RHOBTB1 GTPase cycle

Fort, P., Orlic-Milacic, M., Rivero Crespo, F.

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. For more information see our license.

19/11/2021
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: 78

This document contains 1 pathway and 2 reactions (see Table of Contents)
RHOBTB1 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


## Editions

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
<th>Author</th>
</tr>
</thead>
<tbody>
<tr>
<td>2020-03-06</td>
<td>Authored</td>
<td>Orlic-Milacic, M.</td>
</tr>
<tr>
<td>2020-10-13</td>
<td>Reviewed</td>
<td>Rivero Crespo, F.</td>
</tr>
<tr>
<td>2020-11-09</td>
<td>Edited</td>
<td>Orlic-Milacic, M.</td>
</tr>
<tr>
<td>2021-02-05</td>
<td>Reviewed</td>
<td>Fort, P.</td>
</tr>
<tr>
<td>2021-02-14</td>
<td>Revised</td>
<td>Orlic-Milacic, M.</td>
</tr>
</tbody>
</table>
**RHOBTB1 binds GTP**

**Location:** RHOBTB1 GTPase cycle

**Stable identifier:** R-HSA-9018774

**Type:** uncertain

**Compartments:** endosome membrane, cytosol

RHOBTB1 shares 80% sequence identity with RHOBTB2, with close to 95% identity in the GTPase domain (reviewed by Ji and Rivero 2016). Based on studies in RHOBTB2 (Manjarrez et al. 2014), as well as on the primary structure of the GTPase domain, RHOBTB1 is expected to bind to GTP, but not to cycle between GTP- and GDP-bound states. There are no known RHOBTB1 GAPs - DEBDC1B was reported to bind RHOBTB1 by Bagci et al. 2020, but its RHOBTB1-directed GAP activity has not been tested.

**Followed by:** RHOBTB1 binds interacting proteins at the endosome membrane

**Literature references**


**Editions**

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
<th>Author/Reviewer</th>
</tr>
</thead>
<tbody>
<tr>
<td>2020-03-06</td>
<td>Authored</td>
<td>Orlic-Milacic, M.</td>
</tr>
<tr>
<td>2020-10-13</td>
<td>Reviewed</td>
<td>Rivero Crespo, F.</td>
</tr>
<tr>
<td>2020-11-09</td>
<td>Edited</td>
<td>Orlic-Milacic, M.</td>
</tr>
<tr>
<td>2021-02-05</td>
<td>Reviewed</td>
<td>Fort, P.</td>
</tr>
</tbody>
</table>
RHOBTB1 binds interacting proteins at the endosome membrane

**Location:** RHOBTB1 GTPase cycle

**Stable identifier:** R-HSA-9018778

**Type:** binding

**Compartments:** plasma membrane, cytosol

RHOBTB1, like the other member of the RHOBTB family, RHOBTB2, as well as the divergent RHOBTB3, which does not belong to the RHO superfamily, binds to CUL3 (cullin-3), a core component of the BTB-CUL3-RBX2 E3 ubiquitin ligase complex (Berthold et al. 2008). RHOBTB1 binds to ROCK1 and ROCK2, and ROCK-mediated phosphorylation of RHOBTB1 may regulate its association with CUL3 (Haga et al. 2019). RHOBTB1 has been proposed as a substrate adaptor for PDE5, targeting it to CUL3 complexes for ubiquitination (Mukohda et al. 2019).

Candidate RHOBTB1 interactors identified in the screen conducted by Bagci et al. 2020 include:

- CCT2 (Bagci et al. 2020)
- CCT7 (Bagci et al. 2020)
- COPS2 (Bagci et al. 2020)
- COPS4 (Bagci et al. 2020)
- CPSF7 (Bagci et al. 2020)
- DBN1 (Bagci et al. 2020)
- GPS1 (Bagci et al. 2020)
- HNRNPC (Bagci et al. 2020)
- MYO6 (Bagci et al. 2020)
- RBBP6 (Bagci et al. 2020)
- RBMX (Bagci et al. 2020)
RNF20 (Bagci et al. 2020)
SPEN (Bagci et al. 2020)
SRRM1 (Bagci et al. 2020)
STK38 (Bagci et al. 2020)
TRA2B (Bagci et al. 2020)
TXNL1 (Bagci et al. 2020)
VIM (Bagci et al. 2020)

Some of the candidate interactors, like CCT2 and CCT7, are part of the CCT chaperone complex, while others (DBN1 and MYO6) are related to the actin cytoskeleton, RNA splicing and export (HNRNPC, RBMX and SRRM1) or COP9 signalosome (COPS2 and COPS4).

**Preceded by:** RHOBTB1 binds GTP

**Literature references**


**Editions**

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
<th>Author</th>
</tr>
</thead>
<tbody>
<tr>
<td>2020-03-06</td>
<td>Authored</td>
<td>Orlic-Milacic, M.</td>
</tr>
<tr>
<td>2020-10-13</td>
<td>Reviewed</td>
<td>Rivero Crespo, F.</td>
</tr>
<tr>
<td>2020-11-09</td>
<td>Edited</td>
<td>Orlic-Milacic, M.</td>
</tr>
<tr>
<td>2021-02-05</td>
<td>Reviewed</td>
<td>Fort, P.</td>
</tr>
<tr>
<td>2021-02-14</td>
<td>Revised</td>
<td>Orlic-Milacic, M.</td>
</tr>
</tbody>
</table>
# Table of Contents

- Introduction .................................................. 1
- RHOBTB1 GTPase cycle ........................................ 2
  - RHOBTB1 binds GTP ....................................... 4
  - RHOBTB1 binds interacting proteins at the endosome membrane ... 5

Table of Contents