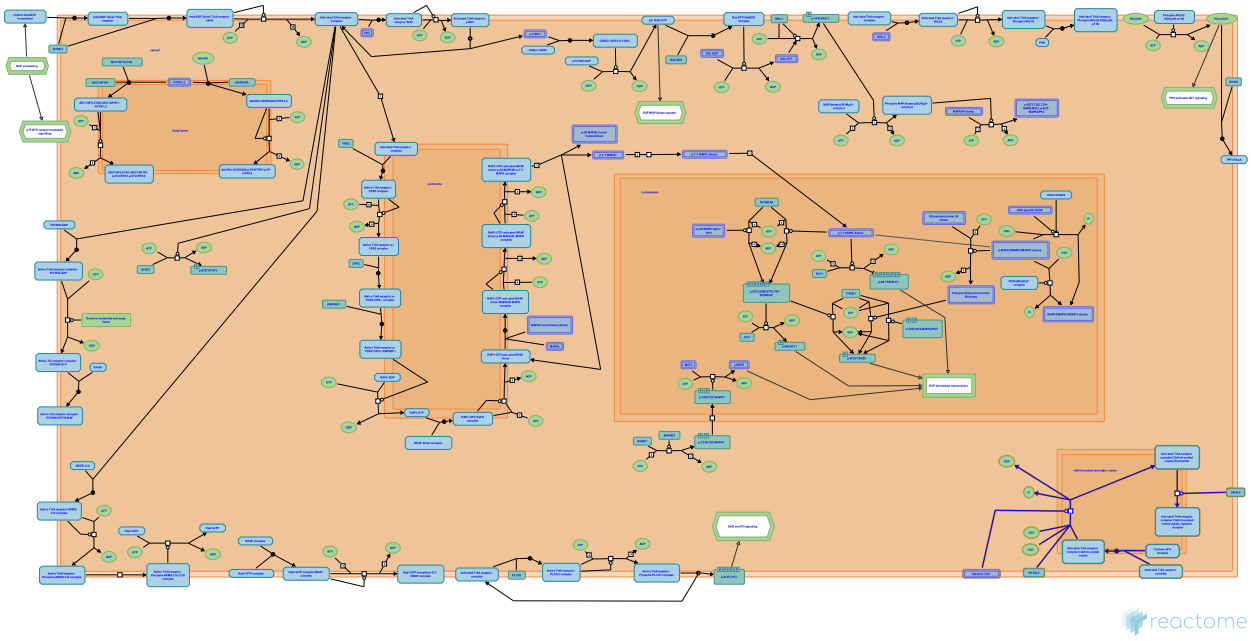
Retrograde neurotrophin signalling



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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 Reactome Textbook.

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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.
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. ↗

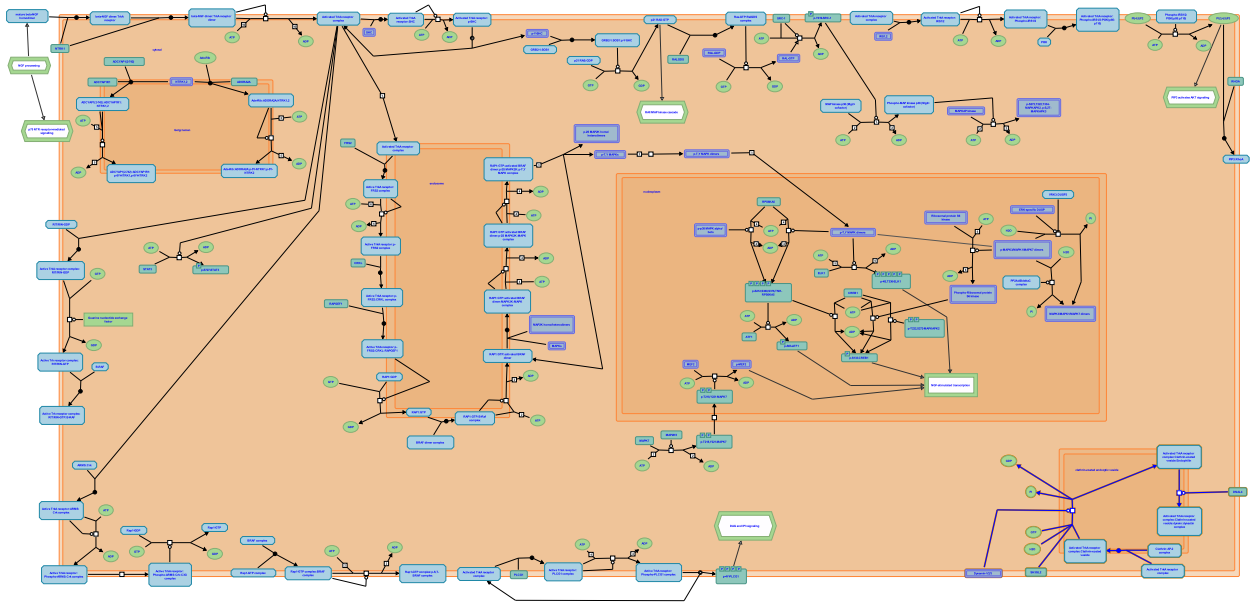
Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

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. ↗

Retrograde neurotrophin signalling ↗

Stable identifier: R-HSA-177504



Neurotrophin-TRK complexes can be internalized and enter signalling vesicles, which travel retrogradely over long distances from distal nerve terminals to neuronal cell bodies. Such retrograde signalling by neurotrophin-TRK complexes regulates survival, synaptogenesis and maintenance of proper neural connectivity. The neurotrophin-TRK complex may use three distinct internalization pathways. Although Clathrin-mediated endocytosys appears to be the major internalization route, it is controversial whether it also represents the dominant pathway for retrograde transport and signalling. Pyncher-mediated endocytosis might be more relevant in this regard. Moreover, also caveolin-mediated endocytosis may play a role in NGF-TrkA internalization.
Retrograde transport of TRKs is microtubule-dependent: TRKs remain activated and bound to neurotrophins during retrograde transport. The current view is reflected in the signalling endosome model. It is a specialized vesicle containing ligand (NGF, BDNF) bound to its activated TRK receptor, together with activated downstream signalling proteins, transported by motor proteins (dyneins) from nerve terminals to remote cell bodies, where the receptors trigger signalling cascades.

Editions

2006-10-10	Edited	Jassal, B.
2006-10-10	Authored	Annibali, D., Nasi, S.
2007-11-08	Reviewed	Greene, LA.

Formation of clathrin-coated vesicle ↗

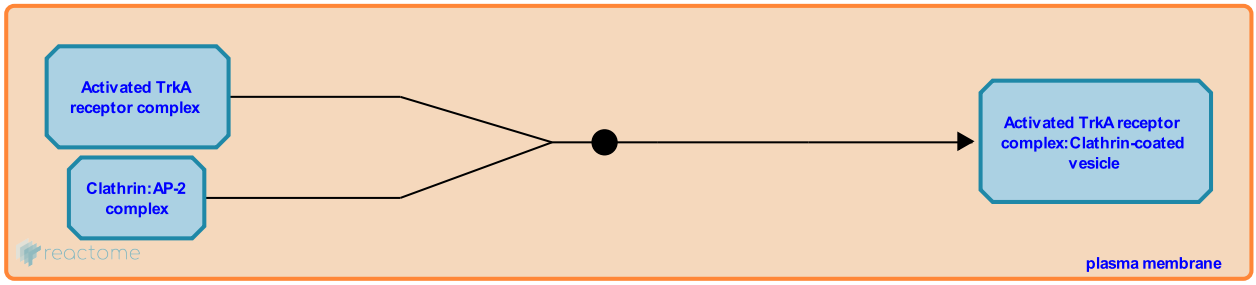
Location: Retrograde neurotrophin signalling

Stable identifier: R-HSA-177491

Type: binding

Compartments: plasma membrane, extracellular region

Inferred from: Formation of clathrin-coated vesicle (Rattus norvegicus)



Both BDNF and NGF treatment recruits clathrin and AP2 (adaptor protein 2) proteins to the plasma membrane. Clathrin is the major protein of the polyhedral coat of vesicles. The AP2 complex mediates both the recruitment of clathrin to membranes and the recognition of sorting signals within the cytosolic tails of transmembrane cargo molecules.

Followed by: Endocytosis (internalization) of clathrin-coated vesicle

Editions

2006-10-10	Edited	Jassal, B.
2006-10-10	Authored	Annibali, D., Nasi, S.
2007-11-08	Reviewed	Greene, LA.

Endocytosis (internalization) of clathrin-coated vesicle ↗

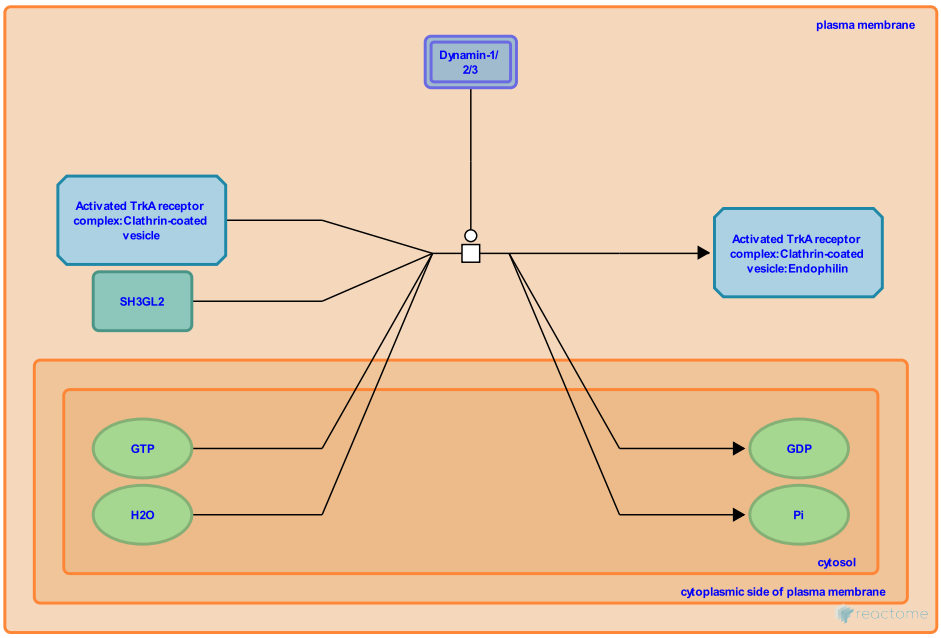
Location: Retrograde neurotrophin signalling

Stable identifier: R-HSA-177501

Type: transition

Compartments: plasma membrane, extracellular region, cytosol

Inferred from: Endocytosis of clathrin-coated vesicle (Rattus norvegicus)



Dynamin is a microtubule-associated force-producing protein involved in producing microtubule bundles and able to bind and hydrolyze GTP. It is involved in vesicle trafficking processes and is necessary for endocytosis. Dynamins are large GTPases that bind to PIP2-containing membranes, several SH3-domain containing proteins and cytoskeletal modifiers. They self-polymerize in a GTP dependent manner, catalyzing the scission of invaginating membranes during endocytosis (Praefcke & McMahon, 2004). There are three dynamins in humans: dynamin I is neuron-specific; dynamin II shows ubiquitous expression; dynamin III is expressed in testis, brain, lung and blood platelets.

Preceded by: Formation of clathrin-coated vesicle

Followed by: Axonal transport of NGF:Trk complexes

Editions

2006-10-10	Edited	Jassal, B.
2006-10-10	Authored	Annibali, D., Nasi, S.
2007-11-08	Reviewed	Greene, LA.

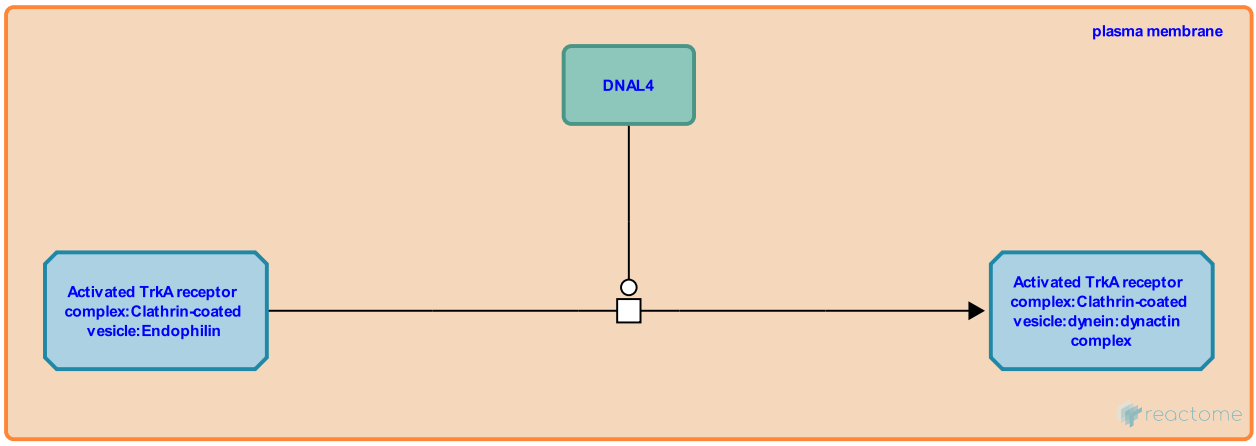
Axonal transport of NGF:Trk complexes ↗

Location: Retrograde neurotrophin signalling

Stable identifier: R-HSA-177479

Type: transition

Compartments: plasma membrane, extracellular region



Of the internalized NGF:TRK complexes, many undergo recycling and/or proteolysis. Only a small fraction is retrogradely transported. Vesicles containing neurotrophin, activated receptors and downstream kinases are transported through axons by the action of dynein, which produces a force towards the end of microtubules.

Preceded by: Endocytosis (internalization) of clathrin-coated vesicle

Literature references

Kong, H., Perez, P., Arevalo, JC., Sung, C., Chuang, J., Yano, H. et al. (2001). Association of Trk neurotrophin receptors with components of the cytoplasmic dynein motor. *J Neurosci, 21*, RC125. ↗

Editions

2006-10-10	Edited	Jassal, B.
2006-10-10	Authored	Annibali, D., Nasi, S.
2007-11-08	Reviewed	Greene, LA.

Table of Contents