



GPCRs ARE MOLECULAR SWITCHES THAT TRANSLATE EXTRACELLULAR SIGNALS

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INTRODUCTION

G protein-coupled receptors (GPCRs) are a large family of important membrane receptors in immune cells, including mast cells (MCs), that are characterized by seven alpha-helical transmembrane domains which recognize ligands such as cytokines, histamine, etc., and activate the G protein within the cell, where it triggers a signalling cascade (1). There are different types of G proteins: Gi decrease cAMP, Gs increases cAMP, and Gq increases intracellular calcium (Ca²⁺).

G PROTEIN-COUPLED RECEPTOR

Immune cells, such as MCs, express GPCRs (2). MCs are sensory immune cells that are ubiquitous in the body. They mediate innate and adaptive immunity and possess numerous and varied receptors such as FcεRI, CCR, CXCR, C3a and C5a, c-Kit (CD117), IL-1R, TNFR, and TLRs, among others, including GPCRs. In MCs, GPCRs trigger degranulation, releasing inflammatory molecules that damage tissue (3). Some of these compounds can be released immediately, while others are generated later through protein synthesis.

GPCRs are important receptors in neurology. They are located on the membranes of neurons and glial cells, where they process extracellular signals in response to intracellular signals. When a neurotransmitter binds to its receptor, it activates an intracellular G protein, which in turn mediates a biochemical cascade involved in neurological diseases. These intracellular events begin with a ligand binding to a GPCR, which in turn activates a G protein, leading to second messengers and the cellular response (4). GPCRs regulate various biological functions, such as neurotransmitter release, neuronal excitability, synaptic plasticity, emotional behavior, memory, pain, and sleep. GPCRs also regulate neurotransmitters such as serotonin, dopamine, GABA, and norepinephrine.

The dopamine receptors D1 and D2 are GPCRs, and are coupled to Gs and Gi, respectively (5). These are involved in various pathological conditions, such as schizophrenia and Parkinson's disease. Several serotonin receptors, except those with GPCRs, are involved in some psychiatric disorders such as anxiety and depression but can also be involved in neurological disorders such as migraine. The μ (mu, MOR), κ (kay, KOR), and δ (delta, DOR) opioid receptors are GPCR A class, and Gi proteins can be activated by opioids, which lower cAMP and cause analgesia. (6). Opioids reduce neuronal excitability and pain transmission. When an opioid, such as morphine, binds to the receptor, it activates the Gi proteins, causing a decrease in adenylate cyclase and cAMP, closing presynaptic Ca²⁺ channels and opening postsynaptic potassium (K⁺) channels. This leads to reduced neurotransmitter release, neuronal hyperpolarization, and analgesia.

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GPCR dysregulation occurs in several neuronal disorders including movement disorders, Parkinson's disease, Alzheimer's disease, headache, depression, and epilepsy. Selective serotonin reuptake inhibitors (SSRIs) modulate these GPCR-related reactions, and about one-third of all drugs in general act by binding to them.

CONCLUSIONS

GPCRs are membrane proteins that receive extracellular signals and convert them into intracellular responses and are important modulators of brain activity and in neurological and psychiatric diseases, where they function primarily as modulators of the set of electrical and biochemical processes by which neurons communicate with each other. GPCRs are important drug targets because they are easily accessible from outside the cell. Various GPCRs are used, including antihistamines that block H1 receptors in allergies, β -blockers that antagonize β -adrenergic receptors for hypertension and heart disease, dopamine agonists used in Parkinson's disease, migraine drugs that act on serotonin receptors, and others.

Conflict of interest

The author declares that they have no conflict of interest.

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