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Purinergic regulation of calcium signaling and exocytosis in rat prostate neuroendocrine cells

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Prostate gland contains neuroendocrine cells (PNECs) are playing important roles in physiological and pathophysiological processes of the prostate gland. Here, we investigated the role of purinoceptors in PNECs freshly isolated from rat ventral prostate (RPNECs) that show immunoreactivity to chromogranin A. Fura-2 ratiometry revealed that ATP evokes both fast Ca^{2+} influx and store Ca^{2+} release in RPNECs. A whole-cell patch clamp study demonstrated fast inactivating cationic current activated by ATP or by α,β-MeATP, which was blocked by ATP-TNP. The activation of P2X inward current was tightly associated with a sharp increase in $[Ca^{2+}]_c$. The presence of P2X1/3 subtypes were proved by RT-PCR analysis. For the stored Ca^{2+} release, ATP and UTP showed similar effects, suggesting the dominant role of P2Y2 subtypes, also confirmed by RT-PCR. Both P2X (α,β-MeATP) and P2Y (UTP) stimulation induced changes in the cell morphology (initial shrinkage and bleb formation on the surface) reversibly. Exocytotic membrane trafficking events were monitored with the membrane-bound fluorescent dye, FM1-43 using confocal microscopy. In spite of the similar Ca^{2+} responses, UTP was far less effective in triggering exocytosis than α,β-MeATP. Since serotonin is reportedly stored in the secretory granule of PNECs, we directly examined whether the aforementioned agonists elicit release of serotonin using carbon fiber electrode-amperometry. In accordance with the results of FM1-43 experiments, α,β-MeATP efficiently evoke serotonin secretion while not with UTP.

In summary, the P2X-mediated Ca^{2+} influx plays crucial roles in the exocytosis of RPNECs. Although a global increase in $[Ca^{2+}]_c$ might be related with the morphological changes, a sharp rise of $[Ca^{2+}]_c$ in the putative sub-plasmalemmal 'microdomains' might be a decisive factor for the exocytosis.

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