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MEETING ABSTRACT Open Access

Tracking the A_{2A} adenosine receptor

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Background

The A_{2A} adenosine receptor has become a drug target in the treatment of Parkinson's disease, psychotic behavior and dementia. In addition, targeted deletion of this receptor in mice leads to hypertension, increased platelet aggregation, male aggressiveness and decreased susceptibility to ischemic brain damage. The potential clinical relevance of this receptor is obvious. The A_{2A} adenosine receptor, a prototypical GPCR, is known to signal via restricted collision coupling with G_s. In addition, it is able to stimulate MAP kinase/ERK in a G_s-independent way but dependent on the lipid microenvironment of the membrane. Hence, we characterized the mobility and the targeting of the A_{2A} receptor in nerve cells.

Methods

Receptor mobility was measured using fluorescence recovery after photobleaching (FRAP). A fluorophore-tagged version of the A_{2A} receptor expressed in the cell membrane was bleached using an intense laser beam and the lateral diffusion rate of the receptor was determined. We also implemented the method of single molecule tracking, which allows for the observation of movements of single receptors in real spatial and temporal resolution.

Results

We introduced a palmitoylation site in the proximal part of the C-terminus of the A_{2A} receptor; this led to the loss of restricted collision coupling of the receptor to its G protein. We also deleted a DVELL motif in the distal part of the C-terminus, which disrupted the interaction of the receptor with a "synaptic associated protein" (SAP102). The mobility of these mutants has been compared with wild-type A_{2A} receptors in different compartments of hippocampal neurons.

Conclusions

The signaling properties of the A_{2A} adenosine receptor depend on its localization within several membrane compartments. Targeting to specific compartments depends on the interaction with "accessory proteins".

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