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Prostaglandin E receptor EP1 forms a complex with dopamine D1 receptor, regulates ligand binding of D1 receptors, and stimulates D1-induced cAMP production through Gβγ in HEK293T cells.

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Abstract

Recent evidence indicates a role for prostaglandin (PG) E_2 and its receptor EP1 in dopaminergic regulation of emotional behaviors. However, a biochemical link between EP1 and dopamine receptor signaling is lacking. Here we report that EP1 forms a complex with dopamine D1 receptors and that EP1 stimulation augments D1-mediated cAMP production in HEK293T cells. Pharmacological blockade of intracellular Ca^{2+} rise, a major signaling pathway of EP1, did not affect EP1-mediated facilitation of D1-induced cAMP production. Rather, EP1 stimulation increased maximal ligand binding of D1 receptors. In addition, consistent with a previous report that $G_{\beta\gamma}$ can augment Gs-mediated cAMP production, overexpression of $G_{t\alpha}$ as a $G_{\beta\gamma}$ scavenger reduced D1-mediated cAMP production with EP1 stimulation, but not that without EP1 stimulation, suggesting a role for $G_{\beta\gamma}$ in the action of EP1 on D1 receptor signaling. Therefore, our study suggests a complex formation of EP1 and D1 receptors as a basis for the crosstalk between these two receptors, and novel actions of PGE_2-EP1 signaling through controlling the ligand binding capacity of D1 receptors and Gβγ subunits.