RET binds GFRA4

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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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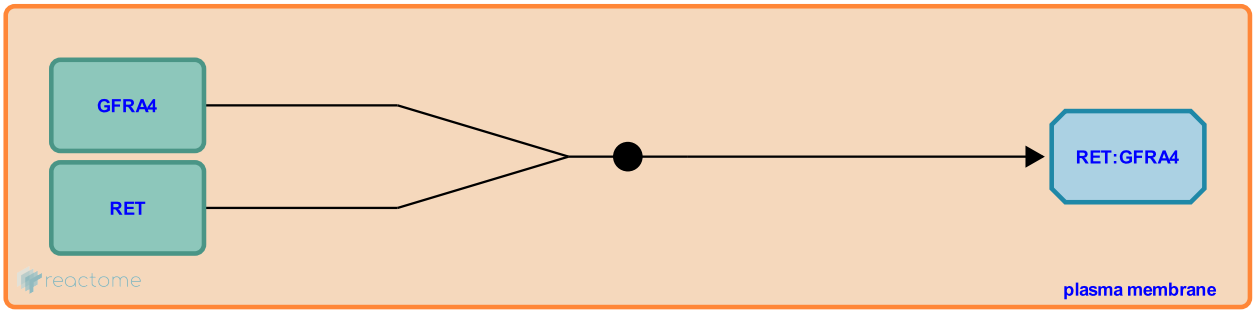
Stable identifier: R-HSA-8871227

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 preassociate 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

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Editions

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