D2 receptor (D_2R) is target for antipsychotic drugs and associated with several neuropsychiatric disorders. The internalization (sequestration) of G protin-coupled receptor is caused by agonist-induced receptor phosphorylation mediated by GRK, followed by the interaction with β-arrestin. In this study, we examined the agonist-dependent sequestration/internalization of dopamine D_2R, which were transiently expressed in HEK 293 cells with or without GRK co-expression. Co-expression of GRK2 or GRK3 markedly enhanced the sequestration of D_2R. GRK-dependent sequestration of D_2R was regulated by the interaction with D_1R and by protein kinase C.

[PA1-8] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

The mechanism of sphingosine-1-phosphate induced contraction in cat esophageal smooth muscle cells.

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We previously shown that sphingosylphosphorylcholine, a lysophosphatidic acid, produced contraction in isolated single cells of cat ilium. We investigated the mechanism of sphingosine-1-phosphate (S1P)-induced contraction of circular smooth muscle cells in cat esophagus. S1P produced esophageal contraction in a dose dependent manner. The maximal contraction (10^{-7}M) induced at 1min. Pertusis toxin (PTX) inhibited contraction induced by S1P, suggesting that the contraction is mediated to a PTX-sensitive G-protein. Among the phospholipase inhibitors, U73122 reduced the contraction. To evaluate the role of PKC, GF109203X or chelerythrine was pretreated prior to S1P, and this contraction was decreased by either inhibitor. MAPK kinase inhibitor PD98059 blocked the contraction significantly, but p38 mitogen-activated protein kinase (MAPK) inhibitor SB202190 did not. However, cotreatment of PD98059 and chelerythrine showed no significant difference when compared with alone treatment of this inhibitors. Western blotting revealed that G-protein coupled endothelial differentiation gene

(EDG)1, EDG3, EDG5 and EDG8 receptor existed in cat esophageal smooth muscle. In conclusion, S1P induces the contraction of cat esophageal smooth muscle cells which mediated by EDG receptor(s) coupled to PTX-sensitive G-protein. PLC was involved in this contraction as well as PKC and p42/44 MAPK.

[PA1-9] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

Sauchinone, a Lignan from Saururus chinensis, Suppresses iNOS Expression through the Inhibition of Transactivation Activity of RelA of NF-kB

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Sauchinone , a known lignan, was isolated from the root of Saururus chinensis as an active principle responsible for inhibiting the production of NO in LPS-stimulated RAW264.7 cells by activity-guided fractionation. Sauchinone dose-dependently inhibited not only the production of NO, but also the expression of iNOS mRNA and protein in LPS-stimulated RAW 264.7 cells. Furthermore, sauchinone prevented LPS-induced NF-kB activation, which is known to play a critical role in iNOS expression, assessed by a reporter assay under the control of NF-kB. However, electrophoretic mobility shift assay (EMSA) demonstrated that sauchinone did not suppress the DNA-binding activity of NF-kB or the degradation of IkB-a induced by LPS. Further analysis revealed that transactivation activity of RelA subunit of NF-kB was dose-dependently suppressed in the presence of sauchinone. Taken together, our results suggested that sauchinone could inhibit production of NO in LPS-stimulated RAW264.7 cells through the suppression of NF-kB by inhibiting transactivation activity of RelA subunit.

[PA1-10] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

Gallocatechin Gallate Inhibits Platelet Aggregation by Arachidonic Acid Liberation and TxA_2 Synthase Activity

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We have previously reported that green tea catechins (GTC) displayed anti-thrombotic activity, and that this might be due to anti-platelet rather than anti-coagulation effects. In the present study, we have studied the anti-platelet activity and mechanism of gallocatechin gallate (GCG), which is a component of GTC. GCG inhibited the collagen- and U46619-induced aggregation of rabbit platelets, with IC_{50} values of 63.0 and 48.3 μM, respectively. GCG also inhibited collagen-induced serotonin release and TxB_2 formation in a similar manner of platelets aggregation. GCG potently inhibited collagen- induced arachidonic acid liberation from membrane phospholipids and diacyglycerol release in a dose-dependent manner. Whereas, GCG had little effect on the level of PGD_2. TxB_2 conversion from arachidonic acid and thromboxane A_2 synthase activity were significantly inhibited by GCG. GCG potently decreased the rise in $[Ca^{2+}]_i$ at a concentration of 200 μM. Taken together, these observations suggest that the anti-platelet activity of GCG may be mainly due to inhibition of arachidonic acid liberation by Ca^{2+}-dependent $cPLA_2$ through the inhibition of Ca^{2+} influx and of thromboxane A_2 synthase activity.

[PA1-11] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

Pharmacological activities of Dongchunghacho strains

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Dongchunghacho (Dong-Chong-Xia-Cho in Chinese) is one of entomogenous fungi that grow as parasites mainly to pupae or larvae. It includes many different genera such as Cordyceps, Paecilomyces, Torrubiella and Podonectria. The ethanolic extract of Cordyceps scarabaeicola, prepared from its fruiting bodies, showed significant inhibitory activity on angiogenesis, which was detected by chick embryo chorioallantoic membrane