ADP signalling through P2Y purinoceptor

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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: 71

This document contains 1 pathway and 4 reactions (see Table of Contents)
Co-activation of P2Y1 and P2Y12 is necessary for complete platelet activation. P2Y1 is coupled to Gq and helps trigger the release of calcium from internal stores, leading to weak and reversible platelet aggregation. P2Y12 is Gi coupled, inhibiting adenylate cyclase, leading to decreased cAMP, a consequent decrease in cAMP-dependent protein kinase activity which increases cytoplasmic [Ca2+], necessary for activation (Woulfe et al. 2001).

In activated platelets, P2Y12 signaling is required for the amplification of aggregation induced by all platelet agonists including collagen, thrombin, thromboxane, adrenaline and serotonin. P2Y12 activation causes potentiation of thromboxane generation, secretion leading to irreversible platelet aggregation and thrombus stabilization.

Literature references
P2RY12 binds ADP

**Location:** ADP signalling through P2Y purinoceptor 12

**Stable identifier:** R-HSA-417829

**Type:** binding

**Compartments:** extracellular region, plasma membrane

P2RY12 (Bodor et al. 2003) is found on the surface of blood platelet cells and is an important regulator in blood clotting. It is one of two ADP receptors expressed in platelets, the other is P2RY1. Activation leads to irreversible platelet aggregation. Defects in this receptor are associated with bleeding disorders. Its preferred ligand is ADP. The platelet anticoagulant drug clopidogrel binds to this receptor (Hollopeter G et al. 2001).

**Followed by:** Activated P2Y purinoceptor 12 binds G-protein Gi

**Literature references**


**Editions**

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Activated P2Y purinoceptor 12 binds G-protein Gi

**Location:** ADP signalling through P2Y purinoceptor 12

**Stable identifier:** R-HSA-392187

**Type:** binding

**Compartments:** plasma membrane

The activated receptor binds the inactive, GDP-bound form of the heterotrimeric G-protein Gi.

**Preceded by:** P2RY12 binds ADP

**Followed by:** Gi activation by P2Y purinoceptor 12

**Literature references**


**Editions**

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**Gi activation by P2Y purinoceptor 12**

**Location:** ADP signalling through P2Y purinoceptor 12

**Stable identifier:** R-HSA-392195

**Type:** transition

**Compartments:** cytosol, plasma membrane

The G-protein alpha subunit exchanges GDP for GTP

**Preceded by:** Activated P2Y purinoceptor 12 binds G-protein Gi

**Followed by:** Dissociation of the P2Y purinoceptor 12:Gi complex

**Literature references**


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Dissociation of the P2Y purinoceptor 12:Gi complex

**Location:** ADP signalling through P2Y purinoceptor 12

**Stable identifier:** R-HSA-392202

**Type:** dissociation

**Compartments:** extracellular region, plasma membrane

The classical view of G-protein signalling is that the G-protein alpha subunit dissociates from the beta:gamma dimer. Activated G alpha (s) and the beta:gamma dimer then participate in separate signalling cascades. Although G protein dissociation has been contested (e.g. Bassi et al. 1996), recent in vivo experiments have demonstrated that dissociation does occur, though possibly not to completion (Lambert 2008).

**Preceded by:** Gi activation by P2Y purinoceptor 12

**Literature references**

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