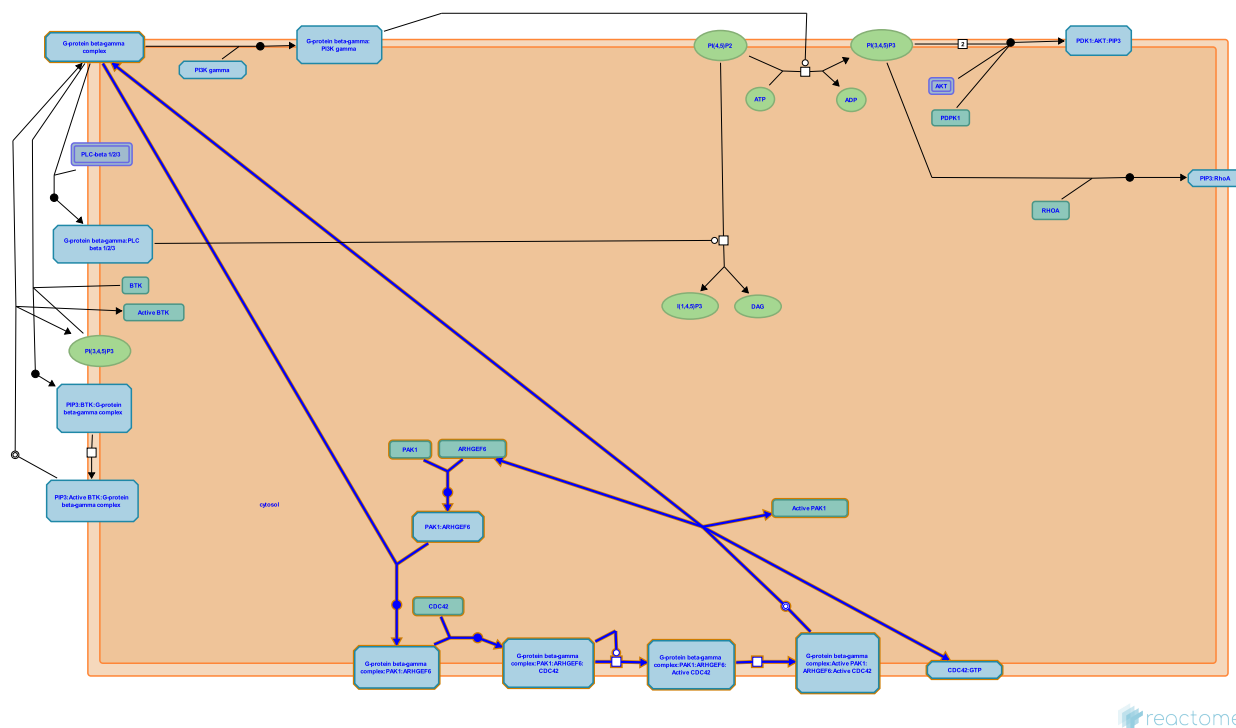


G beta:gamma signalling through CDC42



Goedhart, J., Varusai, TM.

European Bioinformatics Institute, New York University Langone Medical Center, Ontario Institute for Cancer Research, Oregon Health and Science University.

The contents of this document may be freely copied and distributed in any media, provided the authors, plus the institutions, are credited, as stated under the terms of [Creative Commons Attribution 4.0 International \(CC BY 4.0\) License](https://creativecommons.org/licenses/by/4.0/). For more information see our [license](https://reactome.org/page/faq).

This is just an excerpt of a full-length report for this pathway. To access the complete report, please download it at the [Reactome Textbook](https://reactome.org/page/faq).

18/05/2024

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

Fabregat, A., Sidiropoulos, K., Viteri, G., Forner, O., Marin-Garcia, P., Arnau, V. et al. (2017). Reactome pathway analysis: a high-performance in-memory approach. *BMC bioinformatics*, 18, 142. [↗](#)

Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics*, 33, 3461-3467. [↗](#)

Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res*, 46, D649-D655. [↗](#)

Fabregat, A., Korninger, F., Viteri, G., Sidiropoulos, K., Marin-Garcia, P., Ping, P. et al. (2018). Reactome graph database: Efficient access to complex pathway data. *PLoS computational biology*, 14, e1005968. [↗](#)

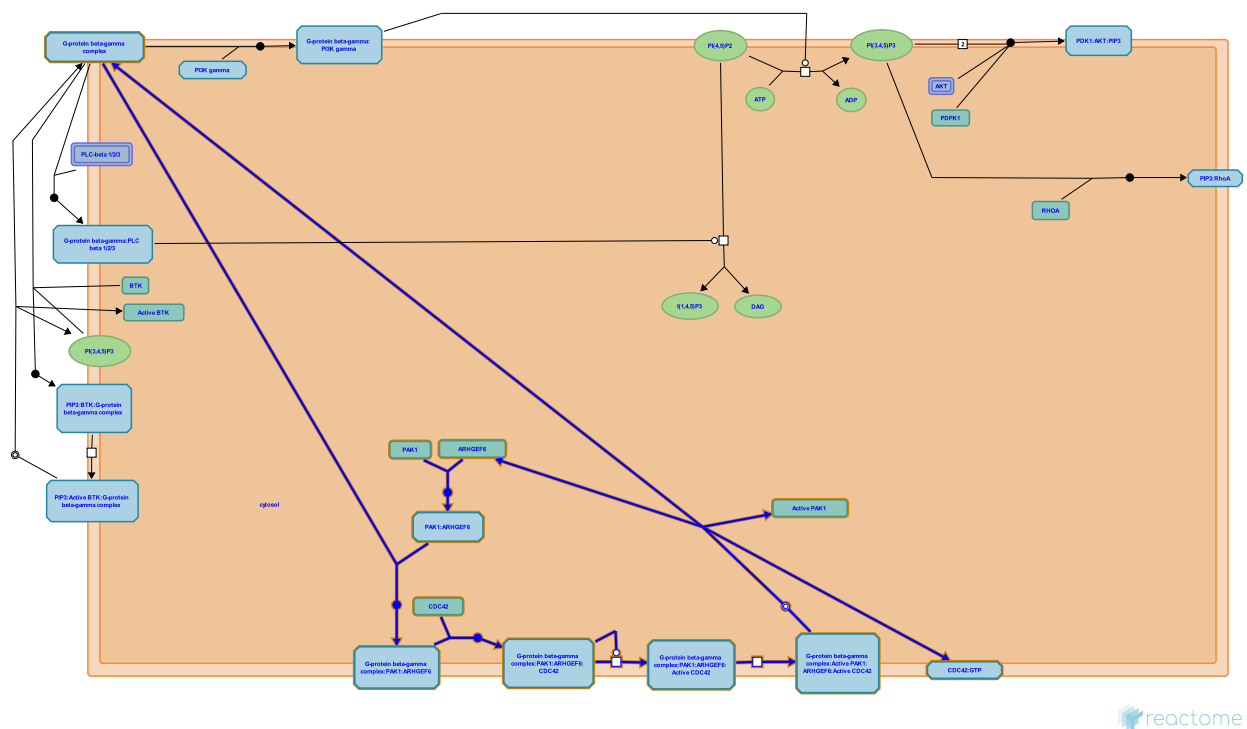
Reactome database release: 88

This document contains 1 pathway and 6 reactions ([see Table of Contents](#))

G beta:gamma signalling through CDC42 ↗

Stable identifier: R-HSA-8964616

Compartments: plasma membrane, cytosol



reactome

G-Protein Coupled Receptors (GPCR) sense extracellular signals and activate different Guanine nucleotide binding proteins (G-proteins) that have alpha, beta and gamma subunits. Upon activation, the alpha subunit of G-proteins dissociates from beta-gamma and the both are then free to regulate downstream effectors. Serine/threonine-protein kinase PAK 1 binds with Rho guanine nucleotide exchange factor 6 (ARHGEF6, PIX-Alpha) in the cytosol and is subsequently translocated by the G-protein beta-gamma complex to the plasma membrane. Here, ARHGEF6 activates Cell division control protein 42 homolog (CDC42) by acting as a GEF. Once active, CDC42 can facilitate the activation of PAK1. CDC42 is known to be involved in epithelial cell polarization processes.

Literature references

Wu, Y., Li, Z., Mo, Z., Smrcka, AV., Huang, CK., Liu, B. et al. (2003). Directional sensing requires G beta gamma-mediated PAK1 and PIX alpha-dependent activation of Cdc42. *Cell*, 114, 215-27. ↗

Editions

2017-07-27	Authored, Edited	Varusai, TM.
2018-08-29	Reviewed	Goedhart, J.

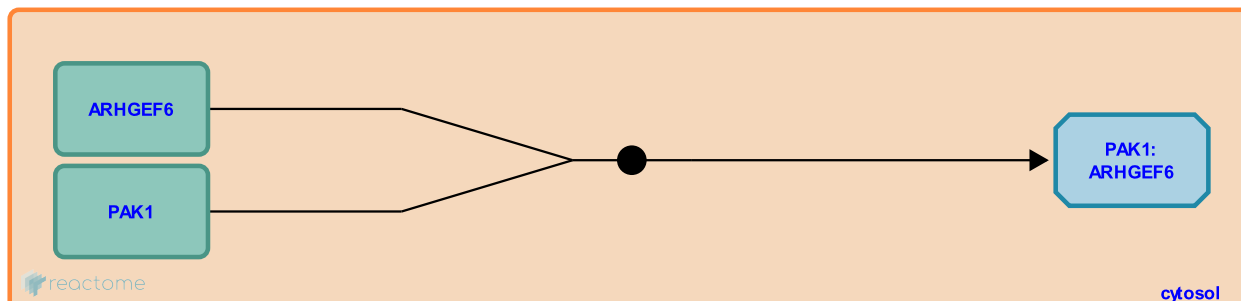
PAK1 binds ARHGEF6 ↗

Location: [G beta:gamma signalling through CDC42](#)

Stable identifier: R-HSA-8964619

Type: binding

Compartments: cytosol



G-Protein Coupled Receptors (GPCR) sense extracellular signals and activate different Guanine nucleotide binding proteins (G-proteins) that have alpha, beta and gamma subunits. Upon activation, the alpha subunit of G-proteins dissociates from beta-gamma and the both are then free to regulate downstream effectors. Serine/threonine-protein kinase PAK 1 can directly bind with Rho guanine nucleotide exchange factor 6 (ARHGEF6, PIX-Alpha) in the cytosol. This complex is then translocated to the plasma membrane where Cell division control protein 42 homolog (CDC42) is activated. CDC42 is known to be involved in epithelial cell polarization processes.

Followed by: [PAK1:ARHGEF6 complex binds G-protein beta-gamma complex](#)

Literature references

Wu, Y., Li, Z., Mo, Z., Smrcka, AV., Huang, CK., Liu, B. et al. (2003). Directional sensing requires G beta gamma-mediated PAK1 and PIX alpha-dependent activation of Cdc42. *Cell*, 114, 215-27. ↗

Editions

2017-07-27	Authored, Edited	Varusai, TM.
2018-08-29	Reviewed	Goedhart, J.

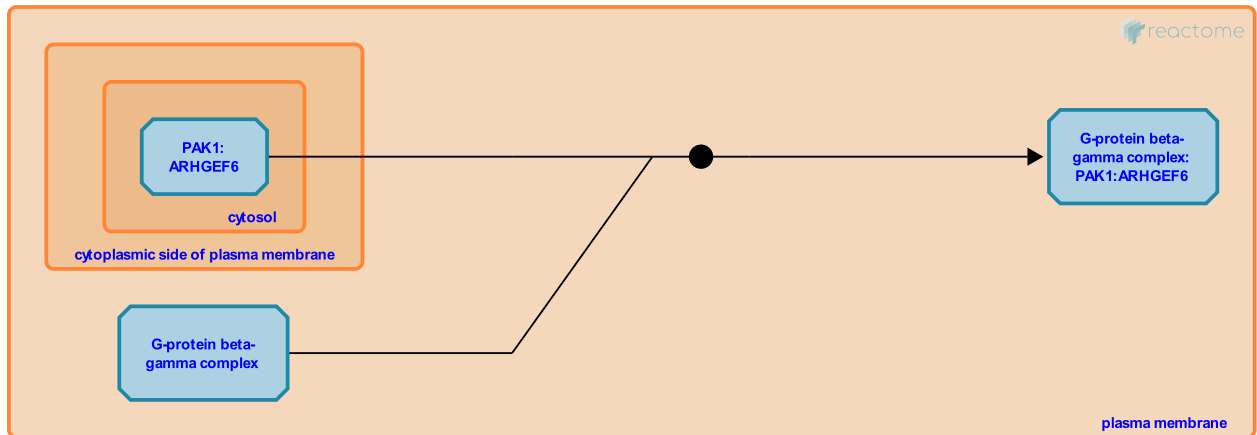
PAK1:ARHGEF6 complex binds G-protein beta-gamma complex ↗

Location: [G beta:gamma signalling through CDC42](#)

Stable identifier: R-HSA-8964605

Type: binding

Compartments: plasma membrane, cytosol



G-Protein Coupled Receptors (GPCR) sense extracellular signals and activate different Guanine nucleotide binding proteins (G-proteins) that have alpha, beta and gamma subunits. Upon activation, the alpha subunit of G-proteins dissociates from beta-gamma and the both are then free to regulate downstream effectors. Serine/threonine-protein kinase PAK 1 binds with Rho guanine nucleotide exchange factor 6 (ARHGEF6, PIX-Alpha) in the cytosol. PAK1 in this complex then binds to G-protein beta-gamma complex and facilitates the translocation of PAK1:ARHGEF6 complex to the plasma membrane, where Cell division control protein 42 homolog (CDC42) is activated. CDC42 is known to be involved in epithelial cell polarization processes.

Preceded by: [PAK1 binds ARHGEF6](#)

Followed by: [CDC42 binds GNB/GNG:PAK1:ARHGEF6 complex](#)

Literature references

Wu, Y., Li, Z., Mo, Z., Smrcka, AV., Huang, CK., Liu, B. et al. (2003). Directional sensing requires G beta gamma-mediated PAK1 and PIX alpha-dependent activation of Cdc42. *Cell*, 114, 215-27. ↗

Editions

2017-07-27	Authored, Edited	Varusai, TM.
2018-08-29	Reviewed	Goedhart, J.

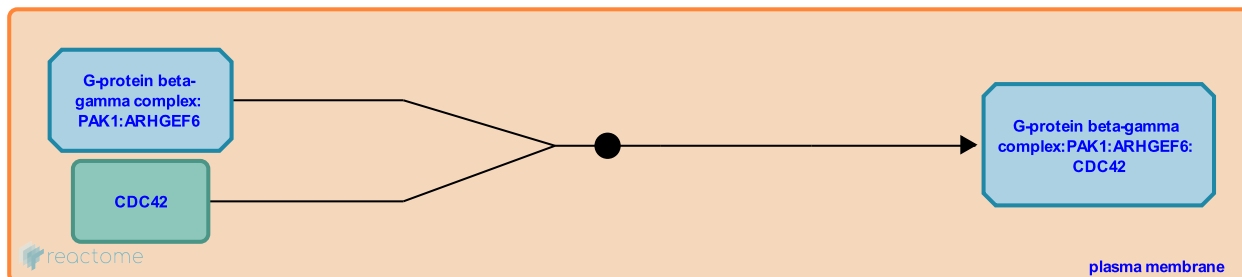
CDC42 binds GNB/GNG:PAK1:ARHGEF6 complex ↗

Location: [G beta:gamma signalling through CDC42](#)

Stable identifier: R-HSA-8964634

Type: binding

Compartments: plasma membrane



G-Protein Coupled Receptors (GPCR) sense extracellular signals and activate different Guanine nucleotide binding proteins (G-proteins) that have alpha, beta and gamma subunits. Upon activation, the alpha subunit of G-proteins dissociates from beta-gamma and the both are then free to regulate downstream effectors. Serine/threonine-protein kinase PAK 1 binds with Rho guanine nucleotide exchange factor 6 (ARHGEF6, PIX-Alpha) in the cytosol and is subsequently translocated by the G-protein beta-gamma complex to the plasma membrane. Here, the GTPase Cell division control protein 42 homolog (CDC42) binds with this complex, following which ARHGEF6 activates CDC42. CDC42 is known to be involved in epithelial cell polarization processes.

Preceded by: [PAK1:ARHGEF6 complex binds G-protein beta-gamma complex](#)

Followed by: [CDC42 in GNB/GNG:PAK1:ARHGEF6:CDC42 is activated](#)

Literature references

Wu, Y., Li, Z., Mo, Z., Smrcka, AV., Huang, CK., Liu, B. et al. (2003). Directional sensing requires G beta gamma-mediated PAK1 and PIX alpha-dependent activation of Cdc42. *Cell*, 114, 215-27. ↗

Editions

2017-07-27	Authored, Edited	Varusai, TM.
2018-08-29	Reviewed	Goedhart, J.

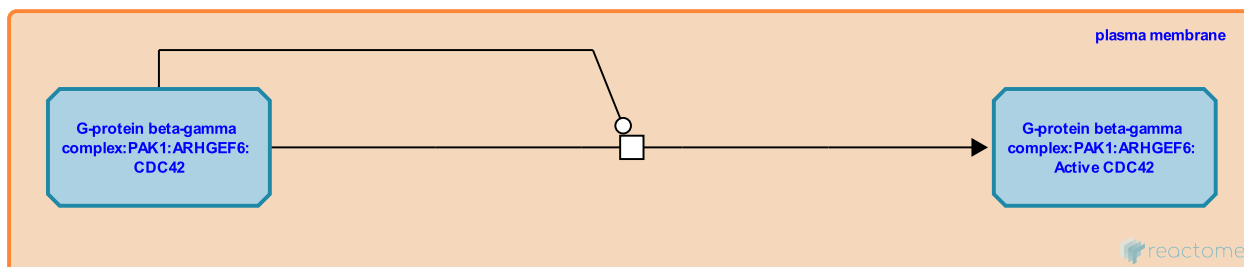
CDC42 in GNB/GNG:PAK1:ARHGEF6:CDC42 is activated ↗

Location: [G beta:gamma signalling through CDC42](#)

Stable identifier: R-HSA-8964604

Type: transition

Compartments: plasma membrane, cytosol



G-Protein Coupled Receptors (GPCR) sense extracellular signals and activate different Guanine nucleotide binding proteins (G-proteins) that have alpha, beta and gamma subunits. Upon activation, the alpha subunit of G-proteins dissociates from beta-gamma and the both are then free to regulate downstream effectors. Serine/threonine-protein kinase PAK 1 binds with Rho guanine nucleotide exchange factor 6 (ARHGEF6, PIX-Alpha) in the cytosol and is subsequently translocated by the G-protein beta-gamma complex to the plasma membrane. Here, the GTPase Cell division control protein 42 homolog (CDC42) binds with this complex. Subsequently, ARHGEF6 acts as a GEF for CDC42 and facilitates the activation of CDC42. CDC42 is known to be involved in epithelial cell polarization processes.

Preceded by: [CDC42 binds GNB/GNG:PAK1:ARHGEF6 complex](#)

Followed by: [PAK1 in GNB/GNG:PAK1:ARHGEF6:Active CDC42 is activated](#)

Literature references

Wu, Y., Li, Z., Mo, Z., Smrcka, AV., Huang, CK., Liu, B. et al. (2003). Directional sensing requires G beta gamma-mediated PAK1 and PIX alpha-dependent activation of Cdc42. *Cell*, 114, 215-27. ↗

Editions

2017-07-27	Authored, Edited	Varusai, TM.
2018-08-29	Reviewed	Goedhart, J.

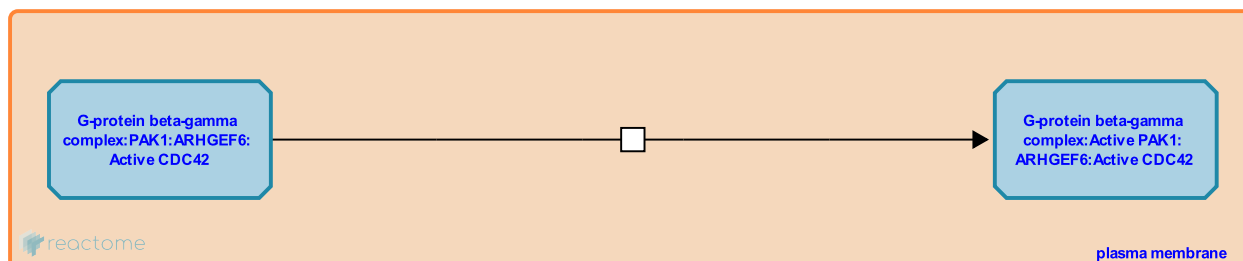
PAK1 in GNB/GNG:PAK1:ARHGEF6:Active CDC42 is activated ↗

Location: [G beta:gamma signalling through CDC42](#)

Stable identifier: R-HSA-8964614

Type: transition

Compartments: plasma membrane, cytosol



G-Protein Coupled Receptors (GPCR) sense extracellular signals and activate different Guanine nucleotide binding proteins (G-proteins) that have alpha, beta and gamma subunits. Upon activation, the alpha subunit of G-proteins dissociates from beta-gamma and the both are then free to regulate downstream effectors. Serine/threonine-protein kinase PAK 1 binds with Rho guanine nucleotide exchange factor 6 (ARHGEF6, PIX-Alpha) in the cytosol and is subsequently translocated by the G-protein beta-gamma complex to the plasma membrane. Here, ARHGEF6 activates the GTPase Cell division control protein 42 homolog (CDC42) by acting as a GEF. Upon activation, CDC42 facilitates the activation of PAK1 by exposing its catalytic domains. PAK1 is a signalling entity playing a key role in cytoskeleton dynamics, cell adhesion, migration, proliferation, apoptosis, mitosis, and vesicle-mediated transport processes.

Preceded by: [CDC42 in GNB/GNG:PAK1:ARHGEF6:CDC42 is activated](#)

Followed by: [Active PAK1 and Active CDC42 dissociates from GNB/GNG:PAK1:ARHGEF6:CDC42 complex](#)

Literature references

Wu, Y., Li, Z., Mo, Z., Smrcka, AV., Huang, CK., Liu, B. et al. (2003). Directional sensing requires G beta gamma-mediated PAK1 and PIX alpha-dependent activation of Cdc42. *Cell*, 114, 215-27. ↗

Editions

2017-07-27	Authored, Edited	Varusai, TM.
2018-08-29	Reviewed	Goedhart, J.

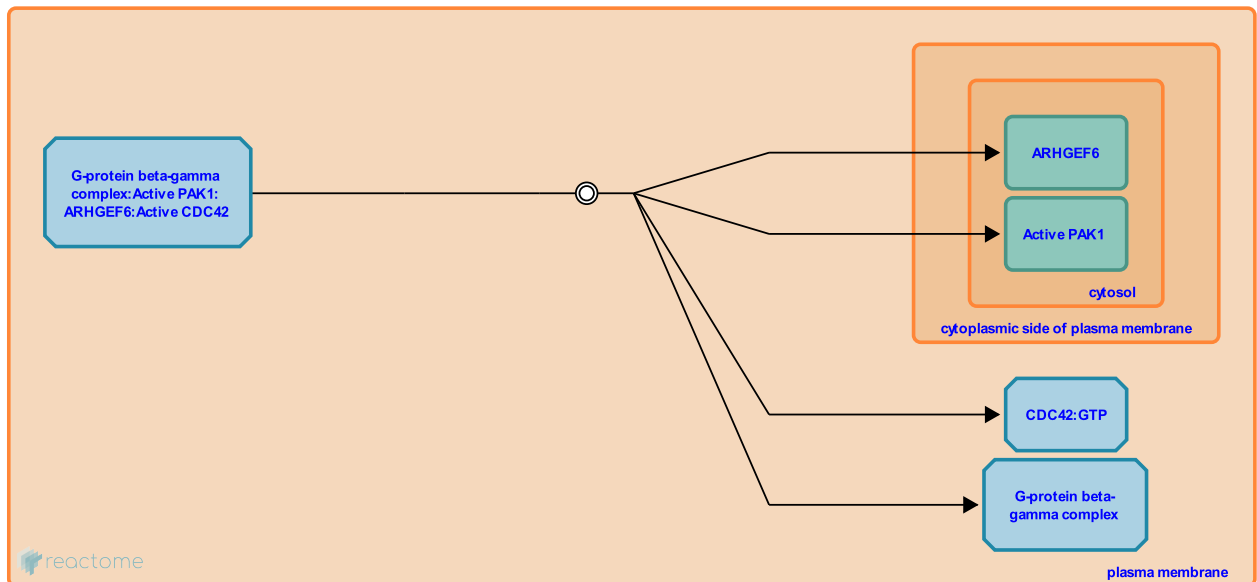
Active PAK1 and Active CDC42 dissociates from GNB/GNG:PAK1:ARHGEF6:CDC42 complex ↗

Location: G beta:gamma signalling through CDC42

Stable identifier: R-HSA-8964599

Type: dissociation

Compartments: plasma membrane, cytosol



G-Protein Coupled Receptors (GPCR) sense extracellular signals and activate different Guanine nucleotide binding proteins (G-proteins) that have alpha, beta and gamma subunits. Upon activation, the alpha subunit of G-proteins dissociates from beta-gamma and the both are then free to regulate downstream effectors. Serine/threonine-protein kinase PAK 1 binds with Rho guanine nucleotide exchange factor 6 (ARHGEF6, PIX-Alpha) in the cytosol and is subsequently translocated by the G-protein beta-gamma complex to the plasma membrane. Here, ARHGEF6 activates Cell division control protein 42 homolog (CDC42) by acting as a GEF. Once active, CDC42 can facilitate the activation of PAK1. At this stage the whole complex dissociates to release the active CDC42 and active PAK1. CDC42 is known to be involved in epithelial cell polarization processes. PAK1 plays an important role in cytoskeleton dynamics and cell adhesion.

Preceded by: PAK1 in GNB/GNG:PAK1:ARHGEF6:Active CDC42 is activated

Literature references

Wu, Y., Li, Z., Mo, Z., Smrcka, AV., Huang, CK., Liu, B. et al. (2003). Directional sensing requires G beta gamma-mediated PAK1 and PIX alpha-dependent activation of Cdc42. *Cell*, 114, 215-27. ↗

Editions

2017-07-27	Authored, Edited	Varusai, TM.
2018-08-29	Reviewed	Goedhart, J.

Table of Contents

Introduction	1
⚡ G beta:gamma signalling through CDC42	2
➤ PAK1 binds ARHGEF6	3
➤ PAK1:ARHGEF6 complex binds G-protein beta-gamma complex	4
➤ CDC42 binds GNB/GNG:PAK1:ARHGEF6 complex	5
➤ CDC42 in GNB/GNG:PAK1:ARHGEF6:CDC42 is activated	6
➤ PAK1 in GNB/GNG:PAK1:ARHGEF6:Active CDC42 is activated	7
➤ Active PAK1 and Active CDC42 dissociates from GNB/GNG:PAK1:ARHGEF6:CDC42 complex	8
Table of Contents	9