

3.6.5.2 Small monomeric GTPases (version 2019.4) in the IUPHAR/BPS Guide to Pharmacology Database

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Abstract

Small G-proteins, are a family of hydrolase enzymes that can bind and hydrolyze guanosine triphosphate (GTP). They are a type of G-protein found in the cytosol that are homologous to the alpha subunit of heterotrimeric G-proteins, but unlike the alpha subunit of G proteins, a small GTPase can function independently as a hydrolase enzyme to bind to and hydrolyze a guanosine triphosphate (GTP) to form guanosine diphosphate (GDP). The best-known members are the Ras GTPases and hence they are sometimes called Ras subfamily GTPases.

Contents

This is a citation summary for 3.6.5.2 Small monomeric GTPases in the [Guide to Pharmacology](#) database (GtoPdb). It exists purely as an adjunct to the database to facilitate the recognition of citations to and from the database by citation analyzers. Readers will almost certainly want to visit the relevant sections of the database which are given here under database links.

[GtoPdb](#) is an expert-driven guide to pharmacological targets and the substances that act on them. GtoPdb is a reference work which is most usefully represented as an on-line database. As in any publication this work should be appropriately cited, and the papers it cites should also be recognized. This document provides a citation for the relevant parts of the database, and also provides a reference list for the research cited by those parts.

Please note that the database version for the citations given in GtoPdb are to the most recent preceding version in which the family or its subfamilies and targets were substantially changed. The links below are to the current version. If you need to consult the cited version, rather than the most recent version, please contact the GtoPdb curators.

Database links

[3.6.5.2 Small monomeric GTPases](#)

<http://www.guidetopharmacology.org/GRAC/FamilyDisplayForward?familyId=896>

[RAS subfamily](#)

<http://www.guidetopharmacology.org/GRAC/FamilyDisplayForward?familyId=897>

[Introduction to RAS subfamily](#)

<http://www.guidetopharmacology.org/GRAC/FamilyIntroductionForward?familyId=897>

Enzymes

[HRAS](#)

<http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=2822>

NRAS

<http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=2823>

KRAS

<http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=2824>

RAB subfamily

<http://www.guidetopharmacology.org/GRAC/FamilyDisplayForward?familyId=938>

Enzymes

RAB27A, member RAS oncogene family

<http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=2916>

References

1. Almoguera C, Shibata D, Forrester K, Martin J, Arnheim N and Perucho M. (1988) Most human carcinomas of the exocrine pancreas contain mutant c-k-ras genes. *Cell* **53**: 549-54 [PMID:2453289]
2. Baines AT, Xu D and Der CJ. (2011) Inhibition of Ras for cancer treatment: the search continues. *Future Med Chem* **3**: 1787-808 [PMID:22004085]
3. Bezniakow N, Gos M and Obersztyn E. (2014) The RASopathies as an example of RAS/MAPK pathway disturbances - clinical presentation and molecular pathogenesis of selected syndromes. *Dev Period Med* **18**: 285-96 [PMID:25182392]
4. Blum R, Jacob-Hirsch J, Amariglio N, Rechavi G and Kloog Y. (2005) Ras inhibition in glioblastoma down-regulates hypoxia-inducible factor-1 alpha, causing glycolysis shutdown and cell death. *Cancer Res.* **65**: 999-1006 [PMID:15705901]
5. Bos JL. (1989) ras oncogenes in human cancer: a review. *Cancer Res.* **49**: 4682-9 [PMID:2547513]
6. Braun BS and Shannon K. (2008) Targeting Ras in myeloid leukemias. *Clin. Cancer Res.* **14**: 2249-52 [PMID:18413813]
7. Brzezinska AA, Johnson JL, Munafo DB, Crozat K, Beutler B, Kiosses WB, Ellis BA and Catz SD. (2008) The Rab27a effectors JFC1/Slp1 and Munc13-4 regulate exocytosis of neutrophil granules. *Traffic* **9**: 2151-64 [PMID:18939952]
8. Burner GC and Loeb LA. (1989) Mutations in the KRAS2 oncogene during progressive stages of human colon carcinoma. *Proc. Natl. Acad. Sci. U.S.A.* **86**: 2403-7 [PMID:2648401]
9. Catz SD. (2014) The role of Rab27a in the regulation of neutrophil function. *Cell. Microbiol.* **16**: 1301-10 [PMID:24964030]
10. Collins MA and Pasca di Magliano M. (2013) Kras as a key oncogene and therapeutic target in pancreatic cancer. *Front Physiol* **4**: 407 [PMID:24478710]
11. Cooper WA, Lam DC, O'Toole SA and Minna JD. (2013) Molecular biology of lung cancer. *J Thorac Dis* **5 Suppl 5**: S479-90 [PMID:24163741]
12. Ebi H, Faber AC, Engelman JA and Yano S. (2014) Not just gRASping at flaws: finding vulnerabilities to develop novel therapies for treating KRAS mutant cancers. *Cancer Sci.* **105**: 499-505 [PMID:24612015]
13. Goitre L, Trapani E, Trabalzini L and Retta SF. (2014) The Ras superfamily of small GTPases: the unlocked secrets. *Methods Mol. Biol.* **1120**: 1-18 [PMID:24470015]
14. Hansen R, Peters U, Babbar A, Chen Y, Feng J, Janes MR, Li LS, Ren P, Liu Y and Zarrinkar PP. (2018) The reactivity-driven biochemical mechanism of covalent KRAS^{G12C} inhibitors. *Nat. Struct. Mol. Biol.* **25**: 454-462 [PMID:29760531]
15. Johnson JL, Monfregola J, Napolitano G, Kiosses WB and Catz SD. (2012) Vesicular trafficking through cortical actin during exocytosis is regulated by the Rab27a effector JFC1/Slp1 and the RhoA-GTPase-activating protein Gem-interacting protein. *Mol. Biol. Cell* **23**: 1902-16 [PMID:22438581]
16. Johnson JL, Ramadass M, He J, Brown SJ, Zhang J, Abgaryan L, Biris N, Gavathiotis E, Rosen H and Catz SD. (2016) Identification of Neutrophil Exocytosis Inhibitors (Nexinhibs), Small Molecule Inhibitors of Neutrophil Exocytosis and Inflammation: DRUGGABILITY OF THE SMALL GTPase Rab27a. *J. Biol. Chem.* **291**: 25965-25982 [PMID:27702998]

17. Liu M, Bryant MS, Chen J, Lee S, Yaremko B, Lipari P, Malkowski M, Ferrari E, Nielsen L and Prioli N *et al.*. (1998) Antitumor activity of SCH 66336, an orally bioavailable tricyclic inhibitor of farnesyl protein transferase, in human tumor xenograft models and wap-ras transgenic mice. *Cancer Res.* **58**: 4947-56 [PMID:9810004]
18. O'Bryan JP. (2019) Pharmacological targeting of RAS: Recent success with direct inhibitors *Pharmacol. Res.* **139**: 503-511 [PMID:30366101]
19. Ostrem JM, Peters U, Sos ML, Wells JA and Shokat KM. (2013) K-Ras(G12C) inhibitors allosterically control GTP affinity and effector interactions. *Nature* **503**: 548-51 [PMID:24256730]
20. Rasool S, Rasool V, Naqvi T, Ganai BA and Shah BA. (2014) Genetic unraveling of colorectal cancer. *Tumour Biol.* **35**: 5067-82 [PMID:24573608]
21. Rotblat B, Ehrlich M, Haklai R and Kloog Y. (2008) The Ras inhibitor farnesylthiosalicylic acid (Salirasib) disrupts the spatiotemporal localization of active Ras: a potential treatment for cancer. *Meth. Enzymol.* **439**: 467-89 [PMID:18374183]
22. Spiegel J, Cromm PM, Zimmermann G, Grossmann TN and Waldmann H. (2014) Small-molecule modulation of Ras signaling. *Nat. Chem. Biol.* **10**: 613-22 [PMID:24929527]
23. Stanley LA. (1995) Molecular aspects of chemical carcinogenesis: the roles of oncogenes and tumour suppressor genes. *Toxicology* **96**: 173-94 [PMID:7900159]
24. Tam IY, Chung LP, Suen WS, Wang E, Wong MC, Ho KK, Lam WK, Chiu SW, Girard L and Minna JD *et al.*. (2006) Distinct epidermal growth factor receptor and KRAS mutation patterns in non-small cell lung cancer patients with different tobacco exposure and clinicopathologic features. *Clin. Cancer Res.* **12**: 1647-53 [PMID:16533793]
25. Wennerberg K, Rossman KL and Der CJ. (2005) The Ras superfamily at a glance. *J. Cell. Sci.* **118**: 843-6 [PMID:15731001]
26. Yoshida N, Doisaki S and Kojima S. (2012) Current management of juvenile myelomonocytic leukemia and the impact of RAS mutations. *Paediatr Drugs* **14**: 157-63 [PMID:22480363]
27. Zhang J and Lodish HF. (2007) Endogenous K-ras signaling in erythroid differentiation. *Cell Cycle* **6**: 1970-3 [PMID:17721087]