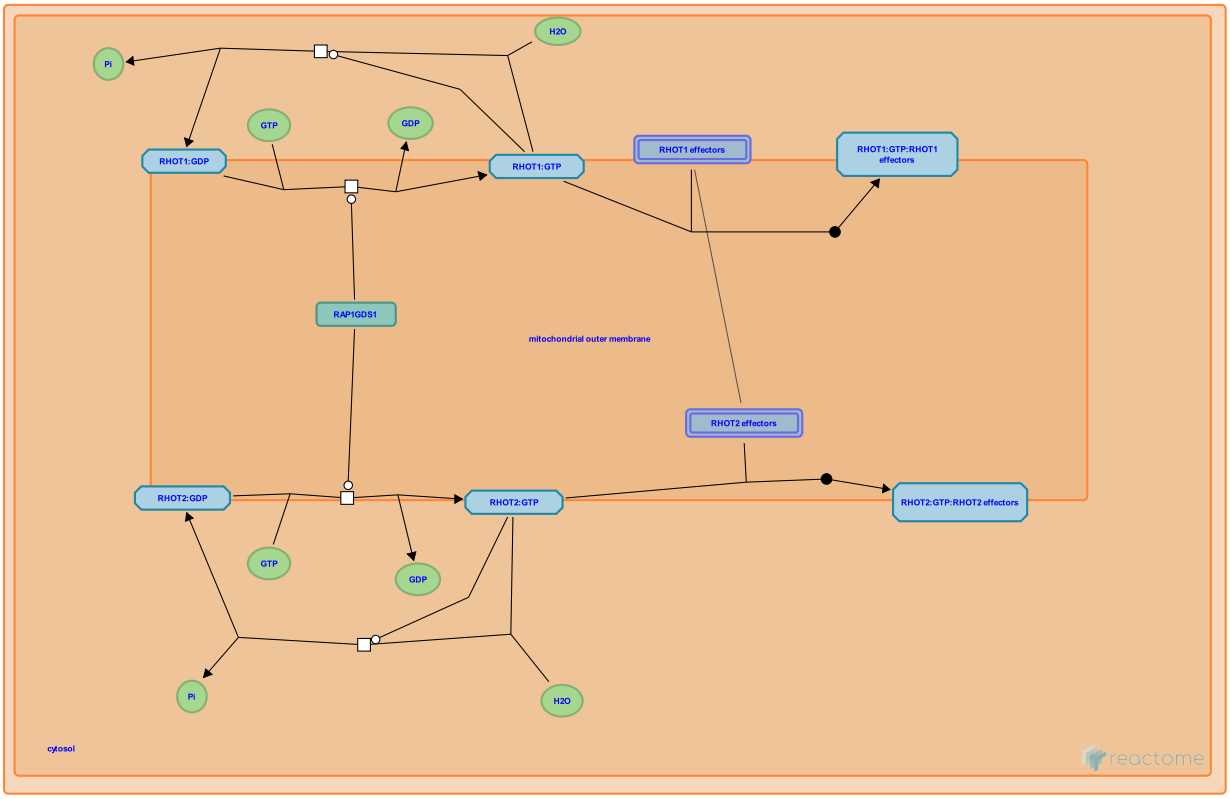
Miro GTPase Cycle



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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.
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Literature references

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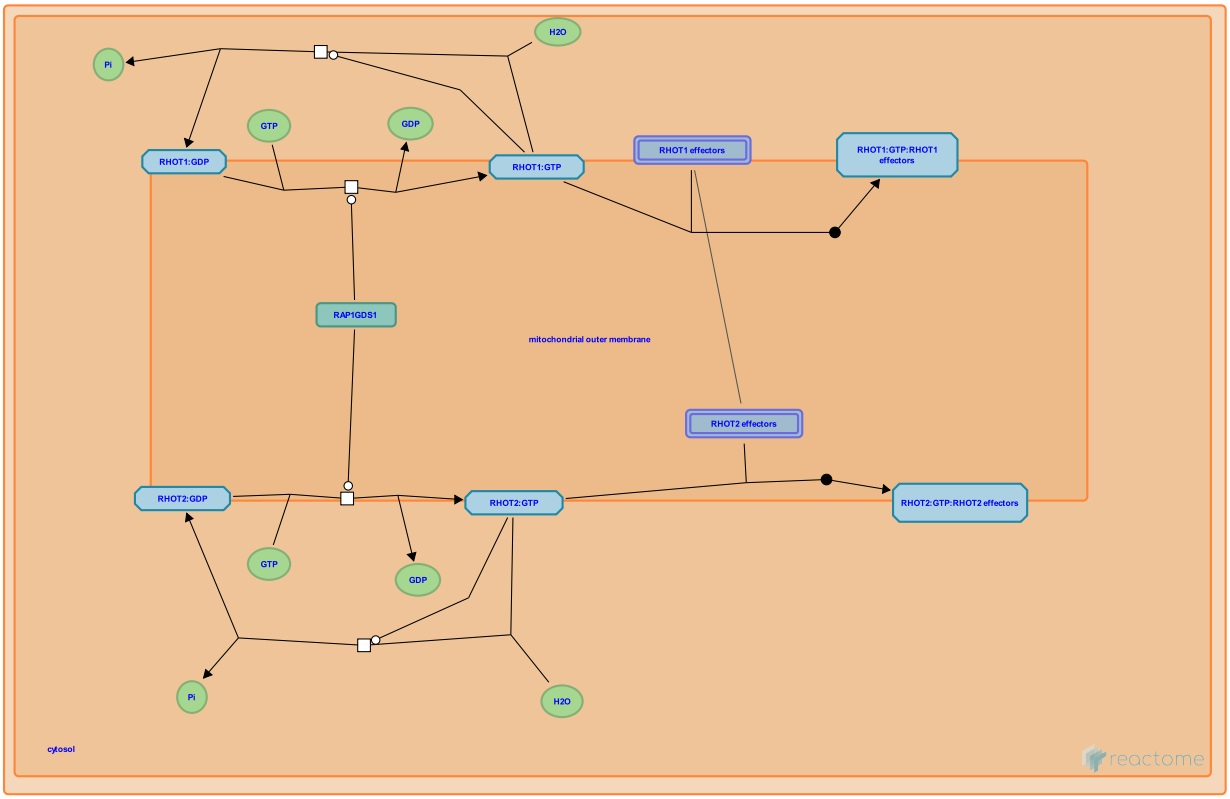
Fabregat, A., Korninger, F., Viteri, G., Sidiropoulos, K., Marin-Garcia, P., Ping, P. et al. (2018). Reactome graph database: Efficient access to complex pathway data. *PLoS computational biology, 14*, e1005968. ↗

Reactome database release: 88

This document contains 3 pathways (see Table of Contents)

Miro GTPase Cycle

Stable identifier: R-HSA-9715370



Miro GTPases are a separate family of Ras-related GTPases that are sometimes included in the atypical RHO GTPases group, but are phylogenetically distinct from the Rho family (Jaffe and Hall 2005; Boureux et al. 2007; Devine et al. 2016; Liu et al. 2017). Miro GTPases possess an additional GTPase domain more closely related to Rheb (Klosowiak et al. 2013). Miro family of RAS-like GTPases includes two members, RHOT1 and RHOT2. RHOT1 and RHOT2 regulate the movement of mitochondria (Schwarz 2013; Devine et al. 2016) and peroxisomes (Castro et al. 2018, Okumoto et al. 2018, Covill-Cooke et al. 2020).

Literature references

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Editions

2020-07-14	Authored	Orlic-Milacic, M.
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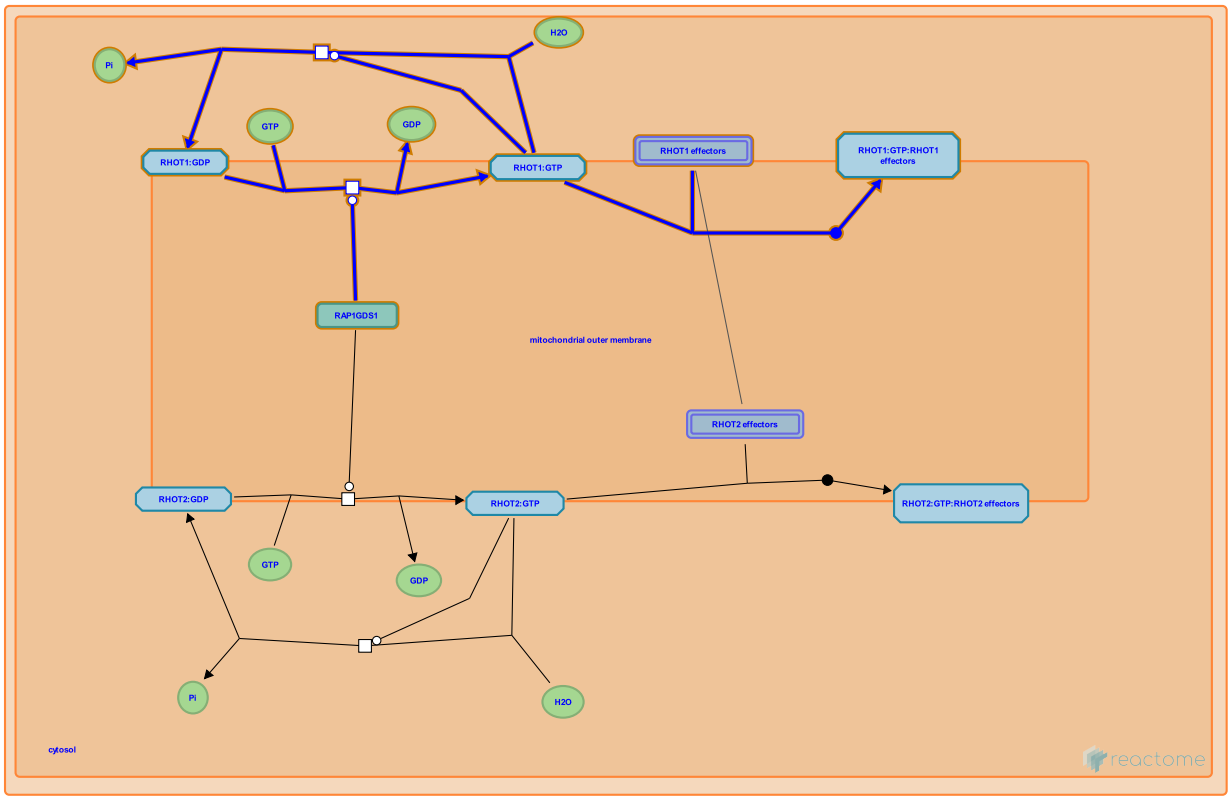
RHOT1 GTPase cycle ↗

Location: Miro GTPase Cycle

Stable identifier: R-HSA-9013425



This pathway catalogues guanine nucleotide exchange factors (GEFs) and effectors of RHOT1 (also known as MIRO-1). RHOT1 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 RHOT1. RHOT1 is a mitochondrial RHO GTPase. Like related RHOT2 (MIRO-2), RHOT1 localizes to the outer mitochondrial membrane. RHOT1 is implicated in mitochondrial movement inside the cells (Schwarz 2013), including the axonal transport of mitochondria in neurons (Saxton and Hollenbeck 2012; Birsa et al. 2013; Devine et al. 2016), as well as mitochondrial fission and fusion (Saxton and Hollenbeck 2012). RHOT1/RHOT2-mediated mitochondrial turnover is affected in neurodegenerative diseases (Birsa et al. 2013; Devine et al. 2016). RHOT1 can localize to peroxisomes and regulate peroxisome motility and fission (Castro et al. 2018, Okumoto et al. 2018, Covill-Cooke et al. 2020). RHOT1 is also involved in the regulation of ER-mitochondria membrane contact sites (Grossmann et al. 2019, Modi et al. 2019).
Upregulation of RHOT1 has a neuroprotective effect in ischemic stroke (Wei et al. 2019).

Literature references

Rapaport, D., Massart, F., Sharma, M., Glaab, E., May, P., Grünewald, A. et al. (2019). Mutations in RHOT1 Disrupt Endoplasmic Reticulum-Mitochondria Contact Sites Interfering with Calcium Homeostasis and Mitochondrial Dynamics in Parkinson's Disease. *Antioxid Redox Signal, 31*, 1213-1234. ↗

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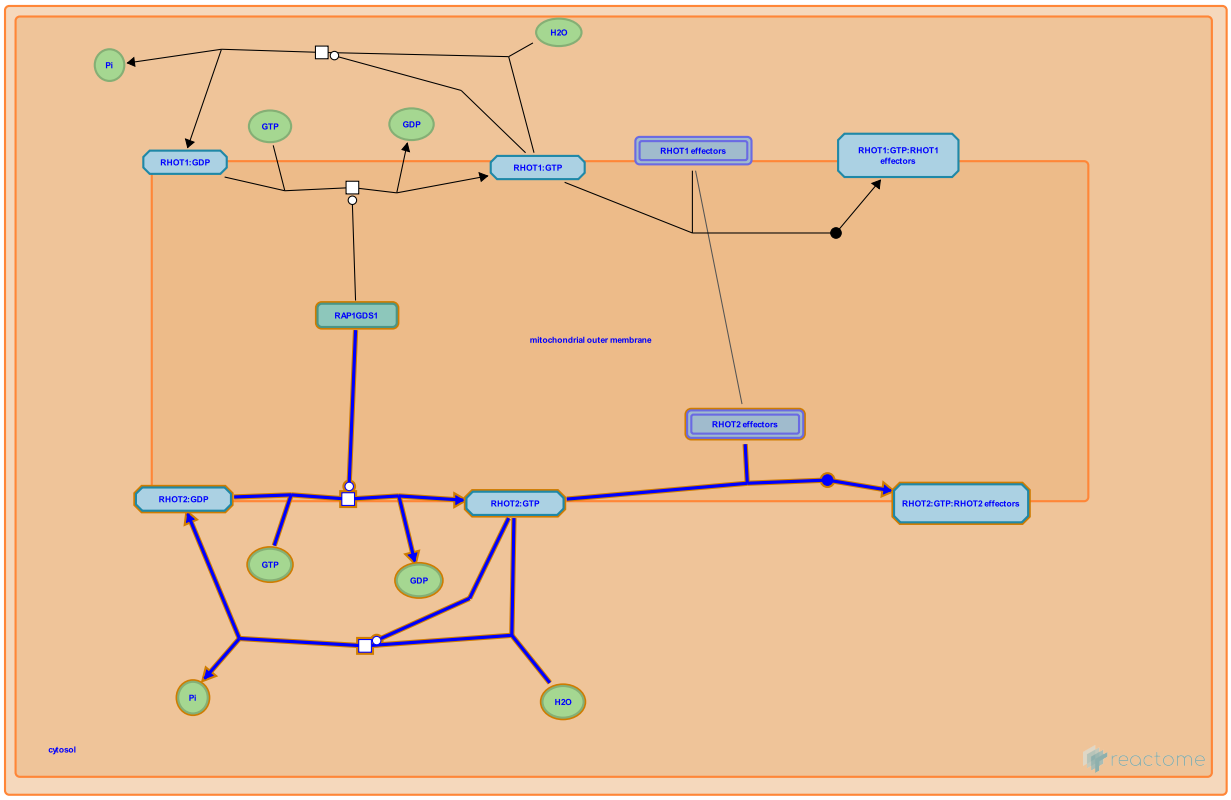
RHOT2 GTPase cycle ↗

Location: Miro 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

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

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