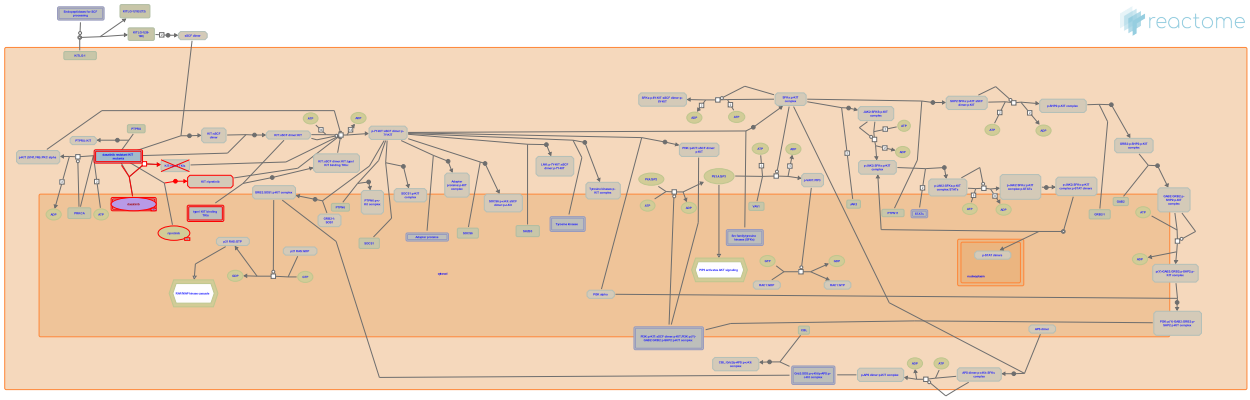
Dasatinib-resistant KIT mutants



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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.

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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. ↗

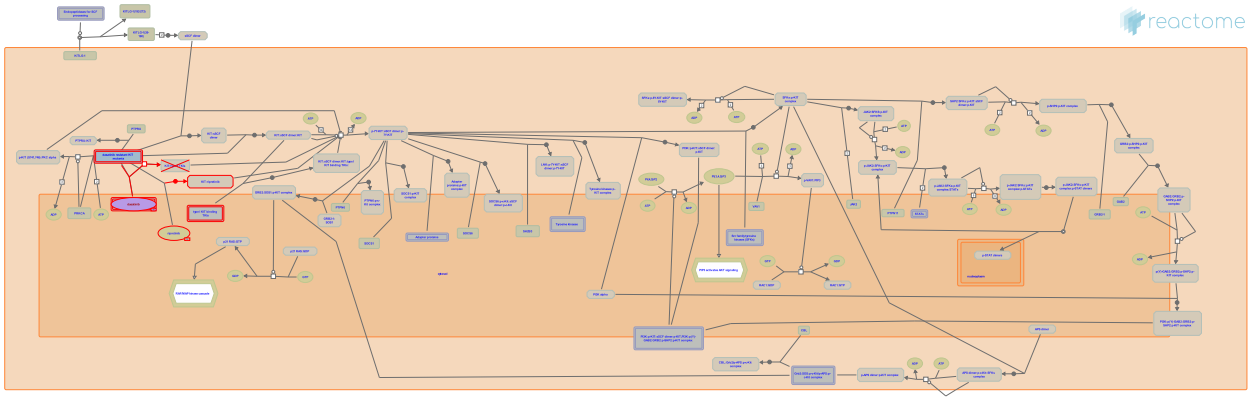
Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

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. ↗

Dasatinib-resistant KIT mutants ↗

Stable identifier: R-HSA-9669914

Diseases: cancer



Dasatinib is a type II tyrosine kinase inhibitor that is active against KIT receptors with mutations in the juxtamembrane and activation loop domains, but shows only partial activity against KIT receptors with mutations at residue V654 (Schittenhelm et al, 2006; Serrano et al, 2019).

Literature references

Heinrich, MC., Ketzer, J., Bauer, S., Zhu, M., Presnell, A., Raut, CP. 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. ↗

Shiraga, S., Schroeder, A., Bokemeyer, C., Deininger, MW., Heinrich, MC., Druker, BJ. et al. (2006). Dasatinib (BMS-354825), a dual SRC/ABL kinase inhibitor, inhibits the kinase activity of wild-type, juxtamembrane, and activation loop mutant KIT isoforms associated with human malignancies. *Cancer Res., 66*, 473-81. ↗

Editions

2020-03-13	Reviewed	Serrano, C., Pilco-Janeta, D., García-Valverde, A.
2020-04-01	Authored	Rothfels, K.
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Dasatinib-resistant KIT mutants do not bind dasatinib ↗

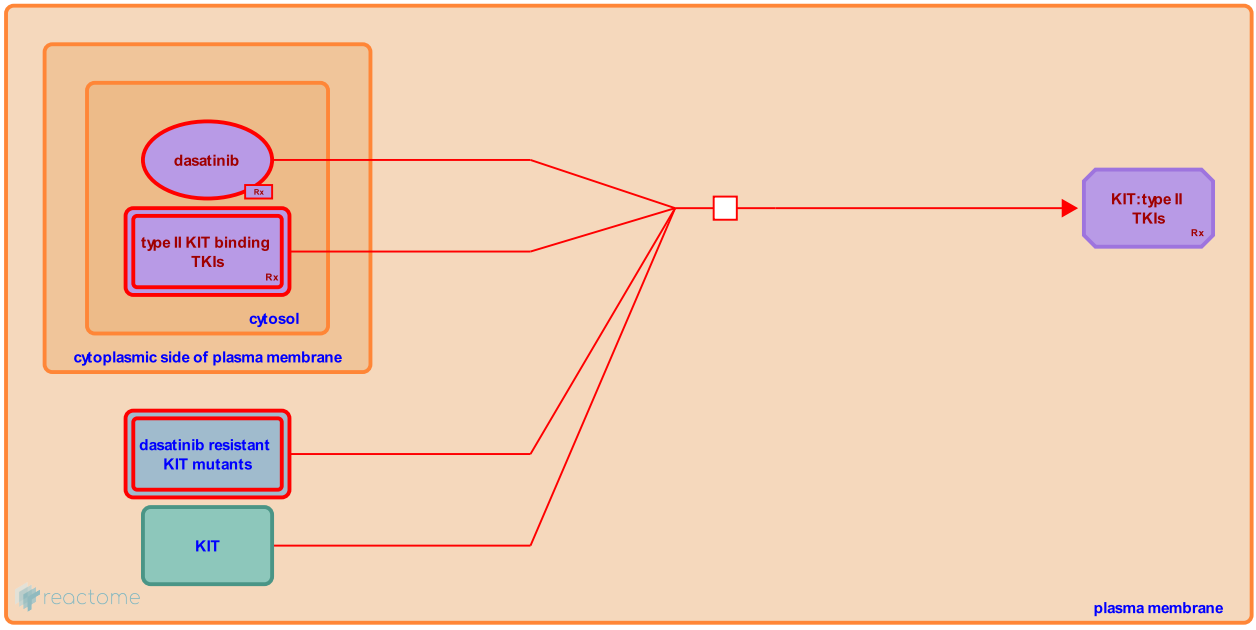
Location: Dasatinib-resistant KIT mutants

Stable identifier: R-HSA-9669855

Type: transition

Compartments: plasma membrane

Diseases: cancer



KIT receptors bearing mutations in the ATP-binding pocket are resistant to treatment with dasatinib (Schittenhelm et al, 2006; Serrano et al, 2019).

Literature references

Heinrich, MC., Ketzer, J., Bauer, S., Zhu, M., Presnell, A., Raut, CP. 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. ↗

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