

Homo- or heterodimerization of RAF downstream of mutant RAS

Rothfels, K., Stephens, RM.

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](#).

18/05/2024

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. [↗](#)

Reactome database release: 88

This document contains 1 reaction ([see Table of Contents](#))

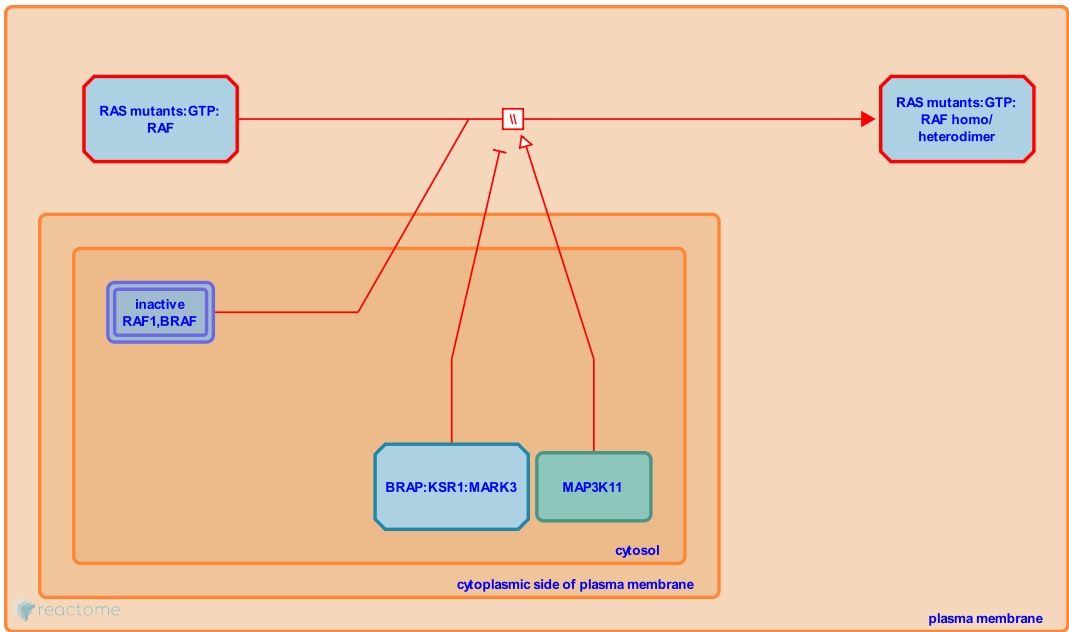
Homo- or heterodimerization of RAF downstream of mutant RAS ↗

Stable identifier: R-HSA-6803240

Type: omitted

Compartments: plasma membrane

Diseases: cancer, Noonan syndrome



Similar to the WT pathway, activation of RAF downstream of oncogenic RAS depends on homo- or heterodimerization of RAF, although the importance of RAF proteins varies among cancer types (Dumaz et al, 2006; Heidorn et al, 2010; Blasco et al, 2011; Karreth et al, 2011; Eser et al, 2013; Heidorn et al, 2010; Poulikakos et al, 2010; Hatzivassiliou et al, 2010; reviewed in Lito et al, 2013). A notable exception to this requirement for RAF dimerization is BRAF V600E, which is RAS-independent and constitutively active as a monomer (Roring et al, 2012; Brummer et al, 2006; Freeman et al, 2013; Garnett et al, 2005).

Literature references

Daly, RJ., Brummer, T., Reth, M., Misawa, Y., Martin, P., Herzog, S. (2006). Functional analysis of the regulatory requirements of B-Raf and the B-Raf(V600E) oncoprotein. *Oncogene*, 25, 6262-76. ↗

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

Barbacid, M., Baccarini, M., Santamaría, D., Francoz, S., Cañamero, M., Charron, J. et al. (2011). c-Raf, but not B-Raf, is essential for development of K-Ras oncogene-driven non-small cell lung carcinoma. *Cancer Cell*, 19, 652-63. ↗

Garnett, MJ., Barford, D., Paterson, H., Rana, S., Marais, R. (2005). Wild-type and mutant B-RAF activate C-RAF through distinct mechanisms involving heterodimerization. *Mol. Cell*, 20, 963-9. ↗

Freeman, AK., Ritt, DA., Morrison, DK. (2013). Effects of Raf dimerization and its inhibition on normal and disease-associated Raf signaling. *Mol. Cell*, 49, 751-8. ↗

Editions

2015-02-12	Edited	Rothfels, K.
2015-05-18	Authored	Rothfels, K.
2016-08-05	Reviewed	Stephens, RM.