

2x p-5Y-RET:GDNF:GFRA complexes binds DOK1,DOK2,DOK4,DOK5,DOK6

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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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Reactome database release: 88

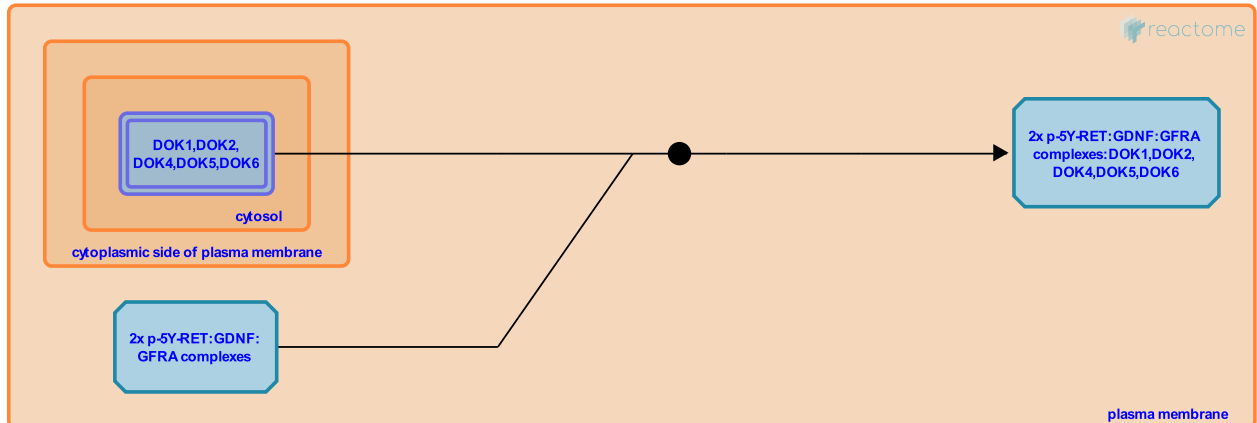
This document contains 1 reaction ([see Table of Contents](#))

2x p-5Y-RET:GDNF:GFRA complexes binds DOK1,DOK2,DOK4,DOK5,DOK6 ↗

Stable identifier: R-HSA-8855617

Type: binding

Compartments: cytosol, extracellular region, plasma membrane



Docking protein 1 (DOK 1), 2, 4, 5, and 6 adaptor proteins all interact with RET at phosphorylated tyrosine-1062 (Y1062) (Grimm et al. 2001, Crowder et al. 2004, Kurotsuchi et al. 2010).

DOKs are adaptor proteins that can inhibit mitogen-activated protein kinase (MAPK) signaling, cell proliferation, and cellular transformation. DOK1 and 2 may exert their inhibitory effects by recruiting Ras GTPase-activating protein 1 (RASA1, RasGAP), which is a negative regulator of Ras signaling, but DOK2 can attenuate EGF receptor-induced MAP kinase activation without RASA1. DOK3 negatively regulates signaling by recruiting INPP5D and CSK (Grimm et al. 2001).

RET promotes neurite outgrowth of the rat pheochromocytoma cell line PC12 via Y1062. RET-DOK4/5 fusion proteins induced ligand-dependent axonal outgrowth of PC12 cells, while RET-DOK2 fusions did not. DOK4/5 do not associate with RASA1 or NCK, and enhance RET-dependent activation of MAPK (Grimm et al. 2001).

Literature references

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Grimm, J., Britsch, S., Alitalo, K., Schwarz-Romond, T., Birchmeier, W., Di Cesare, S. et al. (2001). Novel p62dok family members, dok-4 and dok-5, are substrates of the c-Ret receptor tyrosine kinase and mediate neuronal differentiation. *J. Cell Biol.*, 154, 345-54. ↗

Editions

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