KIT binds ripretinib

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.

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.

15/05/2024

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. ↗

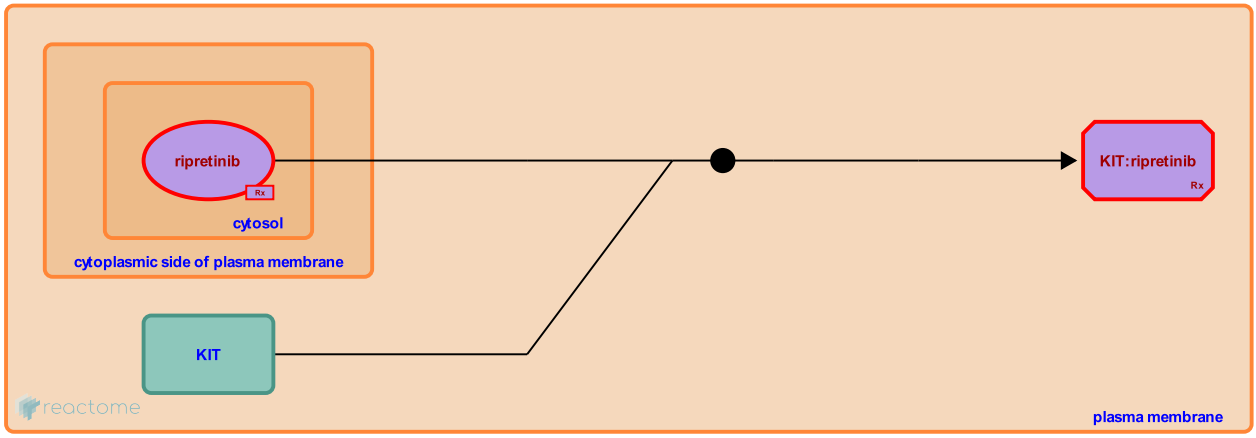
Fabregat, A., Korninger, F., Viteri, G., Sidiropoulos, K., Marin-Garcia, P., Ping, P. et al. (2018). Reactome graph database: Efficient access to complex pathway data. *PLoS computational biology, 14*, e1005968. ↗

KIT binds ripretinib ↗

Stable identifier: R-HSA-9681375

Type: binding

Compartments: plasma membrane, cytosol



Ripretinib is a example of a switch pocket inhibitor, a new type of class II tyrosine kinase inhibitors that is being developed for use against activation and drug resistant mutations in PDGFR and KIT (reviewed in Martin-Broto and Moura, 2020). Switch pocket inhibitors are type II tyrosine kinase inhibitors that force the activation loop (AL) into an inactive conformation, and are therefore active against AL mutants of KIT that are otherwise only sensitive to type I TKIs. Ripretinib is active against mutations affecting extracellular, juxtamembrane, ATP-binding pocket and activation loop domains and is thus the first inhibitor with pan-KIT inhibitory activity. Ripretinib has been successfully studied in TKI-refractory GIST (Smith et al, 2019).

Literature references

Hood, MM., Gupta, A., Su, Y., Ensinger, CL., Caldwell, TM., Bulfer, SL. et al. (2019). Ripretinib (DCC-2618) Is a Switch Control Kinase Inhibitor of a Broad Spectrum of Oncogenic and Drug-Resistant KIT and PDGFRA Variants. *Cancer Cell, 35*, 738-751.e9. ↗

Editions

2020-03-13	Reviewed	Serrano, C., Pilco-Janeta, D., García-Valverde, A.
2020-04-01	Authored	Rothfels, K.
2020-05-22	Edited	Rothfels, K.