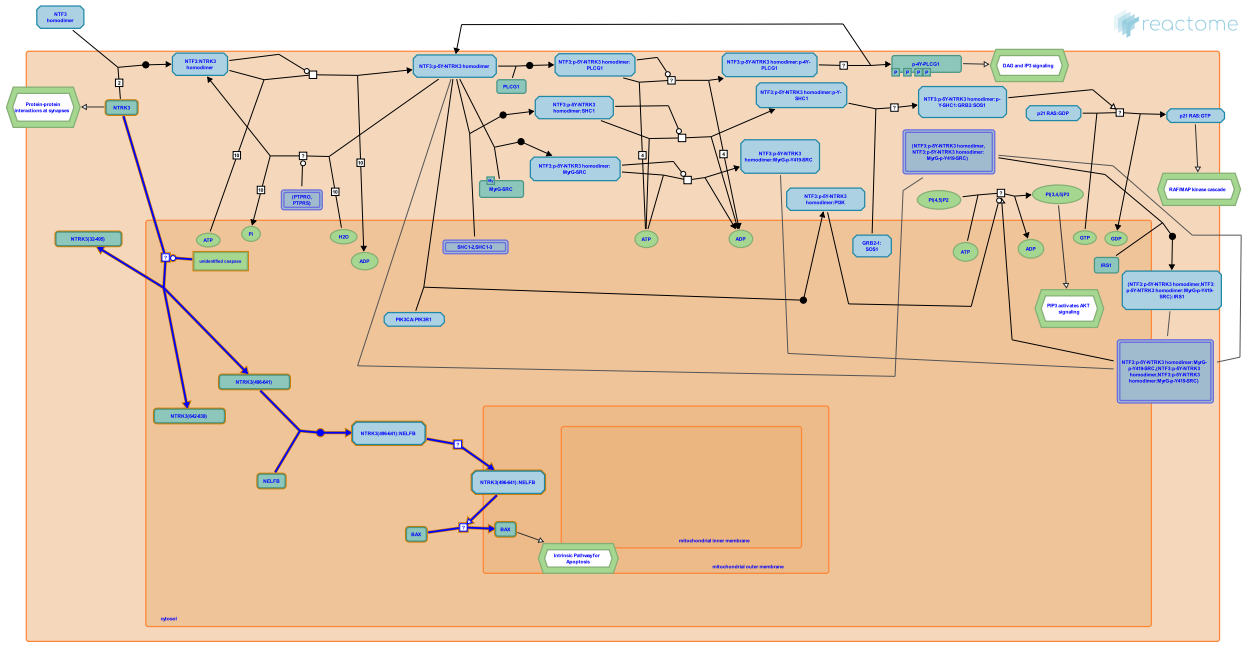
NTRK3 as a dependence receptor



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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.

30/11/2024

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. ↗

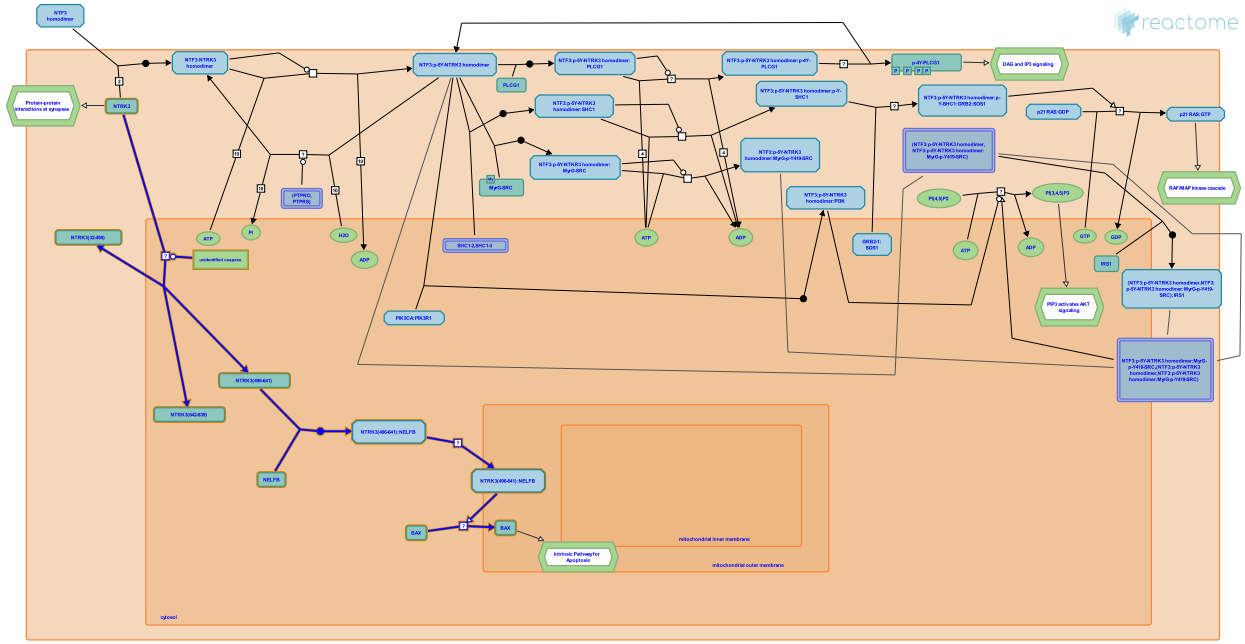
Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

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. ↗

NTRK3 as a dependence receptor ↗

Stable identifier: R-HSA-9603505



When neuronal cells are deprived of the NTRK3 (TRKC) ligand NTF3 (NT-3), NTRK3 functions as a dependence receptor, promoting apoptosis. The pro-apoptotic activity of NTRK3 is implicated in proper nervous system development, by dictating the number of surviving sensory neurons (Tauszig-Delamasure et al. 2007). In the absence of its ligand, NTRK3 undergoes caspase-dependent cleavage (Tauszig-Delamasure et al. 2007), resulting in release of the NTRK3 killer fragment (KF). The NTRK3 KF, in complex with NELFB (COBRA1), inserts into the mitochondrial membrane, promoting cytochrome c release and apoptosome-mediated apoptosis (Ichim et al. 2013).

Literature references

Cabrera, JR., Bouzas-Rodriguez, J., Bordeaux, MC., Tauszig-Delamasure, S., Mehlen, P., Yu, LY. et al. (2007). The TrkC receptor induces apoptosis when the dependence receptor notion meets the neurotrophin paradigm. *Proc. Natl. Acad. Sci. U.S.A., 104*, 13361-6. ↗

Mehlen, P., Coelho-Aguiar, JM., Arumäe, U., Lefebvre, J., Tulasne, D., Le Douarin, N. et al. (2013). The dependence receptor TrkC triggers mitochondria-dependent apoptosis upon Cobra-1 recruitment. *Mol. Cell, 51*, 632-46. ↗

Editions

2018-01-02	Authored	Orlic-Milacic, M.
2018-05-09	Edited	Orlic-Milacic, M.
2018-05-09	Reviewed	Tsoulfas, P.

Unknown caspase cleaves NTRK3 ↗

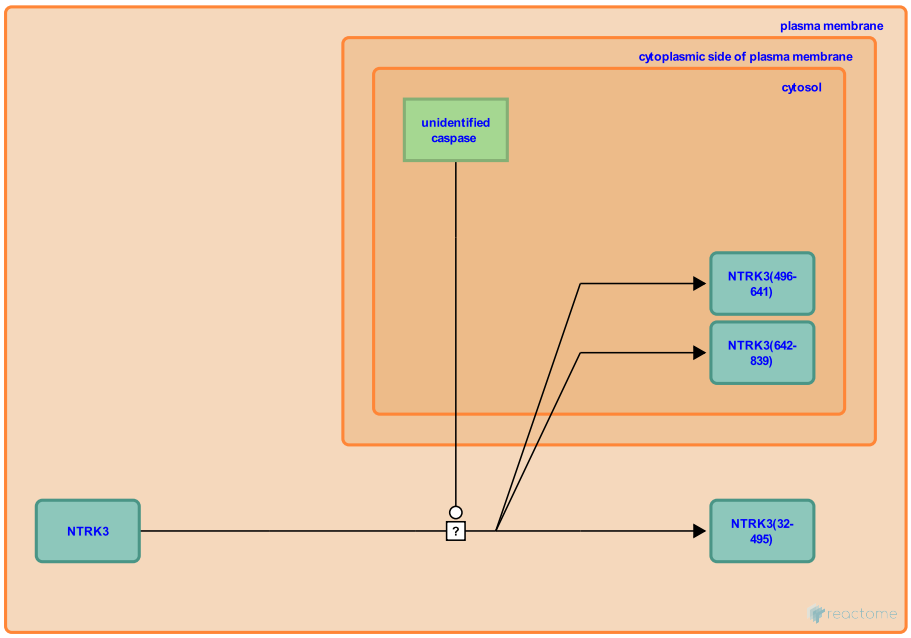
Location: NTRK3 as a dependence receptor

Stable identifier: R-HSA-9603534

Type: uncertain

Compartments: plasma membrane, cytosol

Inferred from: Unknown caspase cleaves Ntrk3 (Mus musculus)



In the absence of ligand, NTRK3 (TRKC) is cleaved by an unknown caspase. CASP3 (caspase-3) cleaves NTRK3 in vitro, but CASP3 inhibitors do not prevent NTRK3 cleavage in live cells. CASP8 (caspase-8) is unable to cleave NTRK3 in vitro. A general caspase inhibitor prevents NTRK3 cleavage in live cells (Tauszig-Delamasure et al. 2007).

Followed by: NTRK3(496-641) binds NELFB

Editions

2018-01-02	Authored	Orlic-Milacic, M.
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NTRK3(496-641) binds NELFB ↗

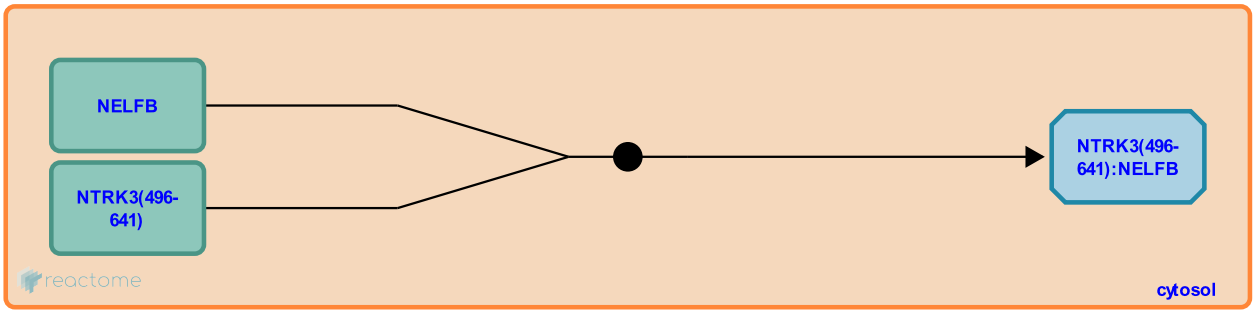
Location: NTRK3 as a dependence receptor

Stable identifier: R-HSA-9603548

Type: binding

Compartments: cytosol

Inferred from: Ntrk3 binds Nelfb (Mus musculus)



NTRK3(496-641), the NTRK3 (TRKC) killer fragment (KF) binds to NELFB in the cytosol. NELFB (COBRA1) is known as a negative regulator of transcriptional elongation and a BRCA1 co-factor. NELFB is predominantly nuclear but is also found outside of the nucleus (Ichim et al. 2013).

Preceded by: Unknown caspase cleaves NTRK3

Followed by: NTRK3(496-641):NELFB translocates to mitochondrion

Editions

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2018-05-09	Reviewed	Tsoulfas, P.

NTRK3(496-641):NELFB translocates to mitochondrion ↗

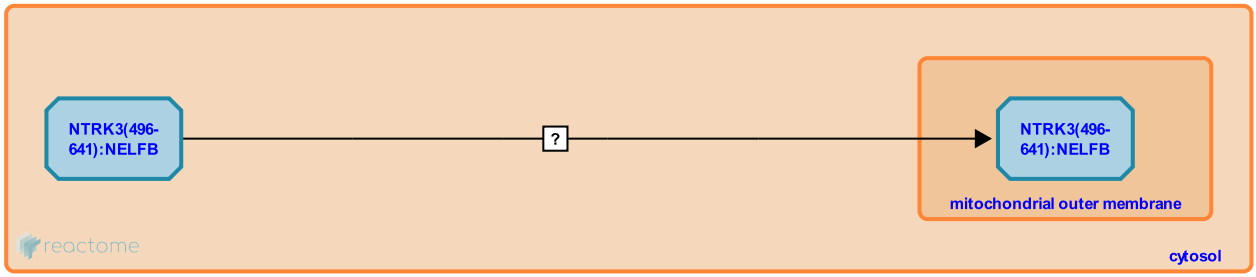
Location: NTRK3 as a dependence receptor

Stable identifier: R-HSA-9603554

Type: uncertain

Compartments: cytosol, mitochondrial outer membrane

Inferred from: Nrk3(496-641):Nelfb translocates to mitochondrion (Mus musculus)



The complex of the NTRK3 (TRKC) killer fragment (KF) and NELFB (COBRA1) translocates to the mitochondrial outer membrane (Ichim et al. 2013).

Preceded by: NTRK3(496-641) binds NELFB

Followed by: BAX activation is stimulated by NTRK3(495-641) and NELFB

Editions

2018-01-02	Authored	Orlic-Milacic, M.
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BAX activation is stimulated by NTRK3(495-641) and NELFB ↗

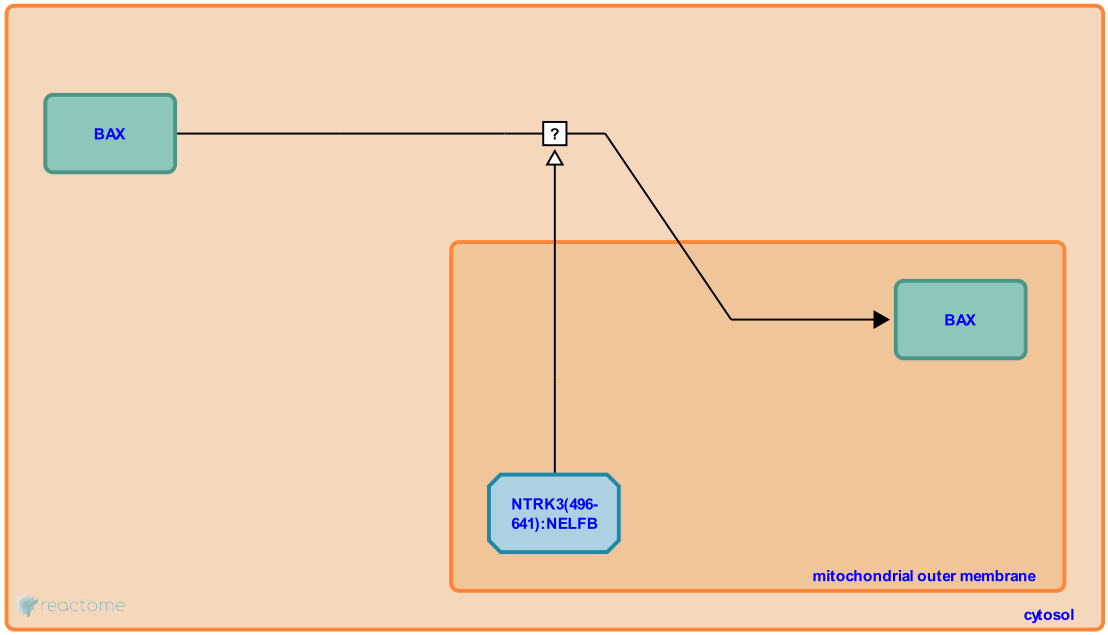
Location: NTRK3 as a dependence receptor

Stable identifier: R-HSA-9603598

Type: uncertain

Compartments: cytosol, mitochondrial outer membrane

Inferred from: BAX activation is stimulated by Ntrk3(496-641) and Nelfb (Chlorocebus sabaeus)



The complex of NTRK3 (TRKC) killer fragment (KF) and NELFB (COBRA1) stimulates BAX activation through an unknown mechanism. This is followed by BAX-dependent cytochrome C release and apoptosome-dependent cell death (Ichim et al. 2013).

Preceded by: NTRK3(496-641):NELFB translocates to mitochondrion

Editions

2018-01-02	Authored	Orlic-Milacic, M.
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Table of Contents