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Meeting abstract

$P2Y_1$ receptors are linked to $K_{Ca}2$ channels in PC12 cells

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Background

$P2Y_1$ receptors are widely expressed in the brain, but their signalling mechanisms in neurons remained largely unknown. In sympathetic neurons, recombinant $P2Y_1$ receptors inhibit voltage-gated Ca^{2+} currents (I_{Ca}) and M-type K^+ currents.

Methods

Patch-clamp recordings were performed in PC12 cell cultures, P2Y receptor ligands and signaling interceptors were applied.

Results

In PC12 cells stably expressing rat $P2Y_1$ receptors (PC12-$P2Y_1$), but not in wild type PC12 cells (PC12-wt), ADP induced rises in intracellular Ca^{2+} with half-maximal effects at 15 ± 1.3 μM. In whole-cell patch-clamp recordings, ADP inhibited I_{Ca} of PC12-$P2Y_1$ cells (EC_{50}: 6.3 ± 1.7 μM) and of PC12-wt (EC_{50}: 3.8 ± 1.3 μM); this effect was not altered by the $P2Y_1$ antagonist MRS 2216 (1 μM), but abolished by $P2Y_{12}$ antagonists. In perforated-patch recordings, ADP inhibited I_M relaxation amplitudes of PC12-$P2Y_1$ cells with half-maximal effects at 2.0 ± 1.8 μM, but in PC12-wt no such effect was observed. In PC12-$P2Y_1$, but not in PC12-wt cells, ADP (1-100 μM) caused transient increases in outward currents determined at -30 mV in the perforated-patch, but not the whole-cell mode. ADP-induced currents had reversal potentials between -80 and -90 mV which was close to the calculated K^+ equilibrium potential (-89 mV). Replacement of 100 mM extracellular Na^+ by K^+ shifted the reversal potential of ADP-induced currents to about -10 mV which was again close to the K^+ equilibrium potential (-17 mV). ADP-induced currents were prevented by thapsigargin (1 μM) and by the phospholipase C inhibitor U73122 (3 μM), but not by an inactive analogue. Finally, the ADP-induced currents were significantly reduced by 100 nM apamin.

Conclusion

These results reveal channels of the $K_{Ca}2$ family as novel targets for $P2Y_1$ receptor signalling.

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