Regulation of Receptor Expression by G Protein

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Angiotensin receptor is classified as type 1 (AT1R) and type 2 (AT2R) that belong to superfamily of G protein-coupled receptors. Among two subtypes, AT1R is mainly involved in regulation of cardiovascular system, and participated in various cardiovascular diseases. The extent of G protein-coupled receptor-mediated responses is determined by the expression levels of receptor, G protein, and effector molecule. Compared with G protein and effector molecule, receptors easily change their expression by various treatments. Therefore, the expression level of receptor is tightly regulated by various mechanisms. While we examined the role of G_i in AT1R-mediated fibrotic responses of rat cardiac fibroblasts using *Pertussis toxin* (PTX), we found that PTX treatment enhances AT1R-mediated Ca^{2+} response. Receptor binding assay revealed that PTX increases the number of AT1R without affecting the affinity for angiotensin II. Among small G proteins, Rac is selectively activated by PTX treatment. PTX treatment increased the expression of IL-1β through Rac-mediated pathway. The treatment with anti-IL-1β antibody or IL-1β siRNAs inhibited the PTX-induced enhancement of angiotensin II-stimulated increases in $[Ca^{2+}]_i$. Thus, secreted IL-1β works as a positive regulator of AT1R expression. The expression of DN-Rac suppressed PTX-induced reactive oxygen species (ROS) production that is necessary for upregulation of AT1R and IL-1β production. These results suggest that Rac plays an essential role in regulation of AT1R expression and AT1R-mediated $[Ca^{2+}]_i$ response through IL-1β production.