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MODULATION OF ATP-GATED CHANNEL BY ADENOSINE RECEPTOR

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The regulatory role of A_{2A} adenosine receptors on the P_2 purinoceptor-mediated calcium signaling was investigated in rat pheochromocytoma (PC12) cells. When PC12 cells were treated with 2-*p*-(2-carboxyethyl)phenethylamino-5'-N-ethylcarboxamido-adenosine (CGS21680), a specific agonist of the A_{2A} adenosine receptor, extracellular ATP-evoked $[Ca^{2+}]_i$ rise was inhibited by 20%. In the presence of adenosine receptor anatgonists, 9-chloro-2-(2-furyl)[1,2,4]triazolo[1,5-c]quinazolin-5-amine (CGS15943) or 8-[4-[[[[(2-aminoethyl)amino]-carbonyl]methyl]oxy]phenyl]-1,3-dipropyl-xanthine (XAC), the inhibitory effect of CGS21680 was abolished. Both intracellular calcium release and IP_3 production evoked by ATP were not influenced by CGS21680 treatment. However, ATP-evoked Ca^{2+} influx was inhibited by CGS21680 stimulation. The CGS21680-mediated inhibition was independent of nifedipine-induced inhibition of $[Ca^{2+}]_i$ rise. The effects of ATP could be roughly dissected by using UTP and 2MeSATP and CGS21680 inhibited 2MeSATP-evoked response without affecting UTP response. The CGS21680-induced inhibition was completely blocked by reactive blue 2. The CGS21680 effect was mimicked by forskolin and dibutyryl-cAMP and blocked by staurosporine, a kinase inhibitor. The data suggest that activation of A_{2A} adenosine receptors inhibits P_2 purinoceptor-mediated Ca^{2+} influx through ATP-gated channels via protein kinase A in PC12 cells.