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Adenosine Inhibits ATP-induced Calcium Influx in PC12 Cells

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The regulatory role of A_{2A} adenosine receptors in 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-ethylcarboxamidoadenosine (CGS21680), a specific agonist of the A_{2A} adenosine receptor, extracellular ATP-evoked $[Ca^{2+}]_i$ rise was inhibited by 20%. Both intracellular calcium release and IP_3 production evoked by ATP were not effected by CGS21680 treatment. However, ATP-evoked Ca^{2+} influx was inhibited following CGS21680 stimulation. The CGS21680-mediated inhibition occurred independently of nifedipine-induced inhibition of the $[Ca^{2+}]_i$ rise. 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 in PC12 cells activation of A_{2A} adenosine receptors leads to inhibition of P_2 purinoceptor-mediated Ca^{2+} influx through ATP-gated cation channels and involves protein kinase A.