BMC Pharmacology

Meeting abstract

Interactions of the G protein-coupled receptor-associated sorting proteins (GASP) 1 and 2 with the novel cannabinoid receptor GPR55

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from 15th Scientific Symposium of the Austrian Pharmacological Society (APHAR) Joint meeting with the Hungarian Society of Experimental and Clinical Pharmacology (MFT) and the Slovenian Pharmacological Society (SDF)
Graz, Austria. 19-21 November 2009

Published: 12 November 2009

BMC Pharmacology 2009, **9**(Suppl 2):A5 doi:10.1186/1471-2210-9-S2-A5

This abstract is available from: http://www.biomedcentral.com/1471-2210/9/S2/A5

Background

GPR55 was recently found to be a novel cannabinoid receptor containing a seven transmembrane-spanning domain and being a member of the G protein-coupled receptor (GPCR) subfamily A. GPR55 is activated by different cannabinoid ligands as well as by the lipid ligand lysophosphatidylinositol (LPI). Generally, the activity of GPCRs is coordinated by receptor signaling, receptor desensitization and receptor resensitization. The latter two mechanisms are typically associated with the sorting of the GPCRs between degradation or recycling pathways and are highly regulated. Several sorting proteins have recently been identified, for example the G protein-coupled receptor-associated sorting protein-1 (GASP1). GASP1 was originally found to target δ opioid receptors (DORs) to lysosomes, hence a degradative pathway. Moreover, it was shown that the interface of the DOR-GASP1 protein-protein interaction is predominantly located in the *C*-terminal portion of the receptor protein.

Results

Here we show that the novel cannabinoid receptor GPR55 can internalize after ligand activation and is subsequently targeted to intracellular vesicles of the lysosomal compartments. This result and the close similarity of GPR55 to the cannabinoid receptor CB_1 - which is targeted to lysosomes via the GASP1 protein - suggested that GASP may be involved in targeting GPR55 to lysosomes. In fact, the *C*-terminus of GPR55 binds GASP1, cGASP1 (the *C*-terminal part of GASP1) and GASP2 (the closest homologue to GASP1) *in vitro*.

Conclusion

This work provides the first evidence that the novel cannabinoid receptor GPR55 is targeted to lysosomes after prolonged agonist stimulation and that this mechanism is likely regulated by members of the newly discovered G protein-coupled receptor-associated sorting proteins, i.e GASP1 and GASP2.