G-protein activation

Castagnoli, L., Jassal, B., Le Novere, N.
**Introduction**

Reactome is open-source, open access, manually curated and peer-reviewed pathway database. Pathway annotations are authored by expert biologists, in collaboration with Reactome editorial staff and cross-referenced to many bioinformatics databases. A system of evidence tracking ensures that all assertions are backed up by the primary literature. Reactome is used by clinicians, geneticists, genomics researchers, and molecular biologists to interpret the results of high-throughput experimental studies, by bioinformaticians seeking to develop novel algorithms for mining knowledge from genomic studies, and by systems biologists building predictive models of normal and disease variant pathways.

The development of Reactome is supported by grants from the US National Institutes of Health (P41 HG003751), University of Toronto (CFREF Medicine by Design), European Union (EU STRP, EMI-CD), and the European Molecular Biology Laboratory (EBI Industry program).

**Literature references**


Reactome database release: 70

This document contains 1 pathway and 6 reactions (see Table of Contents)
Receptor activated heterotrimeric G proteins consist of the Galpha and the tightly associated Gbeta-gamma subunits. When a ligand binds to a G protein-coupled receptor, it stabilises a conformation with an high affinity for the G-protein bound to GDP. GDP is then exchanged for GTP on the Galpha subunit. This exchange triggers the dissociation of the Galpha subunit from the Gbeta-gamma dimer and the receptor. Galpha-GTP and Gbeta-gamma, can then modulate different signalling cascades and effector proteins, while the receptor is able to activate another G protein, resulting in an amplification cascade. The Galpha subunit will eventually hydrolyze the attached GTP to GDP by its inherent enzymatic activity, allowing it to reassociate with Gbeta-gamma and start a new cycle.

**Literature references**


**Editions**

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The high affinity receptor complex binds to G-protein

**Location:** G-protein activation

**Stable identifier:** R-HSA-167408

**Type:** transition

**Compartments:** plasma membrane

The high affinity complex beta-endorphin:mu opioid receptor binds to the heterotrimeric G-protein. This binding stabilises a conformation of the G-protein alpha i subunit presenting a low affinity for GDP, but a high affinity for GTP

**Preceded by:** G-protein beta-gamma subunits rebind the alpha-GDP subunit

**Followed by:** The receptor:G-protein complex releases GDP

**Literature references**


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The receptor:G-protein complex releases GDP

**Location:** G-protein activation

**Stable identifier:** R-HSA-167419

**Type:** dissociation

**Compartments:** cytosol, plasma membrane

G proteins are inactive in the GDP-bound state. The ternary complex neurotransmitter:receptor:G-protein releases GDP.

**Preceded by:** The high affinity receptor complex binds to G-protein

**Followed by:** The receptor:G-protein complex binds GTP

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The receptor:G-protein complex binds GTP

Location: G-protein activation

Stable identifier: R-HSA-167429

Type: transition

Compartments: cytosol, plasma membrane

The ternary complex neurotransmitter:receptor:G-protein binds GTP, resulting in activation of G protein.

Preceded by: The receptor:G-protein complex releases GDP

Followed by: The receptor:G-protein complex dissociates

Literature references


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The ternary complex neurotransmitter:receptor:G-protein dissociates. Both the alpha-i subunit and beta:gamma complex become active, by conformational transition and surface exposure, and both are free to activate downstream effectors.

**Preceded by:** The receptor:G-protein complex binds GTP

**Followed by:** G-protein alpha subunit is inactivated

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G-protein alpha subunit is inactivated

Location: G-protein activation

Stable identifier: R-HSA-167415

Type: transition

Compartments: cytoplasmic side of plasma membrane

Slow intrisinc GTPase activity results in an inactivation of the alpha-i subunit by hydrolyzing GTP to GDP.

Preceded by: The receptor-G-protein complex dissociates

Followed by: G-protein beta-gamma subunits rebind the alpha-GDP subunit

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**G-protein beta-gamma subunits rebind the alpha-GDP subunit**

**Location:** G-protein activation

**Stable identifier:** R-HSA-167433

**Type:** binding

**Compartments:** cytoplasmic side of plasma membrane

Gbetagamma rebinds Galpha-olfactory:GDP, stopping its activity

**Preceded by:** G-protein alpha subunit is inactivated

**Followed by:** The high affinity receptor complex binds to G-protein

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