

Autophosphorylation of PDGFR mutant dimers

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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. [↗](#)

Reactome database release: 88

This document contains 1 reaction ([see Table of Contents](#))

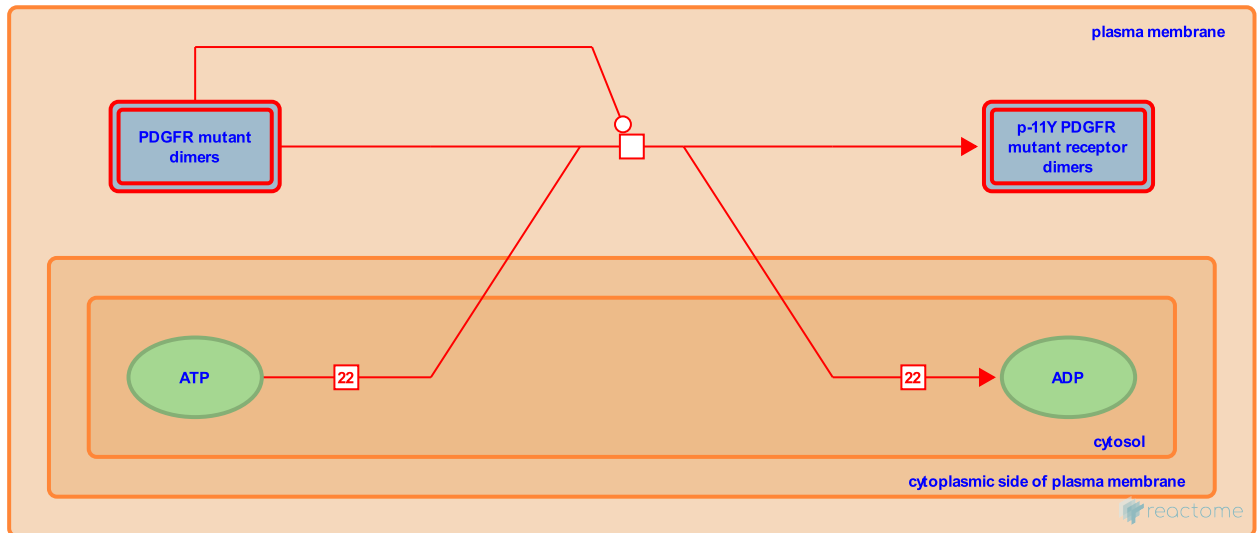
Autophosphorylation of PDGFR mutant dimers [↗](#)

Stable identifier: R-HSA-9672175

Type: transition

Compartments: cytosol, plasma membrane

Diseases: cancer



Activating mutations in the kinase, juxtamembrane and transmembrane domains of PDGFRA lead to constitutive, ligand-independent dimerization and trans-autophosphorylation, and stimulate downstream signaling pathways (Heinrich et al, 2003; Hirota et al, 2003; Corless et al, 2005; Velghe et al, 2014; reviewed in Roskoski et al, 2018; Klug et al, 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. [↗](#)
- Corless, CL., Heinrich, MC., Singer, S., Griffith, DJ., Town, A., Haley, A. et al. (2003). PDGFRA activating mutations in gastrointestinal stromal tumors. *Science*, 299, 708-10. [↗](#)
- Kitamura, Y., Shinomura, Y., Isozaki, K., Nishida, T., Kinoshita, K., Ohashi, A. et al. (2003). Gain-of-function mutations of platelet-derived growth factor receptor alpha gene in gastrointestinal stromal tumors. *Gastroenterology*, 125, 660-7. [↗](#)
- 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. [↗](#)
- Shiraga, S., McGreevey, L., Schroeder, A., Corless, CL., Heinrich, MC., Harrell, P. et al. (2005). PDGFRA mutations in gastrointestinal stromal tumors: frequency, spectrum and in vitro sensitivity to imatinib. *J. Clin. Oncol.*, 23, 5357-64. [↗](#)

Editions

2020-02-06	Reviewed	Ip, CKM.
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