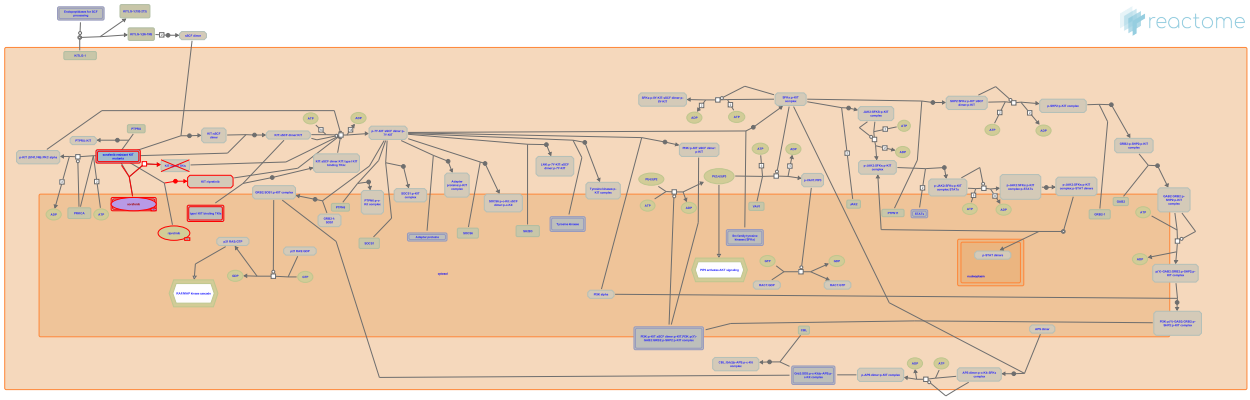
Sorafenib-resistant KIT mutants



García-Valverde, A., Pilco-Janeta, D., Rothfels, K., Serrano, C.

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

26/10/2020

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. ↗

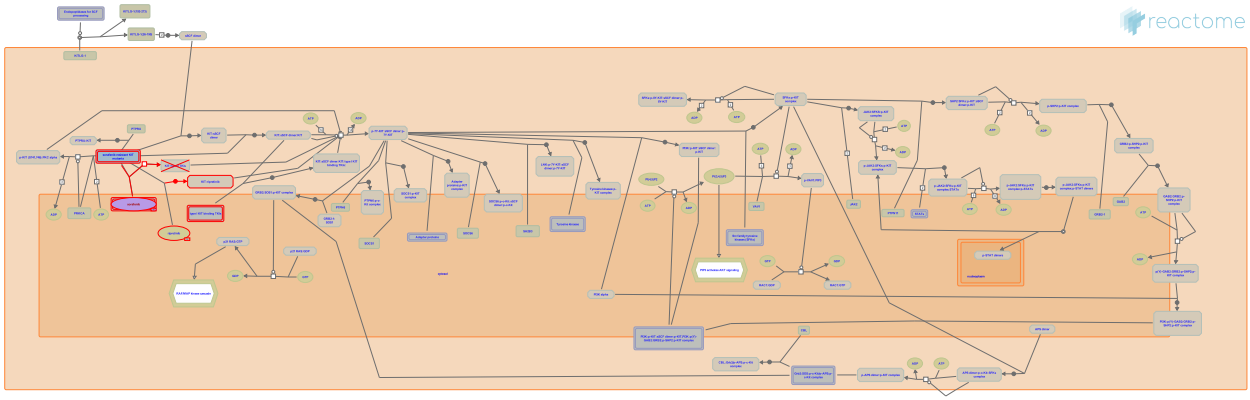
Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

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. ↗

Sorafenib-resistant KIT mutants ↗

Stable identifier: R-HSA-9669936

Diseases: cancer



Sorafenib is a type II tyrosine kinase inhibitor that is approved for use in hepatocellular and renal cell carcinoma. It is active against KIT receptors with mutations in the ATP-binding cleft and the activation loop, with the exception of substitutions at D816, which are resistant (Guida et al, 2007; Heinrich et al, 2012; Serrano et al, 2019; Weisberg et al, 2019; reviewed in Roskoski, 2018; Klug et al, 2012).

Literature references

Serrano, C., Mariño-Enríquez, A., Tao, DL., Ketzer, J., Eilers, G., Zhu, M. et al. (2019). Complementary activity of tyrosine kinase inhibitors against secondary kit mutations in imatinib-resistant gastrointestinal stromal tumours. *Br. J. Cancer, 120*, 612-620. ↗

Klug, LR., Kent, JD., Heinrich, MC. (2018). Structural and clinical consequences of activation loop mutations in class III receptor tyrosine kinases. *Pharmacol. Ther., 191*, 123-134. ↗

Heinrich, MC., Mariño-Enríquez, A., Presnell, A., Donsky, RS., Griffith, DJ., McKinley, A. et al. (2012). Sorafenib inhibits many kinase mutations associated with drug-resistant gastrointestinal stromal tumors. *Mol. Cancer Ther., 11*, 1770-80. ↗

Weisberg, E., Meng, C., Case, AE., Sattler, M., Tiv, HL., Gokhale, PC. et al. (2019). Comparison of effects of midostaurin, crenolanib, quizartinib, gilteritinib, sorafenib and BLU-285 on oncogenic mutants of KIT, CBL and FLT3 in haematological malignancies. *Br. J. Haematol., 187*, 488-501. ↗

Guida, T., Anaganti, S., Provitera, L., Gedrich, R., Sullivan, E., Wilhelm, SM. et al. (2007). Sorafenib inhibits imatinib-resistant KIT and platelet-derived growth factor receptor beta gatekeeper mutants. *Clin. Cancer Res., 13*, 3363-9. ↗

Editions

2020-03-13	Reviewed	Serrano, C., Pilco-Janeta, D., García-Valverde, A.
2020-04-01	Authored	Rothfels, K.
2020-05-04	Edited	Rothfels, K.

Sorafenib-resistant KIT mutants do not bind sorafenib ↗

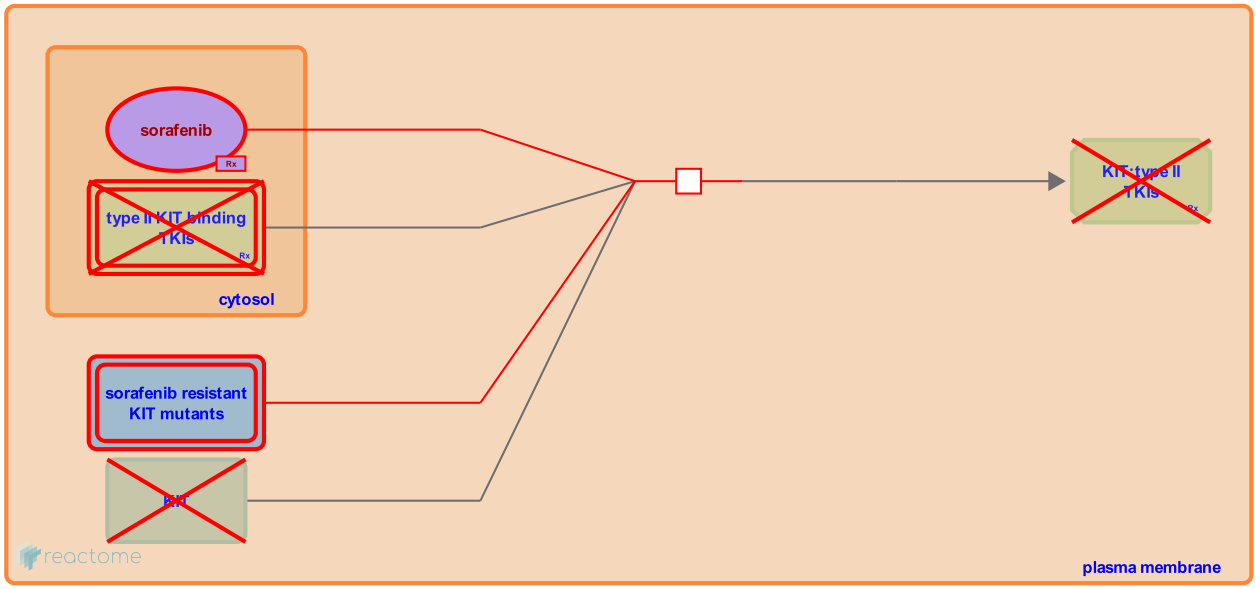
Location: Sorafenib-resistant KIT mutants

Stable identifier: R-HSA-9669874

Type: transition

Compartments: plasma membrane

Diseases: cancer



KIT receptors with mutations at residue D816 are resistant to inhibition by sorafenib, while other activation loop mutations show variable sensitivity (Guida et al, 2007; Heinrich et al, 2012; Serrano et al, 2019).

Literature references

Guida, T., Anaganti, S., Provitera, L., Gedrich, R., Sullivan, E., Wilhelm, SM. et al. (2007). Sorafenib inhibits imatinib-resistant KIT and platelet-derived growth factor receptor beta gatekeeper mutants. *Clin. Cancer Res., 13*, 3363-9. ↗

Heinrich, MC., Mariño-Enríquez, A., Presnell, A., Donsky, RS., Griffith, DJ., McKinley, A. et al. (2012). Sorafenib inhibits many kinase mutations associated with drug-resistant gastrointestinal stromal tumors. *Mol. Cancer Ther., 11*, 1770-80. ↗

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