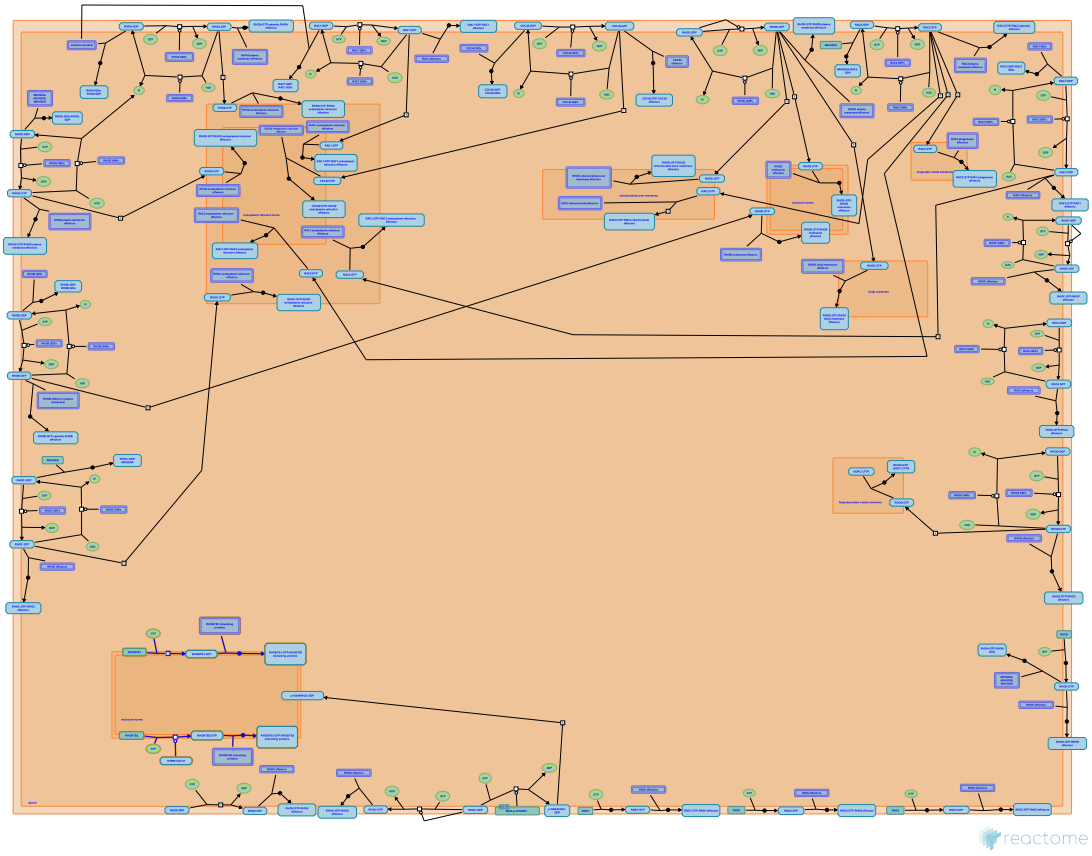
RHOBTB GTPase Cycle



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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

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. ↗

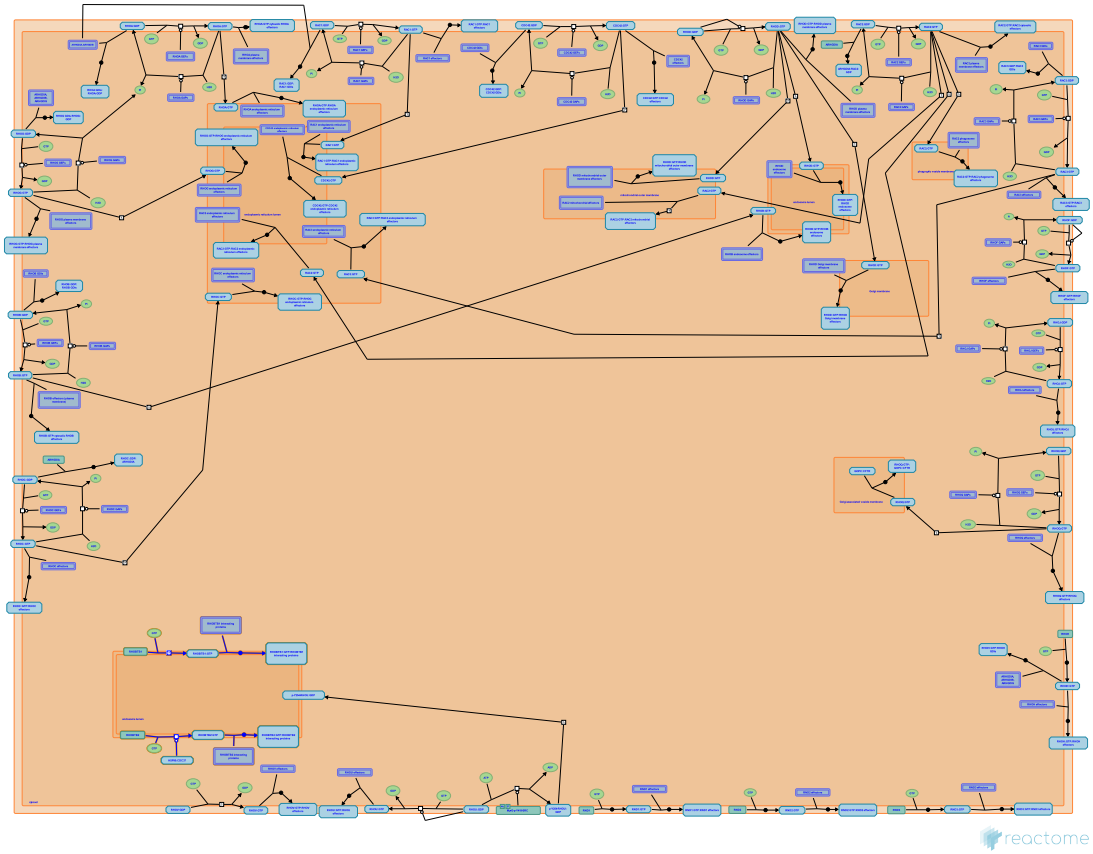
Fabregat, A., Korninger, F., Viteri, G., Sidiropoulos, K., Marin-Garcia, P., Ping, P. et al. (2018). Reactome graph database: Efficient access to complex pathway data. *PLoS computational biology, 14*, e1005968. ↗

Reactome database release: 88

This document contains 3 pathways (see Table of Contents)

RHOBTB GTPase Cycle ↗

Stable identifier: R-HSA-9706574



RHO BTB family belongs to atypical RHO GTPases, which are characterized by the absence of GTPase activity. RhoBTB family includes RHOBTB1 and RHOBTB2. RHOBTB3 is sometimes classified as the third RhoBTB family member, but it is divergent from the other two RHOBTBs and from Rho GTPases in general. RHOBTB1 is a component of a signaling cascade that regulates vascular function and blood pressure (Ji and Rivero 2016). RHOBTB2 is involved in COP9 signalosome-regulated and CUL3-dependent protein ubiquitination (Berthold et al. 2008; Ji and Rivero 2016).

Literature references

Ji, W., Rivero, F. (2016). Atypical Rho GTPases of the RhoBTB Subfamily: Roles in Vesicle Trafficking and Tumorigenesis. *Cells, 5*. ↗

Editions

2020-03-06	Authored	Orlic-Milacic, M.
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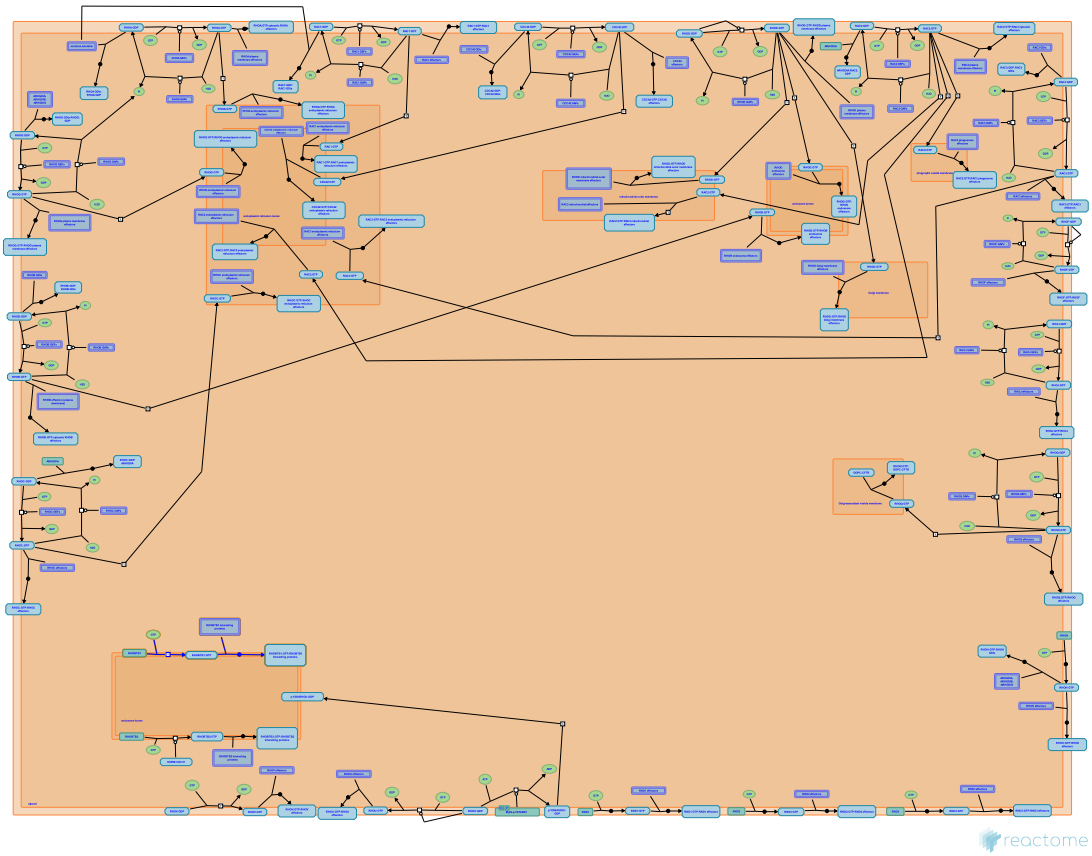
RHOBTB1 GTPase cycle ↗

Location: RHOBTB GTPase Cycle

Stable identifier: R-HSA-9013422



RHOBTB1 is an atypical member of the RHO GTPase family that is predicted not to cycle between a GTP-bound form and a GDP-bound form (Berthold et al. 2008). RHOBTB family proteins, in contrast to other RHO GTPases, possess other conserved domains in addition to the GTPase domain. The GTPase domain at the N-terminus is followed by a proline-rich region, a tandem of two BTB (broad-complex, tramtrack, bric à brac) domains, and a conserved C-terminal BACK (BTB and C-terminal Kelch) domain (Berthold et al. 2008, Ji and Rivero 2016). RHOBTB proteins can form homo- and heterodimers, but the role of dimerization in RHOBTB function is not known (Berthold et al. 2008, Ji and Rivero 2016). RHOBTB1 is highly expressed in skeletal muscle, placenta, stomach, kidney, testis, ovary, uterus and adrenal gland (Berthold et al. 2008). RHOBTB1 is a component of a signaling cascade that regulates vascular function and blood pressure (Ji and Rivero 2016). RHOBTB1 level is decreased in many cancer types and it is proposed to function as a tumor suppressor, but no mutations in RHOBTB1 have been detected in cancer (Berthold et al. 2008; Ji and Rivero 2016). RHOBTB1 localizes at early endosomes and participates in the architecture of the endosomal-lysosomal system (Long et al. 2020).

Literature references

Ji, W., Rivero, F. (2016). Atypical Rho GTPases of the RhoBTB Subfamily: Roles in Vesicle Trafficking and Tumorigenesis. *Cells, 5*. ↗

Schenkova, K., Berthold, J., Rivero, F. (2008). Rho GTPases of the RhoBTB subfamily and tumorigenesis. *Acta Pharmacol. Sin., 29*, 285-95. ↗

Mysior, MM., Long, M., Simpson, JC., Kranjc, T. (2020). RNA Interference Screening Identifies Novel Roles for RhoBTB1 and RhoBTB3 in Membrane Trafficking Events in Mammalian Cells. *Cells, 9*. ↗

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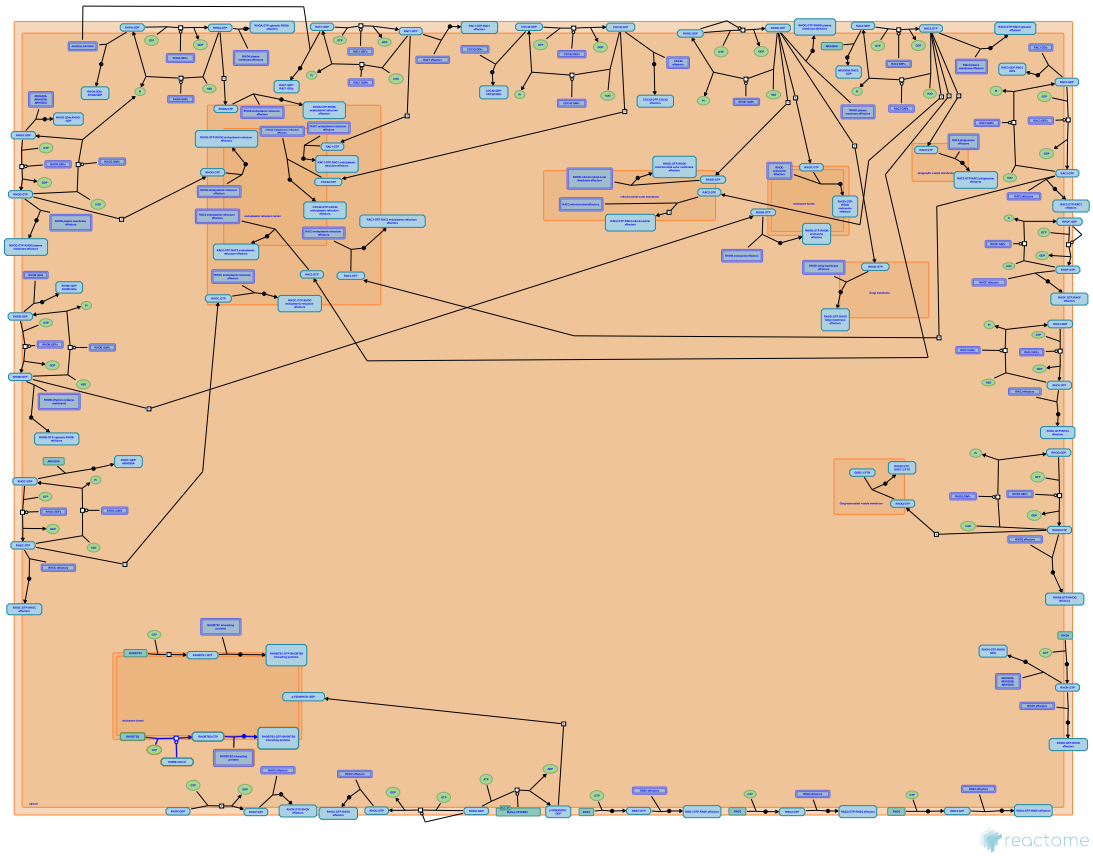
RHOBTB2 GTPase cycle ↗

Location: RHOBTB GTPase Cycle

Stable identifier: R-HSA-9013418



RHOBTB2 is an atypical member of the RHO GTPase family that is predicted not to cycle between a GTP-bound form and a GDP-bound form (Berthold et al. 2008). RHOBTB family proteins, in contrast to other RHO GTPases, possess other conserved domains in addition to the GTPase domain. The GTPase domain at the N terminus is followed by a proline rich region, a tandem of two BTB (broad complex, tramtrack, bric à brac) domains, and a conserved C terminal BACK (BTB and C terminal Kelch) domain (Berthold et al. 2008, Ji and Rivero 2016). RHOBTB proteins can form homo- and heterodimers, but the role of dimerization in RHOBTB function is not known (Berthold et al. 2008, Ji and Rivero 2016). RHOBTB2 is usually expressed weakly (Berthold et al. 2008), at a lower level than RHOBTB1 (Ji and Rivero 2016). Relatively high levels of RHOBTB2 can be detected in neural and cardiac tissues (Berthold et al. 2016). RHOBTB2 is involved in COP9 signalosome-regulated and CUL3-dependent protein ubiquitination (Berthold et al. 2008; Ji and Rivero 2016). RHOBTB2 suppresses cellular proliferation and promotes apoptosis (Ji and Rivero 2016). RHOBTB2 takes part in vesicle transport (Ji and Rivero 2016). RHOBTB2 was initially discovered as the gene homozygously deleted in breast cancer and was named DBC2 (deleted in breast cancer 2) (Berthold et al. 2008). RHOBTB2 level is decreased in many tumor types and it is proposed to act as a tumor suppressor. Genomic deletions and a small number of pathogenic mutations in RHOBTB2 have been reported in cancer (Berthold et al. 2008; Ji and Rivero 2016). Mutations of RHOBTB2 that result in impaired interaction with CUL3 have been found to cause epileptic encephalopathy (Belal et al. 2018).

Literature references

Ji, W., Rivero, F. (2016). Atypical Rho GTPases of the RhoBTB Subfamily: Roles in Vesicle Trafficking and Tumorigenesis. *Cells, 5*. ↗

Schenkova, K., Berthold, J., Rivero, F. (2008). Rho GTPases of the RhoBTB subfamily and tumorigenesis. *Acta Pharmacol. Sin., 29*, 285-95. ↗

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Tran, V., Gingras, AC., Elkholi, IE., Robert, A., Boulais, J., Faubert, D. et al. (2020). Mapping the proximity interaction network of the Rho-family GTPases reveals signalling pathways and regulatory mechanisms. *Nat. Cell Biol., 22*, 120-134. ↗

Editions

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