# PDGFRs bind type I TKI

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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. ↗

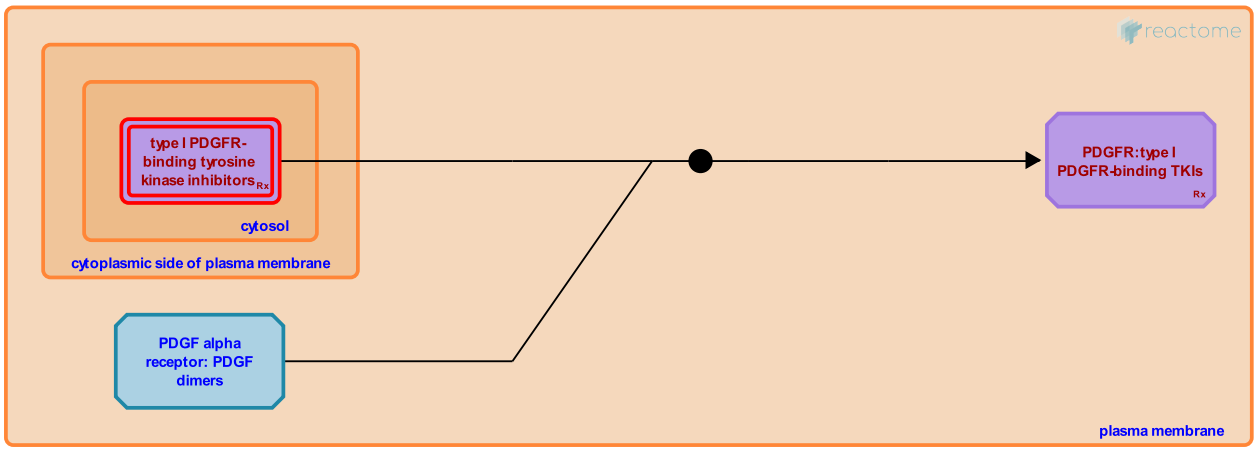
Fabregat, A., Korninger, F., Viteri, G., Sidiropoulos, K., Marin-Garcia, P., Ping, P. et al. (2018). Reactome graph database: Efficient access to complex pathway data. *PLoS computational biology, 14*, e1005968. ↗

## PDGFRs bind type I TKI ↗

**Stable identifier:** R-HSA-9674093

**Type:** binding

**Compartments:** plasma membrane, cytosol




Wild-type PDGFRA and PDGFRB can be bound and inhibited by class I tyrosine kinase inhibitors including pazopanib, avapritinib, and crenolanib (Gril et al, 2013; Wang et al, 2014; Mathias et al, 2015; Meliau et al, 2017; reviewed in Klug et al, 2018). Type I inhibitors bind in the ATP binding site of the active conformation and prevent full activation of the kinase (reviewed in Roskoski, 2018).

## Literature references


Roskoski, R. (2018). The role of small molecule platelet-derived growth factor receptor (PDGFR) inhibitors in the treatment of neoplastic disorders. *Pharmacol. Res., 129*, 65-83. ↗

Liewehr, DJ., Anwar, T., Fernández, P., Palmieri, D., Qian, Y., Steinberg, SM. et al. (2013). Pazopanib inhibits the activation of PDGFRβ-expressing astrocytes in the brain metastatic microenvironment of breast cancer cells. *Am. J. Pathol., 182*, 2368-79. ↗

Natarajan, K., Ambudkar, SV., Doshi, KA., Shukla, S., Mathias, TJ., Baer, MR. et al. (2015). The FLT3 and PDGFR inhibitor crenolanib is a substrate of the multidrug resistance protein ABCB1 but does not inhibit transport function at pharmacologically relevant concentrations. *Invest New Drugs, 33*, 300-9. ↗

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

Heinrich, MC., Zhang, Y., Hodous, BL., Shutes, A., Lengauer, C., Evans, EK. et al. (2017). A precision therapy against cancers driven by KIT/PDGFRA mutations. *Sci Transl Med, 9*. ↗


## Editions

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