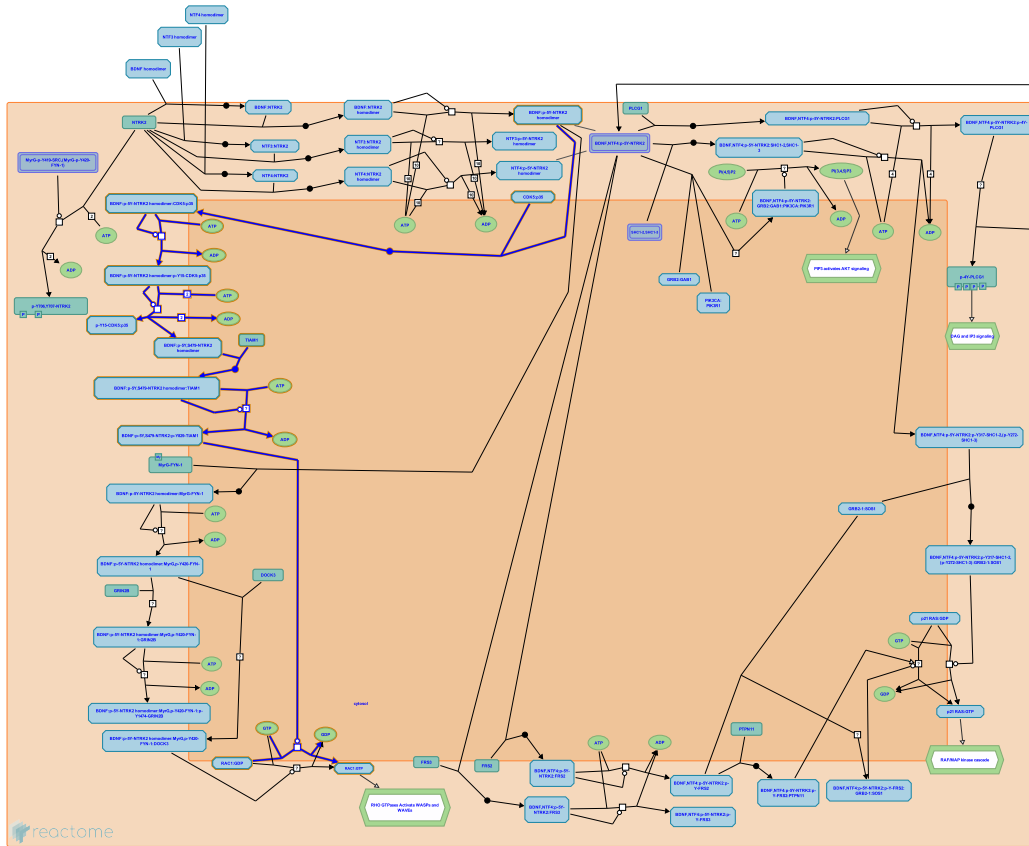


Activated NTRK2 signals through CDK5



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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

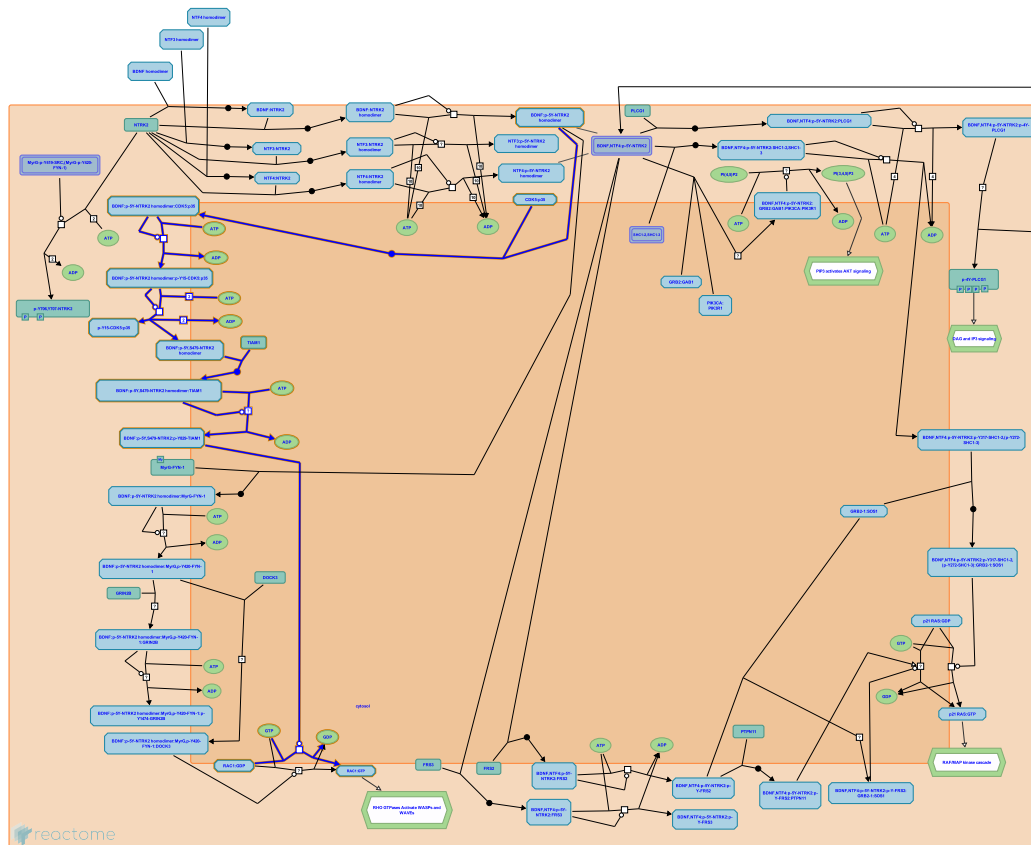
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Reactome database release: 70

This document contains 1 pathway and 6 reactions ([see Table of Contents](#))

Activated NTRK2 signals through CDK5 ↗

Stable identifier: R-HSA-9032845



CDK5, in complex with its activator CDK5R1 (p35), binds to BDNF-activated NTRK2 (TRKB). NTRK2 promotes CDK5 catalytic activity by phosphorylating CDK5 at tyrosine residue Y15 (Cheung et al. 2007), although CDK5 can also be phosphorylated at Y15 independently of NTRK2 (Zhao et al. 2009). CDK5 phosphorylates serine residue S479 of NTRK2 (corresponds to S478 in mouse and rat) (Cheung et al. 2007, Zhao et al. 2009). Phosphorylation of NTRK2 at S479 is needed for BDNF-triggered dendritic growth (Cheung et al. 2007), hippocampal long-term potentiation (LTP) and spatial memory (Lai et al. 2012). These processes involve NTRK2-mediated activation of RHO GTPases RAC1 (Lai et al. 2012) and possibly CDC42 (Cheung et al. 2007). In cultured isolated neurons, phosphorylation at S479 affects localization of NTRK2 (Zhao et al. 2009), but this does not appear to be the case in vivo (Lai et al. 2012).

CDK5-mediated phosphorylation of NTRK2 was suggested to influence the level of AKT activity, downstream mTOR signaling and DLG4 (PSD-95) expression, but further elucidation is needed (Lai et al. 2012).

Signaling by TRKB and CDK5 plays a role in inflammation induced hypersensitivity to heat-triggered pain in rats (Zhang et al. 2014).

Literature references

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Editions

2018-01-05	Authored	Orlic-Milacic, M.
2018-02-13	Reviewed	Castrén, E., Antila, H.
2018-02-20	Edited	Orlic-Milacic, M.

Activated NTRK2 binds CDK5 ↗

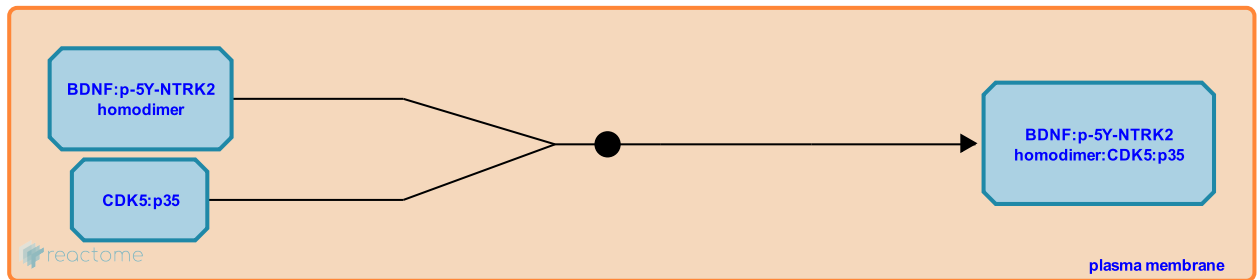
Location: [Activated NTRK2 signals through CDK5](#)

Stable identifier: R-HSA-9032841

Type: binding

Compartments: plasma membrane

Inferred from: [Activated Ntrk2 binds Cdk5 \(Rattus norvegicus\)](#)



BDNF-activated NTRK2 binds CDK5 indirectly, by interacting with p35, a non-cyclin activator of CDK5 which forms a complex with CDK5 (Cheung et al. 2007).

Followed by: [NTRK2 phosphorylates CDK5](#)

Editions

2018-01-05	Authored	Orlic-Milacic, M.
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NTRK2 phosphorylates CDK5 ↗

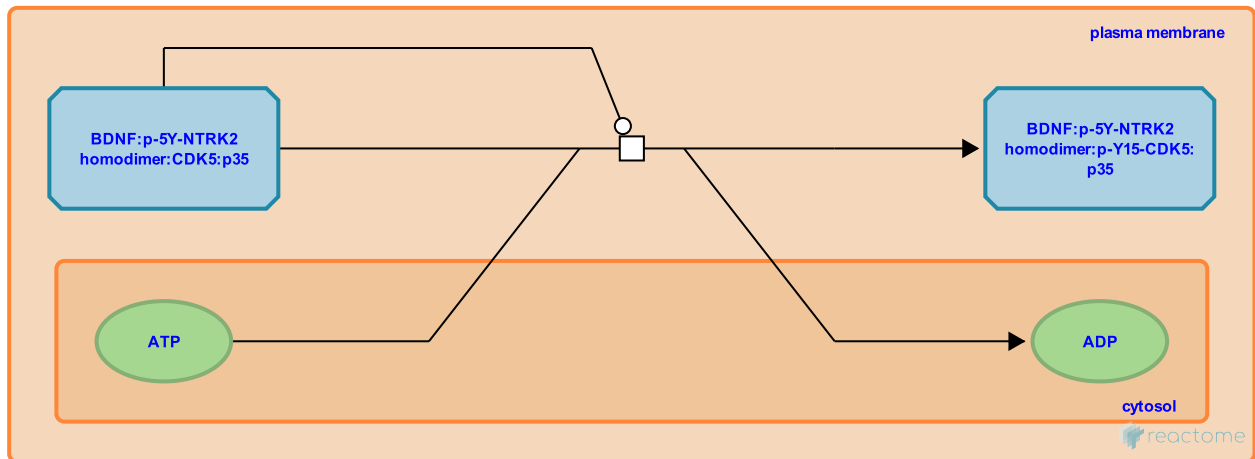
Location: [Activated NTRK2 signals through CDK5](#)

Stable identifier: R-HSA-9032854

Type: transition

Compartments: plasma membrane, cytosol

Inferred from: [Ntrk2 phosphorylates CDK5 \(Homo sapiens\)](#)



BDNF-activated NTRK2 (TRKB) phosphorylates CDK5 on tyrosine residue Y15, thus increasing CDK5 catalytic activity (Cheung et al. 2007).

Preceded by: [Activated NTRK2 binds CDK5](#)

Followed by: [CDK5 phosphorylates NTRK2](#)

Editions

2018-01-05	Authored	Orlic-Milacic, M.
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CDK5 phosphorylates NTRK2 ↗

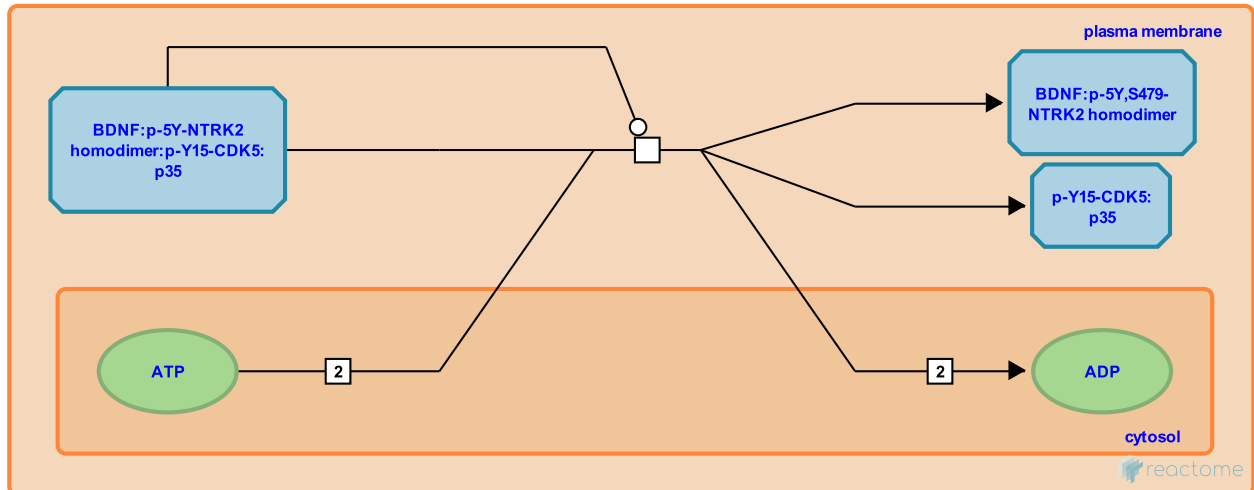
Location: [Activated NTRK2 signals through CDK5](#)

Stable identifier: R-HSA-9032863

Type: transition

Compartments: plasma membrane, cytosol

Inferred from: [Cdk5 phosphorylates Ntrk2 \(Homo sapiens\)](#)



CDK5 phosphorylates NTRK2 (TRKB) on serine residue S479 (corresponds to S478 in mouse and rat Ntrk2). CDK5-mediated phosphorylation does not affect NTRK2-mediated activation of RAS, PLCgamma or PI3K signaling (Cheung et al. 2007, Lai et al. 2012). It was originally suggested that S479 phosphorylation was needed for NTRK2-mediated activation of CDC42, which plays a role in dendritic growth (Cheung et al. 2007), but the involvement of CDC42 was later disputed (Lai et al. 2012).

CDK5 activated by chemical long-term potentiation, independently of BDNF and NTRK2, can phosphorylate intracellular NTRK2 at S479 and promote its insertion into plasma membrane (Zhao et al. 2009), but S479 phosphorylation does not significantly affect NTRK2 localization in vivo (Lai et al. 2012).

Preceded by: [NTRK2 phosphorylates CDK5](#)

Followed by: [NTRK2 binds TIAM1](#)

Editions

2018-01-05	Authored	Orlic-Milacic, M.
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NTRK2 binds TIAM1 [↗](#)

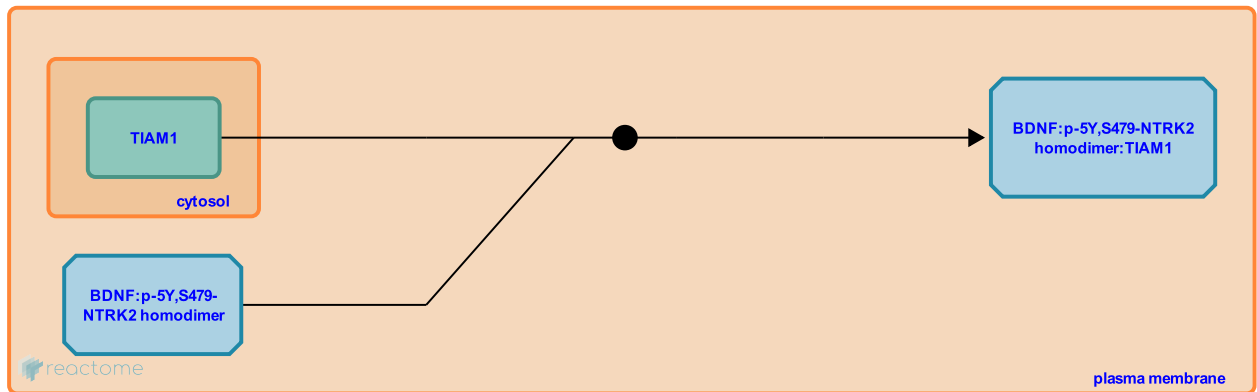
Location: [Activated NTRK2 signals through CDK5](#)

Stable identifier: R-HSA-9033276

Type: binding

Compartments: plasma membrane, cytosol

Inferred from: [Ntrk2 binds Tiam1 \(Mus musculus\)](#)



TIAM1, a guanine nucleotide exchange factor (GEF) for the RHO GTPase RAC1, binds to NTRK2 (TRKB) phosphorylated at serine residue S479 (corresponds to S478 in mice) by CDK5 (Lai et al. 2012).

Preceded by: [CDK5 phosphorylates NTRK2](#)

Followed by: [NTRK2 promotes TIAM1 phosphorylation](#)

Editions

2018-01-05	Authored	Orlic-Milacic, M.
2018-02-13	Reviewed	Castrén, E., Antila, H.
2018-02-20	Edited	Orlic-Milacic, M.

NTRK2 promotes TIAM1 phosphorylation ↗

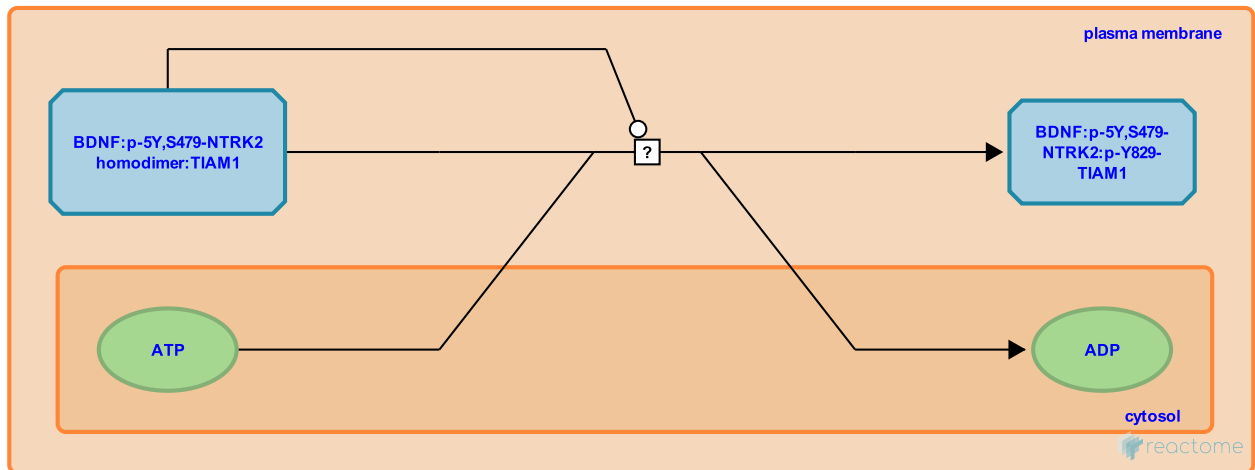
Location: Activated NTRK2 signals through CDK5

Stable identifier: R-HSA-9033284

Type: uncertain

Compartments: plasma membrane, cytosol

Inferred from: Ntrk2 promotes Tiam1 phosphorylation (Homo sapiens)



Upon binding to NTRK2 (TRKB), TIAM1 is phosphorylated at tyrosine residue Y829, presumably by NTRK2, but this has not been shown directly (Lai et al. 2012).

Preceded by: NTRK2 binds TIAM1

Followed by: NTRK2 and CDK5 promote activation of RAC1 by TIAM1

Editions

2018-01-05	Authored	Orlic-Milacic, M.
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2018-02-20	Edited	Orlic-Milacic, M.

NTRK2 and CDK5 promote activation of RAC1 by TIAM1 ↗

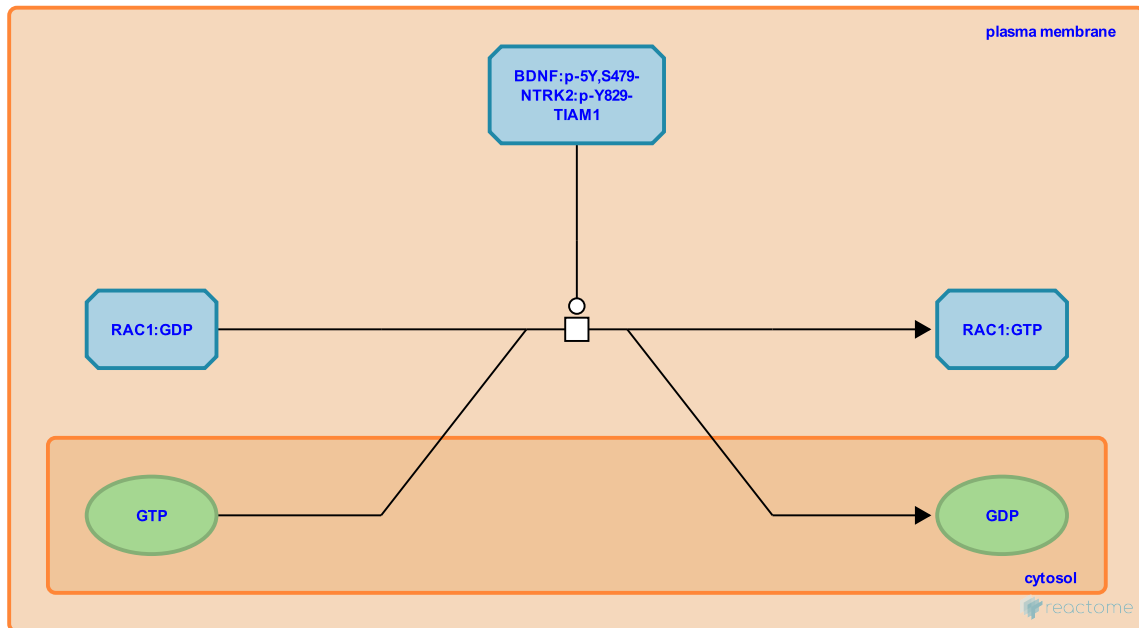
Location: [Activated NTRK2 signals through CDK5](#)

Stable identifier: R-HSA-9033292

Type: transition

Compartments: plasma membrane, cytosol

Inferred from: [Ntrk2 and Cdk5 promote activation of Rac1 by Tiam1 \(Homo sapiens\)](#)



TIAM1, activated by binding to CDK5-phosphorylated and BDNF-activated NTRK2 (TRKB), promotes guanine nucleotide exchange on RAC1, which results in formation of the active RAC1:GTP complex (Lai et al. 2012).

Preceded by: [NTRK2 promotes TIAM1 phosphorylation](#)

Editions

2018-01-05	Authored	Orlic-Milacic, M.
2018-02-13	Reviewed	Castrén, E., Antila, H.
2018-02-20	Edited	Orlic-Milacic, M.

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