Ligand-independent dimerization of cytosolic PDGFRA and PDGFRB fusion proteins

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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

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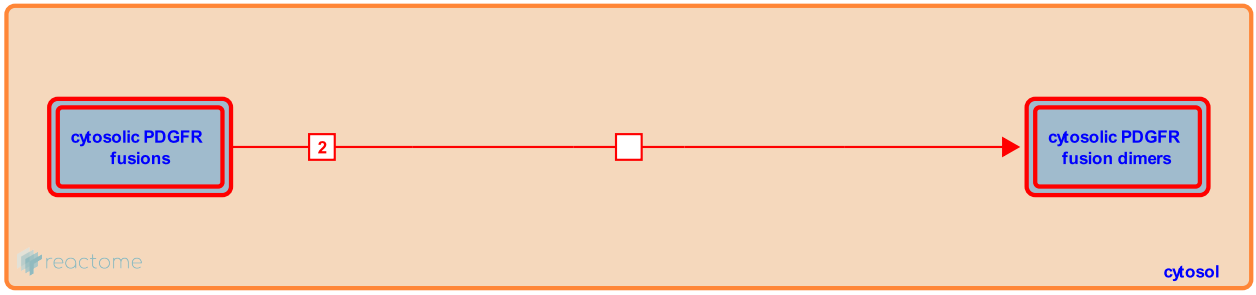
Stable identifier: R-HSA-9673757

Type: transition

Compartments: cytosol

Diseases: cancer



Fusions of an N-terminal partner and the cytosolic domain of PDGFRA or PDGFRB occur at low frequency in some cancers, particularly haematological disease (Cools et al, 2003; Ozawa et al, 2010; Hidalgo-Curtis et al, 2010; reviewed in Wang et al, 2016; Appiah-Kubi et al, 2017). Fusion proteins are constitutively active in the absence of ligand. Constitutive activation is promoted in many cases by the presence of an oligomerization domain in the N-terminal fusion partner, which promotes dimerization and subsequent trans-autophosphorylation. This is not always the case, however. In the instance of FIP1L1-PDGFRA, for example, constitutive activation is independent of the FIP1L1 portion of the protein, and dimerization depends on the relief of PDGFRA autoinhibition through disruption of the juxtamembrane region (Stover et al, 2006; reviewed in Reilly, 2003; Appiah-Kubi et al, 2017).

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Editions

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