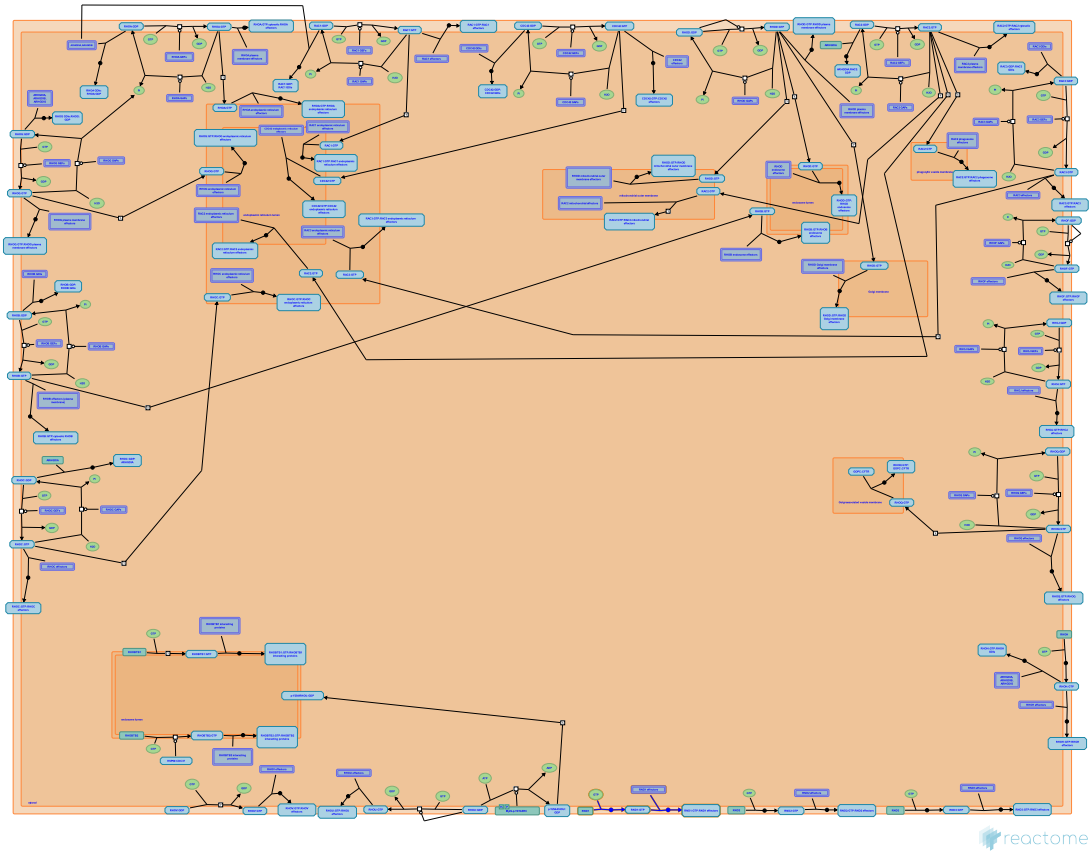
RND1 GTPase cycle



Fort, P., Orlic-Milacic, M.

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

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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. ↗

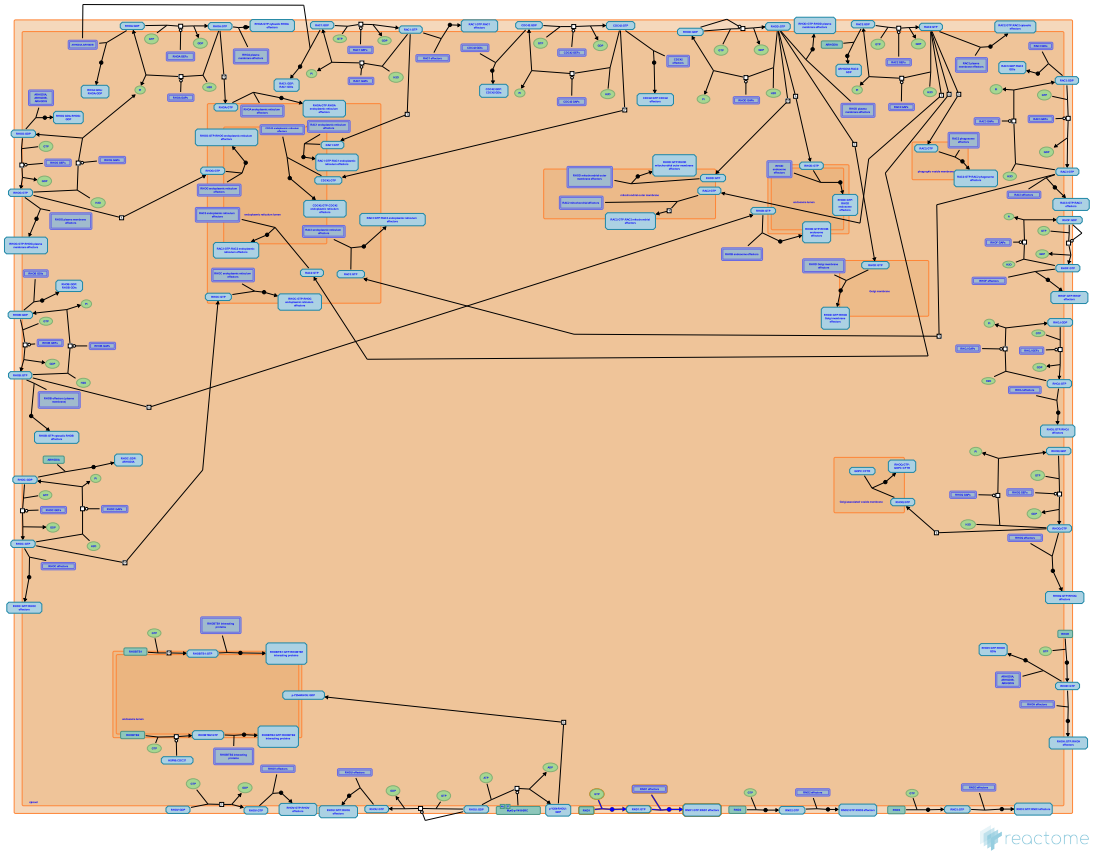
Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

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. ↗

RND1 GTPase cycle ↗

Stable identifier: R-HSA-9696273



RND1 is an atypical RHO GTPase from the RND subfamily. RND1 is constitutively bound to GTP and lacks GTPase activity. No guanine nucleotide exchange factors (GEFs), GTPase activator proteins (GAPs) or guanine nucleotide dissociation inhibitors (GDIs) act on RND1. RND1 localizes to the plasma membrane, but can be extracted from the plasma membrane and sequestered to the cytosol upon phosphorylation-induced binding to 14-3-3 protein. RND1 antagonizes RHOA, leading to reduced actomyosin contractility and loss of stress fibers and focal adhesions, which results in a rounded cell phenotype. RND1 plays a role in embryogenesis, neuronal development, myometrium changes during pregnancy, and angiogenesis. RND1 is frequently downregulated in cancer and is implicated as a tumor suppressor, but may play an oncogenic role in some cancer types. RND1 expression increases in response to anti-cancer agents and in may be involved in resistance to treatment. For review, please refer to Mouly et al. 2019.

Literature references

Monferran, S., Gilhodes, J., Toulas, C., Mouly, L., Lemarié, A., Sordet, O. et al. (2019). The RND1 Small GTPase: Main Functions and Emerging Role in Oncogenesis. *Int J Mol Sci, 20*. ↗

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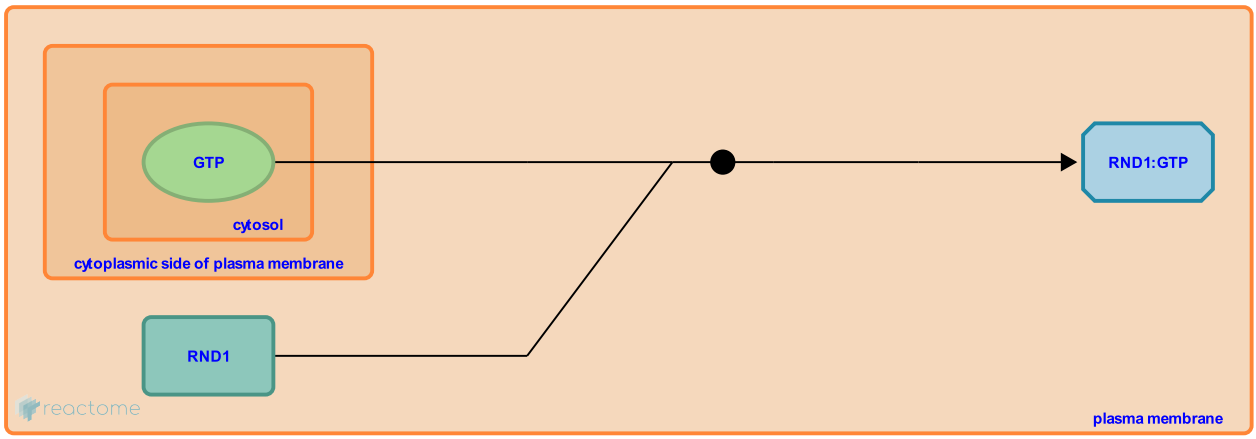
RND1 binds GTP ↗

Location: RND1 GTPase cycle

Stable identifier: R-HSA-9696274

Type: binding

Compartments: plasma membrane, cytosol



RND1 binds GTP with approximately 100 times higher affinity than GDP and is thus considered to be constitutively active (Nobes et al. 1998).

Followed by: RND1 binds effectors

Literature references

Chardin, P., Nobes, CD., Lauritzen, I., Hall, A., Paris, S., Mattei, MG. (1998). A new member of the Rho family, Rnd1, promotes disassembly of actin filament structures and loss of cell adhesion. *J. Cell Biol., 141*, 187-97. ↗

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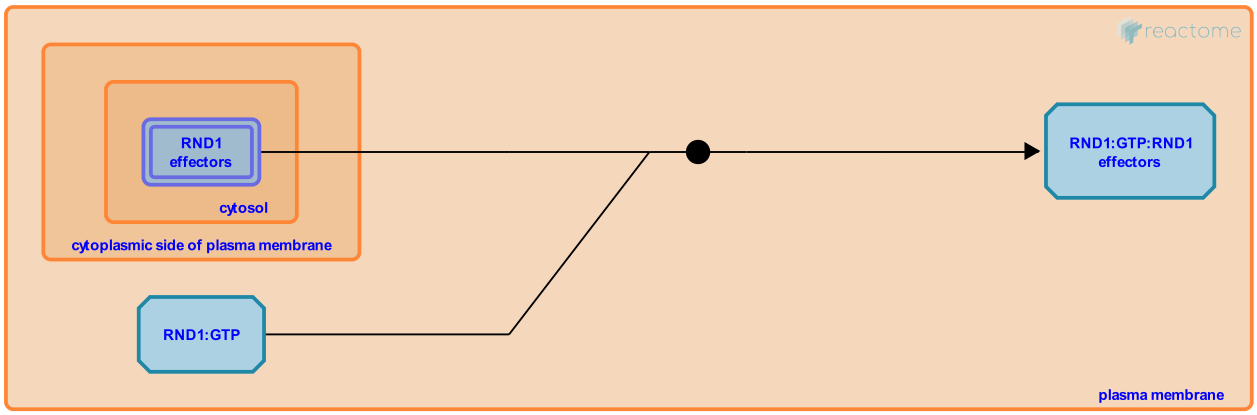
RND1 binds effectors ↗

Location: RND1 GTPase cycle

Stable identifier: R-HSA-9696271

Type: binding

Compartments: plasma membrane, cytosol



Active GTP-bound RND1 binds the following effectors:
ARHGAP5 (Wennerberg et al. 2003; Bagci et al. 2020)
FRS2 (Harada et al. 2005)
FRS3 (Harada et al. 2005)
GRB7 (Vayssiere et al. 2000)
PLEKHG5 (Goh and Manser 2010)
PLXNA1 (Zanata et al. 2002)
STIP1 (de Souza et al. 2014)
STMN2 (Li et al. 2009)
UBXN11 (Katoh et al. 2002)

The following candidate RND1 effectors were reported in the high throughput screen by Bagci et al. 2020 or have been reported as RND1 effectors in some but not all studies:
ALDH3A2 (Bagci et al. 2020)
ANKRD26 (Bagci et al. 2020)
ARHGAP35 (Wennerberg et al. 2003, Mori et al. 2009: binding to active RND1; Bagci et al. 2020: no binding to active RND1)
CAV1 (Bagci et al. 2020)
CCDC88A (Bagci et al. 2020)
CPD (Bagci et al. 2020)
DEPDC1B (Bagci et al. 2020)
DLG5 (Bagci et al. 2020)
DSP (Bagci et al. 2020)
DST (Bagci et al. 2020)
EPHA2 (Bagci et al. 2020)
EPSTI1 (Bagci et al. 2020)
FAM135A (Bagci et al. 2020)
FAM83B (Bagci et al. 2020)
FLOT2 (Bagci et al. 2020)
KIDINS220 (Bagci et al. 2020)
KIF14 (Bagci et al. 2020)
LEMD3 (Bagci et al. 2020)
MUC13 (Bagci et al. 2020)
PKP4 (Bagci et al. 2020)
PIK3R1 (Bagci et al. 2020)
PIK3R2 (Bagci et al. 2020)
PTPN13 (Bagci et al. 2020)
RASAL2 (Bagci et al. 2020)
RBMX (Bagci et al. 2020)
RRAS2 (Bagci et al. 2020)

TFRC (Bagci et al. 2020)
TMEM59 (Bagci et al. 2020)
TXNL1 (Bagci et al. 2020)
VANGL1 (Bagci et al. 2020)
VANGL2 (Bagci et al. 2020)
WDR6 (Bagci et al. 2020)

RND1 does not interact with the following putative effectors that bind to active RND2 and/or RND3:
CKAP4 (Bagci et al. 2020)
CKB (Bagci et al. 2020)
DDX4 (Bagci et al. 2020)
DSG1 (Bagci et al. 2020)
FNBP1 (Bagci et al. 2020)
GOLGA3 (Bagci et al. 2020)
KTN1 (Bagci et al. 2020)
LRRC1 (Bagci et al. 2020)
NISCH (Bagci et al. 2020)
NUDC (Bagci et al. 2020)
PICALM (Bagci et al. 2020)
SCRIB (Bagci et al. 2020)
SEMA4F (Bagci et al. 2020)
TMOD3 (Bagci et al. 2020)
UHRF1BP1L (Bagci et al. 2020)

Preceded by: RND1 binds GTP

Literature references

Nakao, LS., Lopes, MH., Mercadante, AF., Püschel, AW., Martins, VR., Zanata, SM. et al. (2014). STI1 antagonizes cytoskeleton collapse mediated by small GTPase Rnd1 and regulates neurite growth. *Exp. Cell Res., 324*, 84-91. ↗

Harada, A., Katoh, H., Negishi, M. (2005). Direct interaction of Rnd1 with FRS2 beta regulates Rnd1-induced down-regulation of RhoA activity and is involved in fibroblast growth factor-induced neurite outgrowth in PC12 cells. *J. Biol. Chem., 280*, 18418-24. ↗

Rohm, B., Hovatta, I., Zanata, SM., Püschel, AW. (2002). Antagonistic effects of Rnd1 and RhoD GTPases regulate receptor activity in Semaphorin 3A-induced cytoskeletal collapse. *J Neurosci, 22*, 471-7. ↗

Harada, A., Katoh, H., Mori, K., Negishi, M. (2002). Socius is a novel Rnd GTPase-interacting protein involved in disassembly of actin stress fibers. *Mol. Cell. Biol., 22*, 2952-64. ↗

Goh, LL., Manser, E. (2010). The RhoA GEF Syx is a target of Rnd3 and regulated via a Raf1-like ubiquitin-related domain. *PLoS ONE, 5*, e12409. ↗

Editions

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