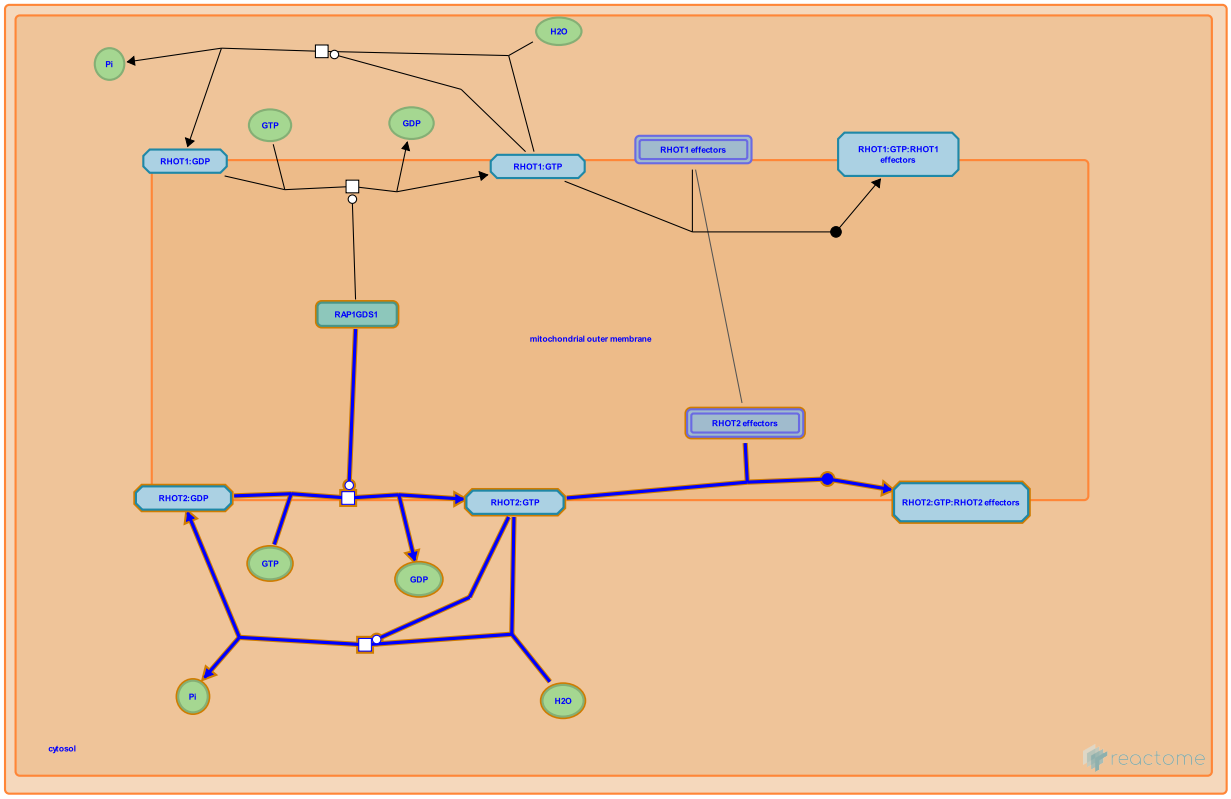
RHOT2 GTPase cycle



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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. ↗

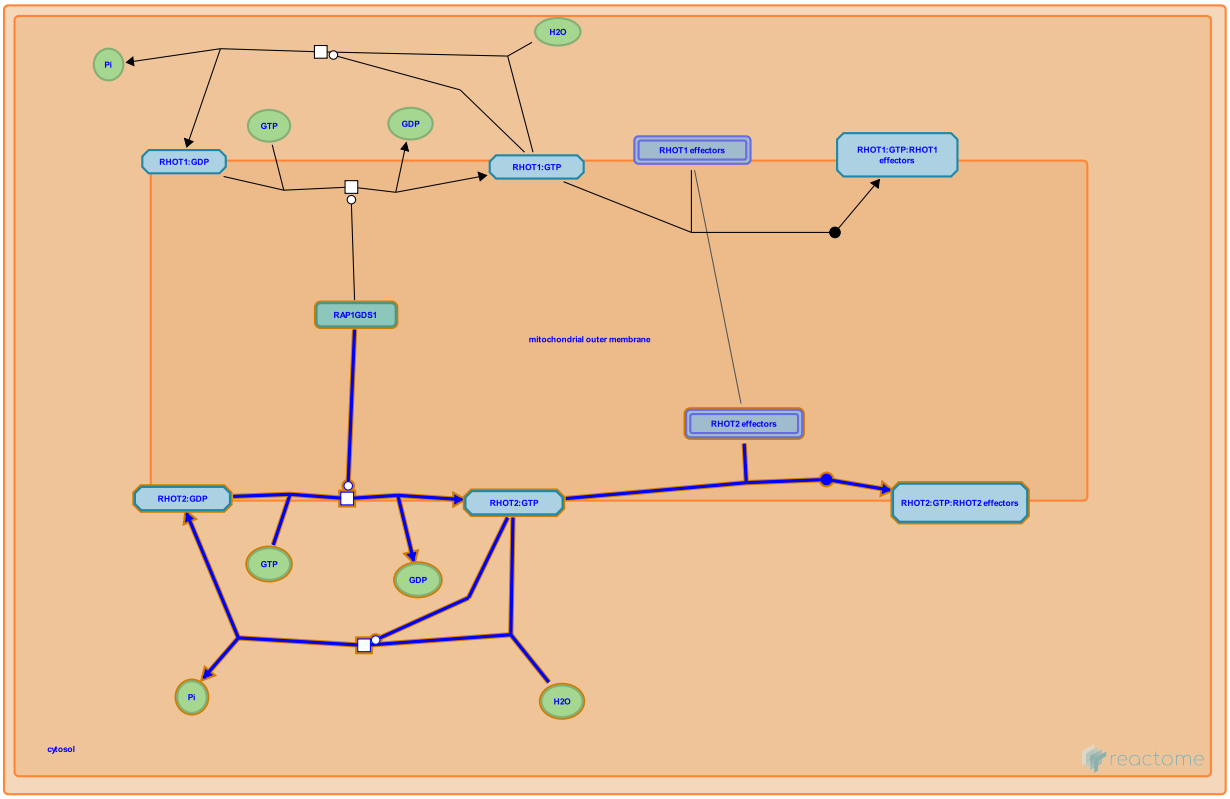
Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

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. ↗

RHOT2 GTPase cycle ↗

Stable identifier: R-HSA-9013419



This pathway catalogues guanine nucleotide exchange factors (GEFs) and effectors of RHOT2 (also known as MIRO-2). RHOT2 possesses a high intrinsic GTP-ase activity and does not require a GTPase activator protein (GAP) (Peters et al. 2018). No GDP dissociation inhibitors (GDIs) have been reported to interact with RHOT2. RHOT2 is a mitochondrial RHO GTPase. Like related RHOT1 (MIRO-1), RHOT2 localizes to the outer mitochondrial membrane. Similar to RHOT1, RHOT2 regulates mitochondrial movement by coupling mitochondria to kinesin and dynein motors that transport them along microtubules (Devine et al. 2016). RHOT2 is also localized to peroxisomes and it is involved in peroxisomal dynamics (Covill-Cooke et al. 2020).

Literature references

Covill-Cooke, C., Lopez-Domenech, G., Birsa, N., Kittler, JT., Toncheva, VS., Drew, J. (2020). Peroxisomal fission is modulated by the mitochondrial Rho-GTPases, Miro1 and Miro2. *EMBO Rep, 21*, e49865. ↗

Lakey, JH., Kay, L., Soundararajan, M., Eswaran, J., Peters, DT. (2018). Human Miro Proteins Act as NTP Hydrolases through a Novel, Non-Canonical Catalytic Mechanism. *Int J Mol Sci, 19*. ↗

Devine, MJ., Birsa, N., Kittler, JT. (2016). Miro sculpts mitochondrial dynamics in neuronal health and disease. *Neurobiol. Dis., 90*, 27-34. ↗

Editions

2020-07-14	Authored	Orlic-Milacic, M.
2021-02-09	Reviewed	Schrader, M., Castro, IG.
2021-02-25	Edited	Orlic-Milacic, M.

RHOT2 GEFs activate RHOT2 ↗

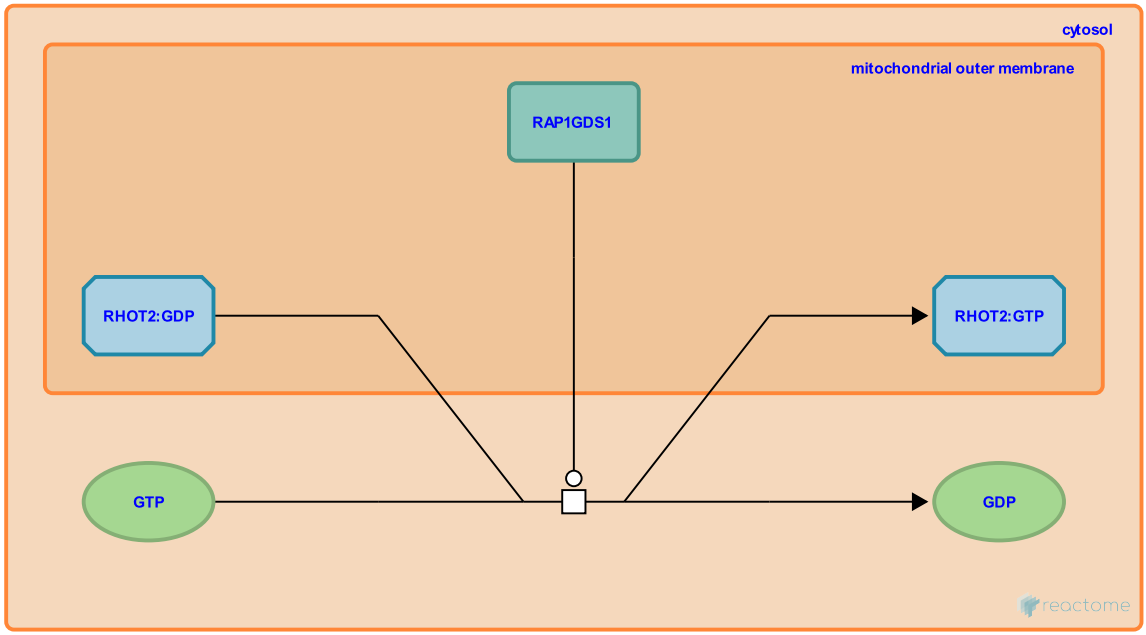
Location: RHOT2 GTPase cycle

Stable identifier: R-HSA-9018825

Type: transition

Compartments: cytosol, mitochondrial outer membrane

Inferred from: Vimar activates Miro (Drosophila melanogaster)



Based on studies in Drosophila, RAP1GDS1, an orthologue of Drosophila Vimar, is a mitochondrial outer membrane-bound atypical guanine nucleotide exchange factor (GEF) that activates mitochondria-associated atypical RHO GTPase RHOT2, an orthologue of Drosophila Miro, by catalyzing GDP to GTP exchange, resulting in formation of the active RHOT2:GTP complex (Ding et al. 2016).

Followed by: RHOT2 hydrolyzes GTP, RHOT2 binds effectors at the mitochondrial outer membrane

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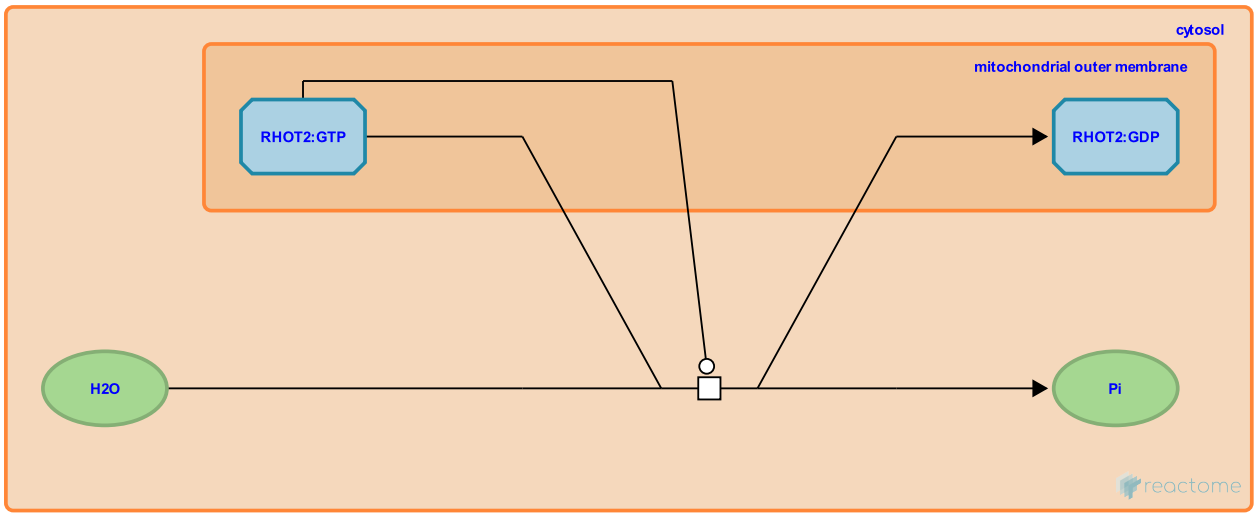
RHOT2 hydrolyzes GTP ↗

Location: RHOT2 GTPase cycle

Stable identifier: R-HSA-9018826

Type: transition

Compartments: cytosol, mitochondrial outer membrane



RHOT2 (Miro2) possesses a high intrinsic GTPase activity and does not require a GTPase activator protein (GAP) to hydrolyze GTP (Peters et al. 2018).

Preceded by: RHOT2 GEFs activate RHOT2

Literature references

Lakey, JH., Kay, L., Soundararajan, M., Eswaran, J., Peters, DT. (2018). Human Miro Proteins Act as NTP Hydrolases through a Novel, Non-Canonical Catalytic Mechanism. *Int J Mol Sci, 19*. ↗

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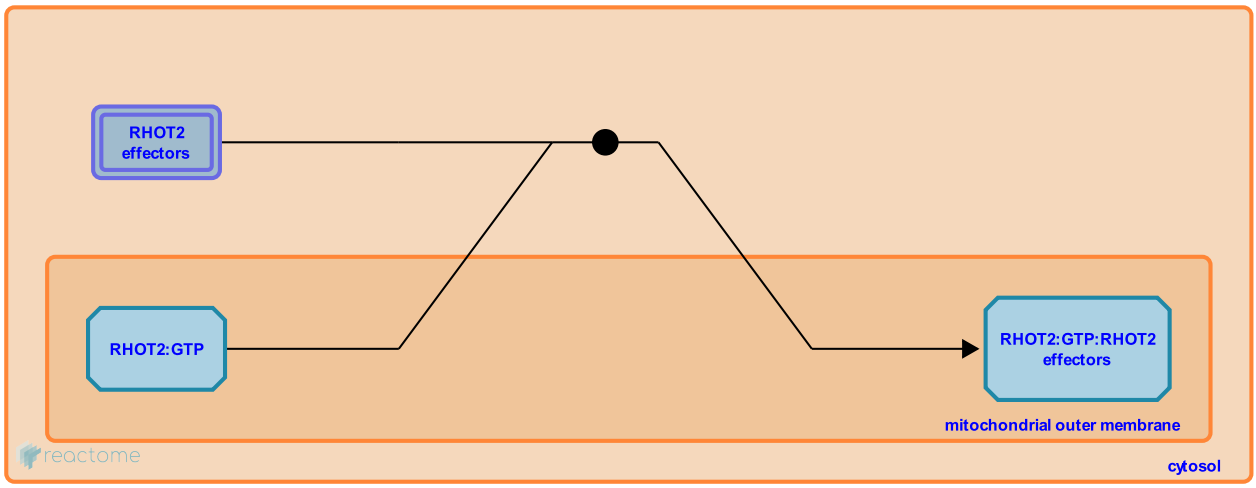
RHOT2 binds effectors at the mitochondrial outer membrane ↗

Location: RHOT2 GTPase cycle

Stable identifier: R-HSA-9018824

Type: binding

Compartments: cytosol, mitochondrial outer membrane



Active GTP-bound RHOT2 interacts with the following effectors:
MFN1 (Nemani et al. 2018)
MFN2 (Nemani et al. 2018)
MYO19 (Oeding et al. 2018; Bocanegra et al. 2020)
TRAK1 (Fransson et al. 2006)
TRAK2 (Fransson et al. 2006)

Preceded by: RHOT2 GEFs activate RHOT2

Literature references

Ruusala, A., Aspenström, P., Fransson, S. (2006). The atypical Rho GTPases Miro-1 and Miro-2 have essential roles in mitochondrial trafficking. *Biochem. Biophys. Res. Commun., 344*, 500-10. ↗

Caplan, J., Sesaki, H., Shanmughapriya, S., Jaña, F., Breves, SL., Craigen, WJ. et al. (2018). MIRO-1 Determines Mitochondrial Shape Transition upon GPCR Activation and Ca²⁺ Stress. *Cell Rep, 23*, 1005-1019. ↗

Schwarz, V., Honnert, U., Freitag, A., Majstrowicz, K., Oeding, SJ., Bähler, M. et al. (2018). Identification of Miro1 and Miro2 as mitochondrial receptors for myosin XIX. *J. Cell. Sci., 131*. ↗

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