

# Signaling by membrane-tethered fusions

## of PDGFRA or PDGFRB



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This is just an excerpt of a full-length report for this pathway. To access the complete report, please download it at the <u>Reactome Textbook</u>.

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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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This document contains 1 pathway and 2 reactions (see Table of Contents)

#### Signaling by membrane-tethered fusions of PDGFRA or PDGFRB 7

#### Stable identifier: R-HSA-9673768



In addition to activating missensse and in-frame deletion mutations, PDGFRA and PDGFRB are also subject to low frequency gene fusion events arising from chromosomal rearrangements. To date there are about 35 identified PDGFRA or B fusion partners, with PDGFRB being the more common partner (reviewed in Appiah-Kubi et al, 2017). Although some of the PDGF fusions proteins are cytosolic by virtue of removal of the PDGFR transmembrane region (TMD), a number of fusions retain the TMD and are linked to the plasma membrane (Hidalgo-Curtis et al, 2010; Ozawa et al, 2010; Curtis et al, 2007; Medves et al, 2010; reviewed in Appiah-Kubi et al, 2017). The most common transmembrane fusion partner of PDGFRA and PDGFRB is ETV6 (also known as TEL1), a transcriptional repressor with known ability to homodimerize (Curtis et al, 2007; Golub et al, 1994; Andrae et al, 2008; reviewed in de Braekeleer et al, 2012; Wang et al, 2016; Appiah-Kubi et al, 2017).

#### Literature references

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#### Editions

2020-02-06	Reviewed	Ip, CKM.
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### Ligand-independent dimerization of membrane-tethered fusions of PDGFRA or PDG-FRB 7

Location: Signaling by membrane-tethered fusions of PDGFRA or PDGFRB

Stable identifier: R-HSA-9673760

Type: transition

Compartments: plasma membrane

#### Diseases: cancer



Transmembrane PDGFR fusion proteins dimerize independent of ligand stimulation, driven by the presence of a dimerization domain provided by the N-terminal fusion partner of the PDGFR protein (Stover et al, 2006; Carroll et al, 1996; Ozawa et al, 2010; Medves et al, 2010; Willbanks et al, 2000; reviewed in Wang et al, 2016; Appiah-Kubi et al, 2017).

Followed by: Autophosphorylation of membrane-tethered fusions of PDGFRA or PDGFRB

#### Literature references

- Yao, X., Chen, Y., Wu, M., Qian, H., Wang, Y., Wu, Y. et al. (2016). The platelet-derived growth factors (PDGFs) and their receptors (PDGFRs) are major players in oncogenesis, drug resistance, and attractive oncologic targets in cancer. *Growth Factors*, *34*, 64-71.
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#### Autophosphorylation of membrane-tethered fusions of PDGFRA or PDGFRB 7

Location: Signaling by membrane-tethered fusions of PDGFRA or PDGFRB

#### Stable identifier: R-HSA-9673761

#### Type: transition

#### Compartments: plasma membrane

Diseases: cancer



Where they have been studied, transmembrane PDGFR fusion proteins have been shown to trans-autophosphorylate in a ligand-independent manner, stimulating downstream signaling and promoting oncogenic transformation (Carroll et al, 1996; Willbanks et al, 2000; Stover et al, 2006; Medves et al, 2010; Ozawa et al, 2010; reviewed in Wang et al, 2016; Appiah-Kubi et al, 2017). Many of the PDGFR fusions appear to signal through the STAT pathway, with some variability in which STAT family members are engaged. Other pathways activated downstream of the transmembrane fusions include MAP kinase, PLC gamma and PI3K signaling cascades (Medves et al, 2010; Ozawa et al, 2010; Ozawa et al, 2010; Ozawa et al, 2010; Willbanks et al, 2000; Carroll et al, 1996).

Preceded by: Ligand-independent dimerization of membrane-tethered fusions of PDGFRA or PDGFRB

#### Literature references

- Yao, X., Chen, Y., Wu, M., Qian, H., Wang, Y., Wu, Y. et al. (2016). The platelet-derived growth factors (PDGFs) and their receptors (PDGFRs) are major players in oncogenesis, drug resistance, and attractive oncologic targets in cancer. *Growth Factors, 34*, 64-71.
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