Signaling specificity of G-protein-coupled receptor (GPCR): Lessons from melanin-concentrating hormone receptor 1

The signaling and trafficking of most GPCRs involves receptor interactions with G proteins, GRKs, arrestins and other receptors. In addition to these widespread GPCR associations, there are many other types of GPCR-interacting proteins that can interact with particular receptors to fine-tune receptor activity. Melanin-concentrating hormone (MCH) is a cyclic neuropeptide exerting its action through two G GPCRs, MCHR1 and MCHR2. The extensive progress using genetic and pharmacological approaches has confirmed that the MCH-MCHR1 system is involved in feeding, energy homeostasis, sleep and emotional processing. In mammalian cells transfected with MCHR1, MCH is able to activate multiple signaling pathways including calcium mobilization, p-ERK activation, and inhibition of cyclic AMP generation through Gi/o- and Gq-coupled pathways. In this seminar, I review the current knowledge regarding: i) the common and distinguishing structural features of MCHR1 for receptor activation and G protein selectivity and ii) the mechanism controlling the fine-tuning of MCHR1 signaling by receptor-selective partners and their possible physiological significance. Lastly, we will discuss our very recent works on functional and physiological roles of MCHR1 selectively located in neuronal primary cilia.

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Basic findings

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