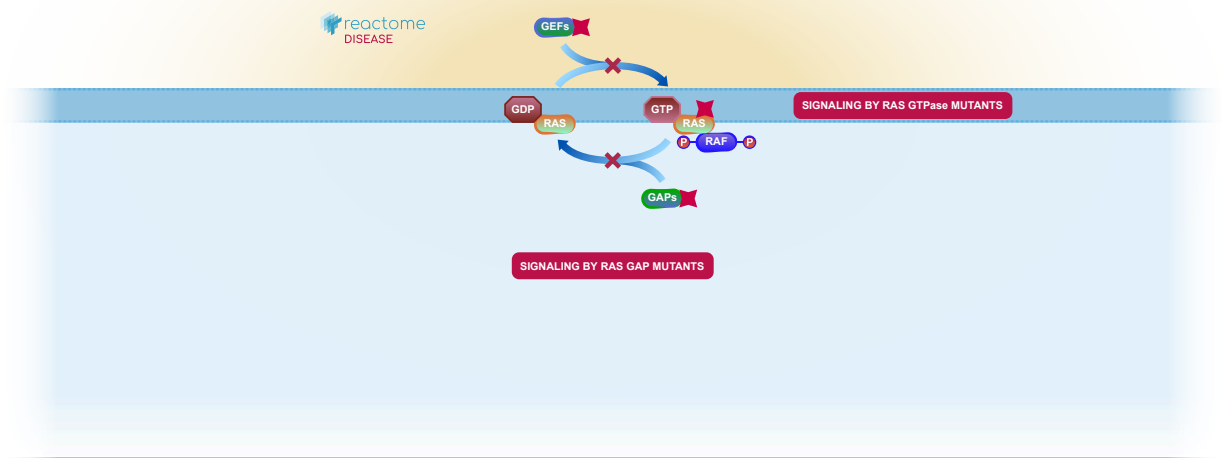
RAS GTPase cycle mutants



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This is just an excerpt of a full-length report for this pathway. To access the complete report, please download it at the Reactome Textbook.

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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. ↗

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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. ↗

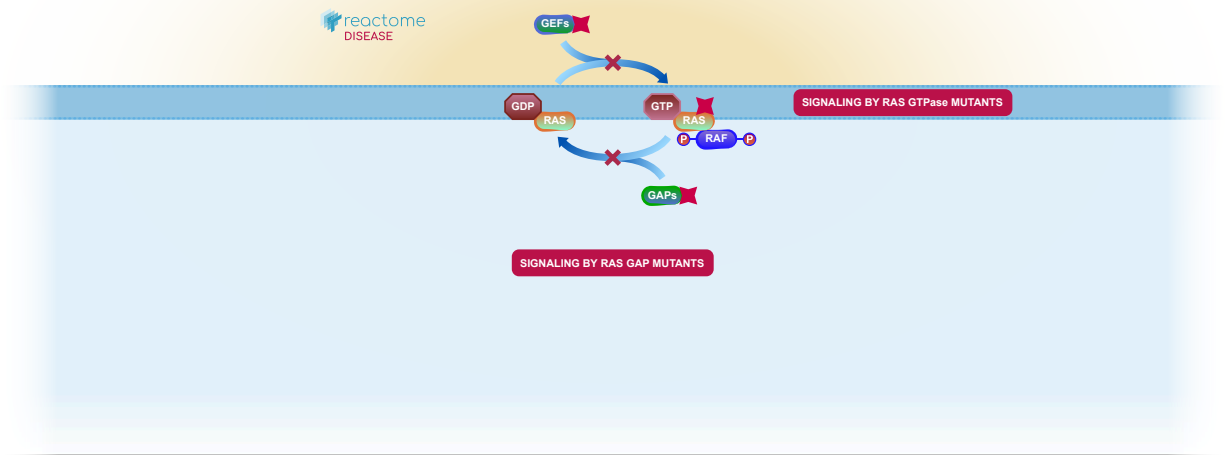
Reactome database release: 88

This document contains 3 pathways (see Table of Contents)

RAS GTPase cycle mutants ↗

Stable identifier: R-HSA-9649913

Diseases: cancer



RAS proteins cycle between an active GTP-bound state and an inactive GDP-bound state. GTPase activating proteins (GAPs) stimulate the low intrinsic GTPase activity of RAS proteins, converting the active to the inactive form, while guanine nucleotide exchange factors (GEFs) stimulate the intrinsic dissociation of GDP, allowing its replacement with GTP and consequent activation of RAS. Disease-causing mutations in RAS promote constitutive signaling by favouring the accumulation of RAS:GTP. The vast majority of these mutations are loss of function mutations at G12, G13 and Q61. These mutations disrupt the GTPase activity of RAS proteins by interfering with nucleophilic attack on the gamma phosphate of GTP. A smaller proportion of RAS mutations increase the intrinsic GDP dissociation rate, while other mutations interfere with RAS interactions with GAPs (reviewed in Prior et al, 2012; Pylayeva-Gupta et al, 2011; Stephen et al, 2014; Samatar and Poulikakos, 2014).

Literature references

Grabocka, E., Pylayeva-Gupta, Y., Bar-Sagi, D. (2011). RAS oncogenes: weaving a tumorigenic web. *Nat. Rev. Cancer, 11*, 761-74. ↗

Lewis, PD., Mattos, C., Prior, IA. (2012). A comprehensive survey of Ras mutations in cancer. *Cancer Res., 72*, 2457-67. ↗

Poulikakos, PI., Samatar, AA. (2014). Targeting RAS-ERK signalling in cancer: promises and challenges. *Nat Rev Drug Discov, 13*, 928-42. ↗

McCormick, F., Stephen, AG., Bagni, RK., Esposito, D. (2014). Dragging ras back in the ring. *Cancer Cell, 25*, 272-81. ↗

Editions

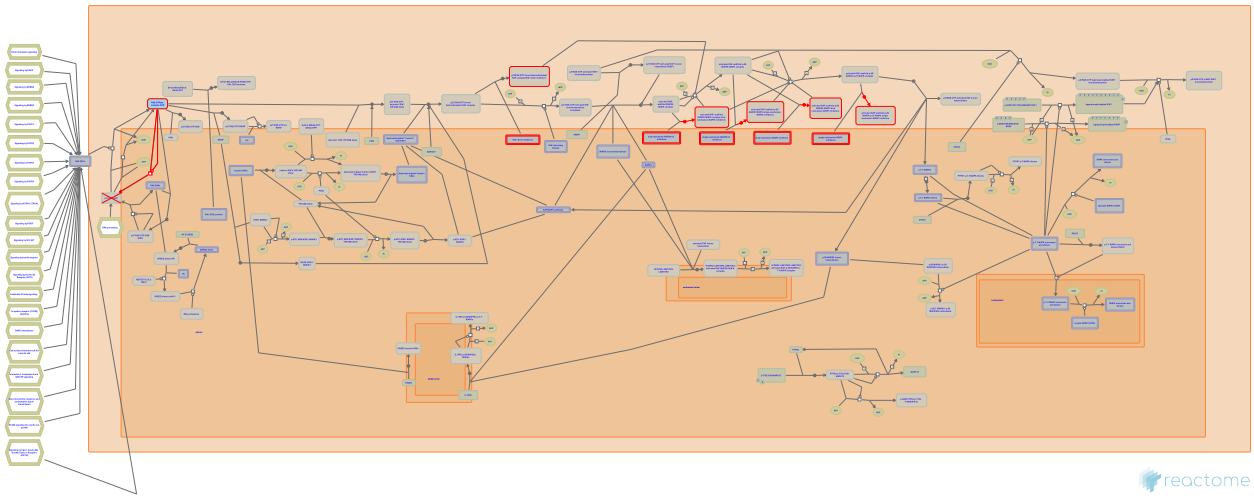
2015-05-18	Authored	Rothfels, K.
2016-08-05	Reviewed	Stephens, RM.

Signaling by RAS GTPase mutants ↗

Location: RAS GTPase cycle mutants

Stable identifier: R-HSA-9753512

Diseases: cancer



This pathway describes RAS mutants with decreased intrinsic GTPase activity that therefore support increased RAS pathway activity (reviewed in Prior et al, 2012; Pylayeva and Gupta, 2011, King et al, 2013; Cox and Der, 2010).

Literature references

Grabocka, E., Pylayeva-Gupta, Y., Bar-Sagi, D. (2011). RAS oncogenes: weaving a tumorigenic web. *Nat. Rev. Cancer, 11*, 761-74. ↗

Lapinski, PE., Lubeck, BA., King, PD. (2013). Nonredundant functions for Ras GTPase-activating proteins in tissue homeostasis. *Sci Signal, 6*, re1. ↗

Lewis, PD., Mattos, C., Prior, IA. (2012). A comprehensive survey of Ras mutations in cancer. *Cancer Res., 72*, 2457-67. ↗

Der, CJ., Cox, AD. (2010). Ras history: The saga continues. *Small GTPases, 1*, 2-27. ↗

Editions

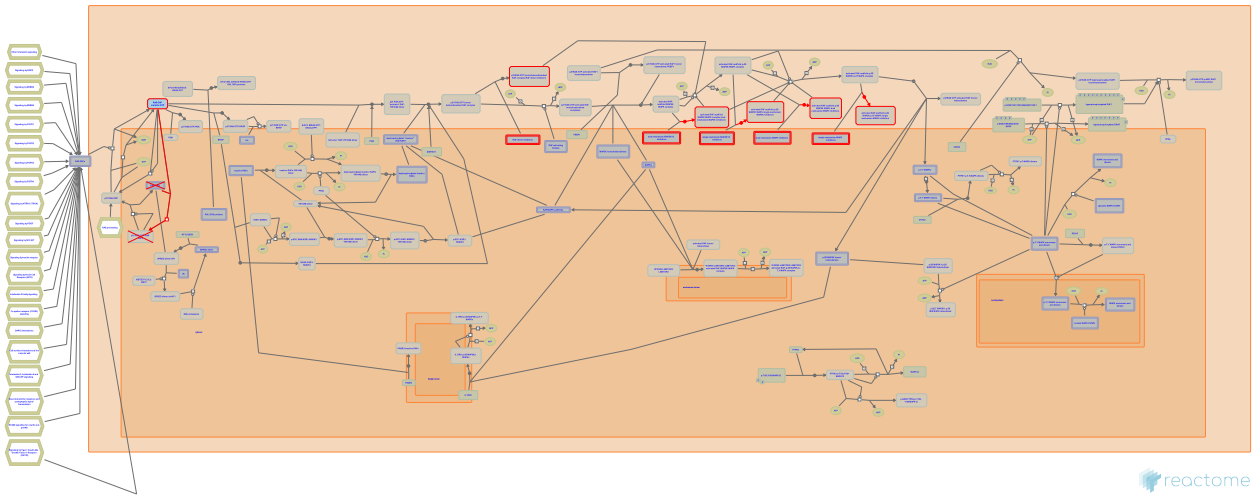
2015-05-18	Authored	Rothfels, K.
2020-05-04	Reviewed	Gavathiotis, E.
2021-09-25	Edited	Rothfels, K.

Signaling by RAS GAP mutants ↗

Location: RAS GTPase cycle mutants

Stable identifier: R-HSA-9753510

Diseases: cancer



This pathway describes RAS mutants whose intrinsic GTPase activity can't be stimulated by GTPase activating proteins (GAPs). These RAS mutants therefore support increased RAS pathway activity (reviewed in Prior et al, 2012; Pylayeva and Gupta, 2011, King et al, 2013; Cox and Der, 2010).

Literature references

Grabocka, E., Pylayeva-Gupta, Y., Bar-Sagi, D. (2011). RAS oncogenes: weaving a tumorigenic web. *Nat. Rev. Cancer, 11*, 761-74. ↗

Lapinski, PE., Lubeck, BA., King, PD. (2013). Nonredundant functions for Ras GTPase-activating proteins in tissue homeostasis. *Sci Signal, 6*, re1. ↗

Lewis, PD., Mattos, C., Prior, IA. (2012). A comprehensive survey of Ras mutations in cancer. *Cancer Res., 72*, 2457-67. ↗

Der, CJ., Cox, AD. (2010). Ras history: The saga continues. *Small GTPases, 1*, 2-27. ↗

Editions

2016-08-05	Reviewed	Stephens, RM.
2021-09-25	Edited	Rothfels, K.

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