Structure and Function of Novel G Protein Regulatory Molecules

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Heterotrimeric GTP-binding regulatory proteins (G proteins) transduce many extracellular signals, such as photons, odorants, hormones, and neurotransmitters, from heptahelical G protein-coupled receptors (GPCRs) to intracellular signaling molecules. G proteins are composed of α, β, and γ subunits, and the latter two subunits usually form a heterodimer. G protein activity is regulated by GDP/GTP exchange and GTP hydrolysis, and its guanine nucleotide cycle is controlled by three classes of regulators, guanine nucleotide exchange factors (GEFs), GTPase activating proteins (GAPs), and GDP dissociation inhibitors (GDIs). A ligand-activated GPCR acts as GEF, which stimulates the exchange of bound GDP for GTP on the G protein α subunit (Gα). GTP binding allows the G protein to dissociate Gα-GTP from Gβγ, and GTP-bound Gα and Gβγ independently or cooperatively regulate effectors. Signal termination is achieved by GTP hydrolysis, resulting in the reformation of an inactive heterotrimer. RGS proteins that act as GAPs for Gα accelerate the GTP hydrolysis activity, leading to the rapid termination of the signal. Recently, several Gα-interacting molecules, which act as other candidate effectors and regulators of G protein signaling, were found. In this symposium, I will introduce the novel type of G protein-interacting molecules, including Ric-8, Flotillin, and YM-254890. Studies on the molecular mechanism of these molecules should help in our understanding of the general principle of G protein activation, and the role of each G protein in divergent G protein signaling systems.