relations for E-4031 of hERG channel block were obtained in the concentrations between 1, 10 and 100 nM. At 26°C(room temperature), 1, 10 and 100 nM E-4031 decreased hERG currents by 17, 36 and 99% respectively. IC_{50} was 14.18 nM. At 30°C(middle temperature), 1, 10 and 100 nM E-4031 decreased hERG currents by 13, 28 and 67% respectively. IC_{50} was, 6.55 nM. At 35°C(physiological temperature), 1, 10 and 100 nM E-4031 decreased hERG currents by 21, 43 and 99% respectively. IC_{50} was 9.98 nM. It may be concluded that the effect of E-4031 on hERG currents was temperature-independent.

[PA1-41] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

Studies of the functional roles of DRY motif in dopamine D2 and D3 receptors

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Asparate-arginine-tyrosine (DRY) motif is highly conserved among GPCRs, and the alternation of this motif has been reported to exist naturally and involved with various diseases that involves constitutive activation or desensitization of receptor. To understand the interaction between G protein and β-arrestin more systemically, we produced the DHY mutants for the D2R and D3R. The introduction of R to H mutation in DRY motif caused differential effects on the characteristics of D2R and D3R: for both receptors receptor-effector coupling and agonist-induced translocation of b arrestins were disrupted; for D2R agonist-induced receptor phosphorylation and receptor sequestration were blocked; the subcellular localization was not changed for D2R but more receptors were observed intracellularly for D3R; the ligand binding properties of D2R were not changed but the affinity for the antagonists was slightly increased for D3R.

[PA1-42] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

Induction of cell cycle arrest and apoptosis by an indirubin analog, a CDK inhibitor, in human lung cancer cells

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Cyclin-dependent kinases (CDKs) regulate the cell division cycle, apoptosis, transcription and differentiation. Inhibition of CDK is a promising target in development of anti-cancer agents. An indirubin analog (AGM011), a CDK inhibitor, is a synthetic compound that inhibits human cancer cell growth in vitro. AGM011 showed a potent cytotoxicity in cultured human cancer cell lines (IC_{50}= 5.43 μM for A549, human lung cancer cell; IC_{50}= 1.21 μM for SNU-638, human stomach cancer cell; IC_{50}= 25.49 μM for Col2, human colon cancer cell; IC_{50}= 5.87 μM for HT1080, human fibrosarcoma cell; IC_{50}= 9.23 μM for HL-60, human leukemia cell). Prompted by the potent cytotoxicity, additional action mechanism studies were performed with cultured A549 human lung cancer cells. Using flow cytometric analysis, AGM011 showed G2/M phase cell cycle arrest and induction of apoptosis in a concentration- and time-dependent manner with characterizing apoptotic features under microscopic observation and DNA fragmentation by agarose gel electrophoresis. These results indicate that AGM011 induces the cell cycle arrest and apoptosis against human cancer cells. Therefore, it might be developed as an effective anti-cancer agent.

[PA1-43] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

Chronic administration of quercetin in rats causes the suppression of glutathione metabolism

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The present study was performed to investigate the effects of chronic administration of quercetin on lipid