

RGS Proteins and Ion Channel Modulation

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Regulator of G protein signaling (RGS) proteins are a diverse family of greater than 20 proteins that interact with GTP-bound $G\alpha$ subunits of the heterotrimeric G-protein family. RGS proteins augment the intrinsic GTPase activity of the $G\alpha$ subunit thereby accelerating the termination of G-protein signaling following agonist removal. The participation of RGS proteins in the G-protein cycle provide an explanation for why physiological responses deactivate following agonist removal at a rate greater than that predicted from measurements of $G\alpha$ subunit GTPase activity. To explore how RGS proteins influence ion channel modulation in neuronal systems, two approaches were employed. First, RGS proteins were heterologously overexpressed and the impact on ion channel modulation determined. Second, G-protein signaling pathways were “reconstructed” by expressing $G\alpha$ subunits rendered insensitive to both Pertussis toxin (PTX) and RGS proteins. The latter methodology lends insight into the role of native RGS proteins. The results of these studies suggest that endogenous RGS proteins play an integral role in controlling both the strength and duration of G-protein-coupled receptor mediated ion channel modulation.