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Author(s)	KITAMURA, Naoki
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ATP modulates Ca^{2+} channels via the pathway related to GTP-binding protein. P_1 and P_2 receptors seem to coexist in guinea-pig adrenal chromaffin cells.

In the smooth muscle tissues contracted by acetylcholine, ATP, 2-methylthio ATP (2MeSATP) and α, β -methylene ATP (α, β -meATP) each caused relaxation. Reactive blue 2 (RB2) and suramin inhibited the relaxant responses to ATP and α, β -meATP. PPADS and DIDS inhibited the relaxation caused by α, β -meATP but not by ATP. Both ATP- and α, β -meATP-induced relaxations were inhibited by apamin.

In tissues at resting tone, ATP and its related compounds caused contractions with the rank order of potency ; 2MeSATP>> ATP \geq UTP>> α, β -meATP. RB2 and suramin inhibited both ATP- and UTP-induced contractions. PPADS inhibited the contraction

caused by UTP but not by ATP. Desensitization with UTP slightly decreased ATP-induced contraction. UTP-induced contraction was not inhibited by desensitization with ATP. ATP- and UTP-induced contractions were inhibited by the removal of extracellular Ca^{2+} or the application of nifedipine. These results suggest that there are two purinoceptors mediating relaxation, and that apamin-sensitive K^+ channels are involved in the relaxant responses to these adenine nucleotide. In addition, it was suggested that ATP and UTP caused contractions via P_{2Y} receptors and pyrimidinoceptors, respectively, and that these contractions were caused by the Ca^{2+} entry through voltage-dependent Ca^{2+} channels. In summary, there are some purino- and pyrimidinoceptors in both chromaffin cells and smooth muscle cells. ATP and its related compounds may play a role as a transmitter in these tissues.

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Voltage-dependent calcium channels in porcine adrenal chromaffin cells : Channel subtypes and mechanisms of their facilitation.

Naoki KITAMURA

*Laboratory of Pharmacology,
Department of Biomedical Sciences,
Graduate School of Veterinary Medicine,
Hokkaido University,
Sapporo 0600818, Japan*

To study the characteristics of voltage-dependent Ca channels in porcine adrenal chromaffin cells, Ca currents (I_{Ca}), rise of intracellular Ca concentration ($[\text{Ca}^{2+}]_i$) and catecholamine release responses induced by stimulation with high K^+ (60 mM) were measured by whole-cell voltage clamp technique, microfluorometry and HPLC-ECD method, respectively. The results

obtained were as follows :

Voltage-current relationship of I_{Ca} indicated that porcine adrenal chromaffin cells possess only high voltage-activated type of Ca channels. The I_{Ca} was inhibited by ω -conotoxin GVIA (ω -CgTx), nifedipine and ω -agatoxin IVA (ω -AgTx) dose-dependently, though the magnitudes of inhibition were various. The degree of inhibition

by maximal doses of these three agents was 78%, 15% and 6%, respectively. When these three agents were applied onto the same cell, I_{Ca} was inhibited additively. Rises in $[Ca^{2+}]_i$ and catecholamine release in response to stimulation by high K^+ were inhibited to about 50% by either ω -CgTx (1 μ M) or nifedipine (10 μ M) but not by ω -AgTx (0.1 μ M). In addition, these responses were almost abolished by the combined application of ω -CgTx and nifedipine. A strong depolarizing pulse (a prepulse to +100 mV) applied prior to a test pulse caused about 20% increase of amplitude of I_{Ba} evoked by the test pulse (facilitation of I_{Ba}). The degree of the facilitation of I_{Ba} was increased with the increase in the voltage (in a range over +20 mV) and duration of the prepulses. Moreover the facilitation of I_{Ba} was decreased with increase in intervals between the prepulses and the test pulses. The application of 8-Bromo-cAMP (1 mM) or forskolin (10 μ M) decreased the amplitudes of I_{Ba} without affecting the degree of facilitation of I_{Ba} by the prepulses. In addition, an intracellular application of Rp-cAMPS, an inhibitor of PKA, did not have any effects on the amplitudes of I_{Ba} and the degree of

facilitation of I_{Ba} . The intracellular application of GTP γ S (100 μ M) decreased the amplitudes of I_{Ba} , but not affected those in the presence of prepulses. On the other hand, the application of GDP β S (100 μ M) caused a slight increase in the amplitudes of I_{Ba} but had no effects on the amplitudes of I_{Ba} in the presence of prepulses. GTP γ S-sensitive component of I_{Ba} was sensitive to ω -CgTx but not to nifedipine. The facilitation of I_{Ba} by the prepulses was abolished by ω -CgTx but not by either ω -AgTx or nifedipine.

Based on these results, it is clarified that porcine adrenal chromaffin cells possess ω -CgTx-sensitive N- and nifedipine-sensitive L- and ω -AgTx-sensitive P/Q-type Ca channels and that L- and N-type channels mainly contribute to the rise in $[Ca^{2+}]_i$ and catecholamine release by depolarizing the cells. N-type Ca channels are mainly involved in the depolarizing prepulse-induced facilitation of I_{Ba} . The facilitation seems to result from the prepulse-induced relief of tonic inhibition on Ca channels by G-protein but not from PKA-induced phosphorylation of channels during the prepulse.

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Effects of tacrine on catecholamine secretion from guinea-pig adrenal chromaffin cells : in comparison with the effects of a cholinesterase inhibitor, physostigmine

Takeshi Sugawara

*Laboratory of Pharmacology,
Department of Biomedical Sciences
Graduate School of Veterinary Medicine,
Hokkaido University, Sapporo 060-0818, Japan*

1. Effects of tacrine and physostigmine (Phys) on catecholamine (CA) secretion induced by acetylcholine (ACh) and their mechanisms were stu-

died in perfused adrenal glands and dispersed adrenal chromaffin cells of the guinea-pig.
2. In perfused adrenal glands, tacrine and Phys