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MEETING ABSTRACT Open Access

Functional and physical interactions between P2Y receptors and ion channels

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Background

Neuronal P2Y receptors, i.e. nucleotide-sensitive G protein-coupled receptors (GPCRs), are known to control various voltage-gated ion channels, in particular K_V7 K^+ and $Ca_V2.2$ Ca^{2+} channels. The differential modulation of these ion channels via GPCRs was shown to rely on the presence or absence of scaffolding proteins such as AKAP79/150 and NHERF-2. Since scaffold proteins are believed to bring GPCRs and ion channels in close proximity to guarantee efficient G protein-mediated modulation, this project evaluates whether a tight contact between P2Y receptors and ion channels is a prerequisite for their functional interaction.

Methods

$P2Y_1$ or $P2Y_{12}$ receptors with fluorescent tags (CFP or YFP) were expressed together with fluorescently labeled $K_V7.2/7.3$ or $Ca_V2.2$ channels in tsA 201 cells and the channel modulation by nucleotides was determined by measuring the according currents. To evaluate the behavior of the receptors and channels in the membrane, fluorescence recovery after photobleaching (FRAP) was determined by confocal laser microscopy.

Results

Activation of $P2Y_1$ but not of $P2Y_{12}$ receptors by ADP inhibited the K^+ currents in a concentration-dependent manner by up to 20.5 ± 1.9%. Conversely, activation of both, $P2Y_1$ and $P2Y_{12}$ receptors, reduced the Ca^{2+} currents by up to 60.1 ± 7.4% and 76.3 ± 4.2%, respectively. In initial FRAP experiments, the YFP-labeled receptors showed similar half-times of around 80 seconds. Upon coexpression of the $P2Y_1$ receptor with the K_V7 channel the half-time increased significantly ($p < 0.009$) to 116 seconds compared to single expression of receptor or channel only. In the case of $P2Y_{12}$, coexpression with K_V7 showed no significant change compared to $P2Y_{12}$ or K_V7 alone.

Conclusions

These findings suggest that distinct ion channels are modulated by different P2Y receptors. K_V7 currents are inhibited by $P2Y_1$ whereas $Ca_V2.2$ currents are reduced by both $P2Y_1$ and $P2Y_{12}$. Additionally, FRAP data show that the presence of K_V7 slows down the movement of $P2Y_1$ in the membrane, but not that of $P2Y_{12}$. This suggests that there is a physical interaction between $P2Y_1$ and K_V7 which is not present between $P2Y_{12}$ and K_V7. The influence on movement of $P2Y_1$ and $P2Y_{12}$ receptors in the membrane by the presence $Ca_V2.2$ remains to be elucidated.

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