

[PA1-1] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

The Mechanism of Contraction Response to EFS in Cat Esophageal Circular Muscle

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Low-frequency electrical field stimulation of transmural nerves of cat esophageal circular smooth muscle produces an "off contraction", which occurs after electrical field stimulation (EFS) of transmural nerves is stopped. We previously examined signal transduction pathways mediating ACh-induced contraction of circular smooth muscle of esophagus. The extracellular Ca^{2+} is needed for the contraction, results in the activation PKC. EFS-induced contraction was abolished by the pretreatments of tetrodotoxin (1 μ M) and atropine (1 μ M). In the present study, we investigated whether EFS-induced contraction would be affected by inhibitors of phospholipases and protein kinases. This contraction was not blocked by D609 (10 μ M, PC-PLC inhibitor), pCMB (10 μ M, PLD inhibitor), DEDA (10 μ M, PLA_2 inhibitor). PKC inhibitor, GF109203X (10 μ M), did not reduce the response. We further studied whether extracellular Ca^{2+} may be required or not for the contraction. Nimodipine (100nM, L-type Ca^{2+} channel blocker) decreased the contractile response by 50% approximately. Our study suggests that the off contraction in cat esophageal circular smooth muscle may be mediated through different signals when compared with agonist-induced contraction.

[PA1-2] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

Comparison of conotoxin G_{VIA} and cilnidipine on nicotinic receptor stimulation-induced catecholamine release in the rat Adrenal Gland

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The present study was designed to compare the effects of conotoxin G_{VIA}, a selective blocker of N-type voltage-dependent calcium channels (VDCC) and cilnidipine, a blocker of both L- and N-type VDCC, on the secretion of catecholamines (CA) evoked by cholinergic stimulation and membrane-depolarization in the isolated perfused rat adrenal gland, and also to establish the mechanism of action. 1. The inhibition of the CA secretory response evoked by acetylcholine (5.32 x 10⁻³ M) was stronger in cilnidipine-treated glands than in conotoxin G_{VIA}-treated glands. However, the CA secretion evoked by high potassium (5.6 x 10⁻² M), a membrane depolarizer, was more significantly inhibited in conotoxin G_{VIA}-treated glands than in cilnidipine-treated glands. 2. The secretory responses of CA evoked by DMPP (10⁻⁴ M for 2 min), a selective agonist of neuronal nicotinic receptors, and McN-A-343 (10⁻⁴ M for 2 min), a selective agonist of neuronal muscarinic receptors, were also more depressed in cilnidipine-treated glands than in conotoxin G_{VIA}-treated glands. 3. The CA release evoked by Bay-K-8644 (10⁻⁵ M), a dihydropyridine-sensitive Ca^{2+} channel activator, was more significantly inhibited in cilnidipine-treated glands than in conotoxin G_{VIA}-treated glands. The inhibition by conotoxin G_{VIA} of the CA release evoked by cyclopiazonic acid (10⁻⁵ M), a selective inhibitor of Ca^{2+} -ATPase in the endoplasmic reticulum, was similar to that by cilnidipine. 4. Taken together, these experimental results demonstrate that the CA secretion evoked by stimulation of cholinergic (nicotinic and muscarinic) receptors is more strongly inhibited by cilnidipine than conotoxin G_{VIA}, but the CA secretion evoked by membrane depolarization is rather more depressed by conotoxin G_{VIA}. It seems that there is some difference in the inhibition of the CA release between conotoxin G_{VIA} (a selective blocker of N-type VDCC) and cilnidipine (a blocker of both L- and N-type VDCC).

[PA1-3] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

Mitogen-activated protein kinase signaling pathway mediates 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD)-induced apoptosis in Jurkat T cells.

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The present study was performed to examine mitogen-activated protein kinase associated pathways in mediation of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD)-induced cell apoptosis in cultured Jurkat T cells. TCDD significantly decreased cell viability in a concentration-dependent manner ($p < 0.05$ at 10-300 nM). TCDD (10 nM) also time-dependently decreased cell viability ($p < 0.05$ at 12-48 h). c-Jun NH₂-terminal kinase was significantly phosphorylated with TCDD treatment in a time dependent manner. p38 MAPK was not significantly changed with TCDD treatment. Extracellular signal-regulated protein kinase was significantly phosphorylated with TCDD treatment for 8 h and gradually returned to baseline. TCDD induced up-regulation of ASK1 and C-Jun, which are up- and down-stream of JNK, respectively, and up-regulation of cytosolic cytochrome c and Caspase-3. These results demonstrate that MAPK signaling pathways including JNK and ERK 1/2, are activated with the treatment of TCDD in Jurkat T cells, which suggest that MAPK pathways may be involved in the TCDD-induced cell death.

[PA1-4] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

The protective mechanism of melatonin on carrageenan-induced paw edema generation in rats

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The influence of melatonin on carrageenan-induced paw edema in Sprague-Dawley rats has been studied. The injection of 1% carrageenan (given at 0.1ml/paw) into the intraplantar induced an inflammatory response, and the maximal increase of paw volume, edema, was observed at 4hour. The levels of nitric oxide (NO), malondialdehyde (MDA) or prostaglandin E₂ (PGE₂) were increased after edema generation. Also, the expression of the inducible NO synthase (iNOS) were increased in the western blot. Melatonin pretreatment (given at 0.1 to 10 mg/kg) reduced this edema at 1, 2, 3 and 4h in a dose-dependent manner. Melatonin treatment also decreased the levels of NO, MDA and PGE₂. Our data suggest that these inflammatory effects of carrageenan may be derived from an increase of the expression iNOS, the production of NO or MDA. Melatonin may prevent this inflammatory responses; increases of the expression iNOS and the levels of NO, MDA or PGE₂.

[PA1-5] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

Sphingosine-1-phosphate Inhibits Human Keratinocyte Proliferation via Akt/PKB Inactivation

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Although sphingosine-1-phosphate (S1P) is a well-known mitogen, our results show that S1P potently inhibits keratinocyte proliferation, and that this leads the inhibition of DNA synthesis. Interestingly, the prolonged activation of extracellular signal-regulated protein kinase (ERK) and the transient inactivation of Akt/protein kinase B (PKB) were also observed in concert with the inhibition of keratinocyte proliferation by S1P. To further verify the anti-proliferative action of S1P, we examined changes in cell cycle related proteins. S1P inhibited cyclin D₂ synthesis but stimulated p21^{WAF1/CIP1} (p21) and p27^{KIP1} (p27) synthesis; all are inhibitors of cyclin-dependent kinase. Furthermore, we found that the growth inhibition by S1P was in part abolished by pertussis toxin (PTX) treatment, but that ERK activation and Akt/PKB inhibition were not abrogated, suggesting that S1P functions both intracellularly, as a second messenger, and extracellularly, as a ligand for cell surface receptors. Insulin-like growth factor I (IGF-I) is a well established human keratinocyte mitogen and is known to stimulate Akt/PKB in various cell types. In the present study, S1P was found to inhibit the keratinocyte proliferation and Akt/PKB activation induced by IGF-I. Our results suggest that S1P may play an important role in the negative regulation of keratinocyte proliferation by inhibiting the Akt/PKB pathway.