

# RET binds GFRA1,GFRA3

Jupe, S., Luo, W., Morales, D.

European Bioinformatics Institute, New York University Langone Medical Center, Ontario Institute for Cancer Research, Oregon Health and Science University.

The contents of this document may be freely copied and distributed in any media, provided the authors, plus the institutions, are credited, as stated under the terms of [Creative Commons Attribution 4.0 International \(CC BY 4.0\) License](https://creativecommons.org/licenses/by/4.0/). For more information see our [license](https://reactome.org/licenses/).

18/09/2024

## 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.

The development of Reactome is supported by grants from the US National Institutes of Health (P41 HG003751), University of Toronto (CFREF Medicine by Design), European Union (EU STRP, EMI-CD), and the European Molecular Biology Laboratory (EBI Industry program).

## 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: 89

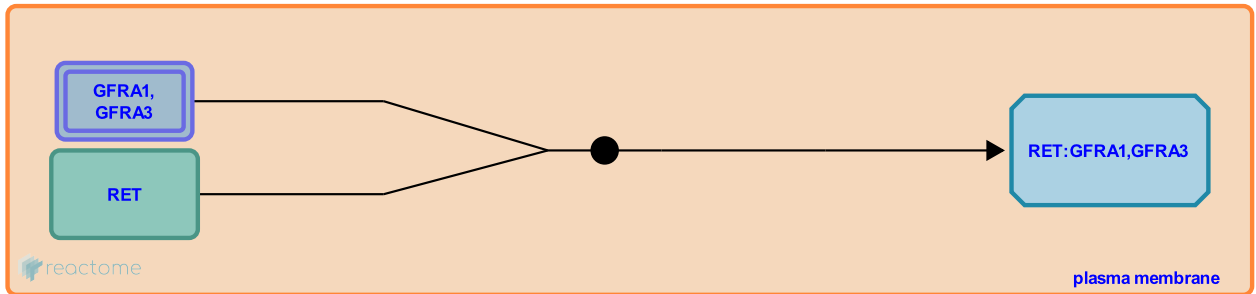
This document contains 1 reaction ([see Table of Contents](#))

# RET binds GFRA1,GFRA3 ↗

**Stable identifier:** R-HSA-8853745

**Type:** binding

**Compartments:** plasma membrane



RET is a receptor tyrosine kinase with a cadherin-related motif and a cysteine-rich domain in the extracellular domain (Takahashi et al. 1988). It is the receptor for members of the glial cell-derived neurotrophic factor (GDNF) family of ligands (Lin et al. 1993, Kotzbauer et al. 1996, Baloh et al. 1998, Milbrandt et al. 1998). RET can only bind these ligands in the presence of a co-receptor from the family of glycosylphosphatidylinositol (GPI)-anchored co-receptors collectively termed GDNF family receptor-alpha (GFRA) (Treanor et al. 1996, Jing et al. 1996, Plaza-Menacho et al. 2006). Early models proposed that GDNF formed a complex with GFRA1 and subsequently recruited RET (Massagué et al. 1996). Current models suggest that GFRA and RET pre-associate before ligand binding, based on binding and site-directed mutagenesis studies (Eketjäll et al. 1999, Cik et al. 2000). An alternative model suggests that GPI-anchored GFRA recruits RET to lipid rafts after GDNF stimulation (Tansey et al. 2000). The stoichiometry as well as the kinetics of ligand-receptor complex formation are not well understood. It is believed that all GDNF family members interact with their cognate co-receptor and activate RET in a similar manner to GDNF (Airaksinen & Saarma 2002).

## Literature references

Lampe, PA., Johnson, EM., Heuckeroth, RO., Milbrandt, J., Osborne, PA., Creedon, DJ. et al. (1997). Neurturin shares receptors and signal transduction pathways with glial cell line-derived neurotrophic factor in sympathetic neurons. *Proc. Natl. Acad. Sci. U.S.A.*, 94, 7018-23. ↗

Enomoto, H., Lampe, PA., Simburger, KS., Johnson, EM., Milbrandt, J., Fahrner, TJ. et al. (1998). Artemin, a novel member of the GDNF ligand family, supports peripheral and central neurons and signals through the GFRalpha3-RET receptor complex. *Neuron*, 21, 1291-302. ↗

Antonio, L., Luo, Y., Altrock, BW., Jing, S., Hu, S., Wen, D. et al. (1996). GDNF-induced activation of the ret protein tyrosine kinase is mediated by GDNFR-alpha, a novel receptor for GDNF. *Cell*, 85, 1113-24. ↗

## Editions

2016-01-25	Authored	Jupe, S.
2016-04-28	Edited	Jupe, S.
2016-05-06	Reviewed	Morales, D.
2016-05-17	Reviewed	Luo, W.