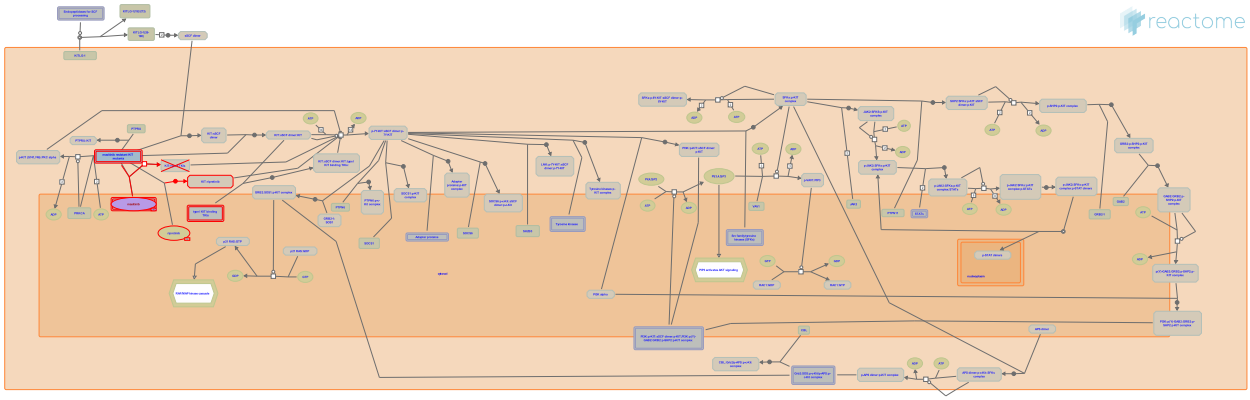
Masitinib-resistant KIT mutants



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.

19/05/2024

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. ↗

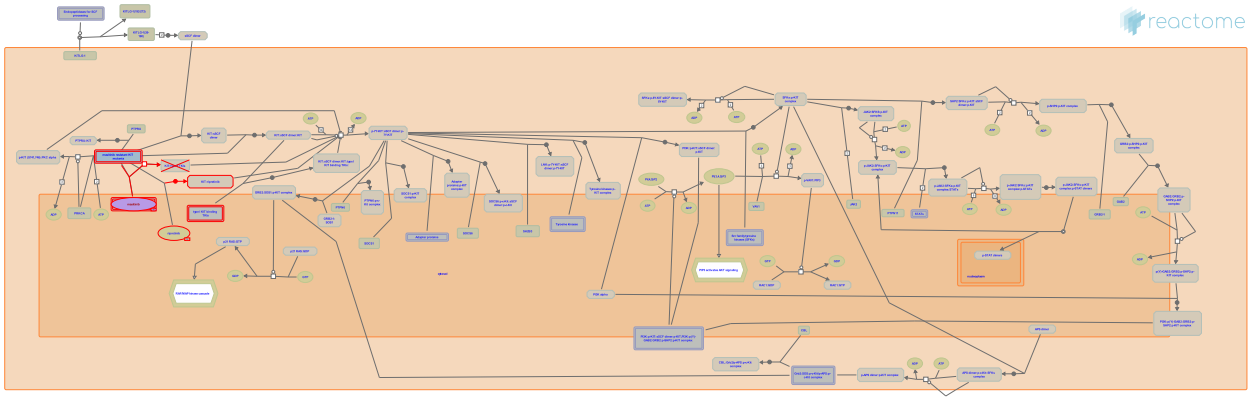
Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

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. ↗

Masitinib-resistant KIT mutants ↗

Stable identifier: R-HSA-9669924

Diseases: cancer



Mastinib is a class II tyrosine kinase inhibitor that targets mutant and wild-type FGFR3, PDGFR and c-KIT (Dubreuil, 2009). Masitinib, like imatinib, is effective in inhibiting the activity of juxtamembrane mutant forms of KIT, but is ineffective against many of the mutations in the activation loop and ATP-binding cleft of the receptor (Dubreuil, 2009; Serrano et al, 2019; reviewed in Demetri, 2011).

Literature references

Gros, L., Hajem, B., Hermine, O., Humbert, M., Lermet, A., Letard, S. et al. (2009). Masitinib (AB1010), a potent and selective tyrosine kinase inhibitor targeting KIT. *PLoS One, 4*, e7258. ↗

Demetri, GD. (2011). Differential properties of current tyrosine kinase inhibitors in gastrointestinal stromal tumors. *Semin. Oncol., 38*, S10-9. ↗

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. ↗

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.

Masitinib-resistant KIT mutants do not bind masitinib ↗

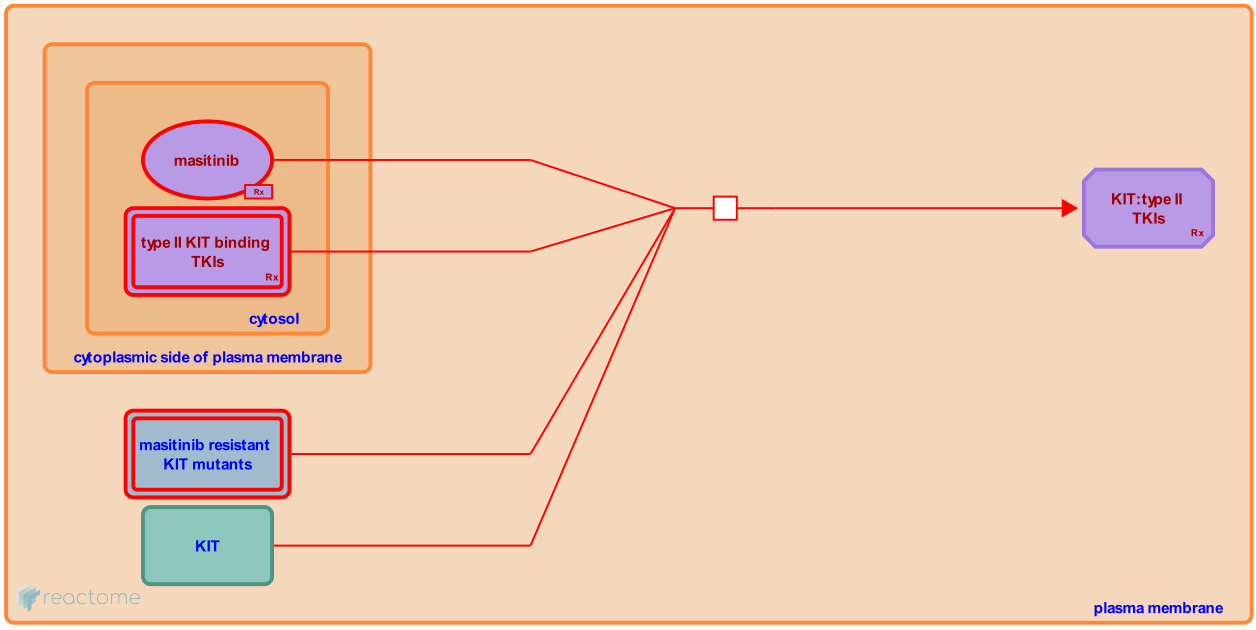
Location: Masitinib-resistant KIT mutants

Stable identifier: R-HSA-9669863

Type: transition

Compartments: plasma membrane

Diseases: cancer



Activated KIT receptors with oncogenic mutations in the ATP-binding cleft and the activation loop of the kinase are resistant to inhibition with masitinib (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. ↗

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.

Table of Contents