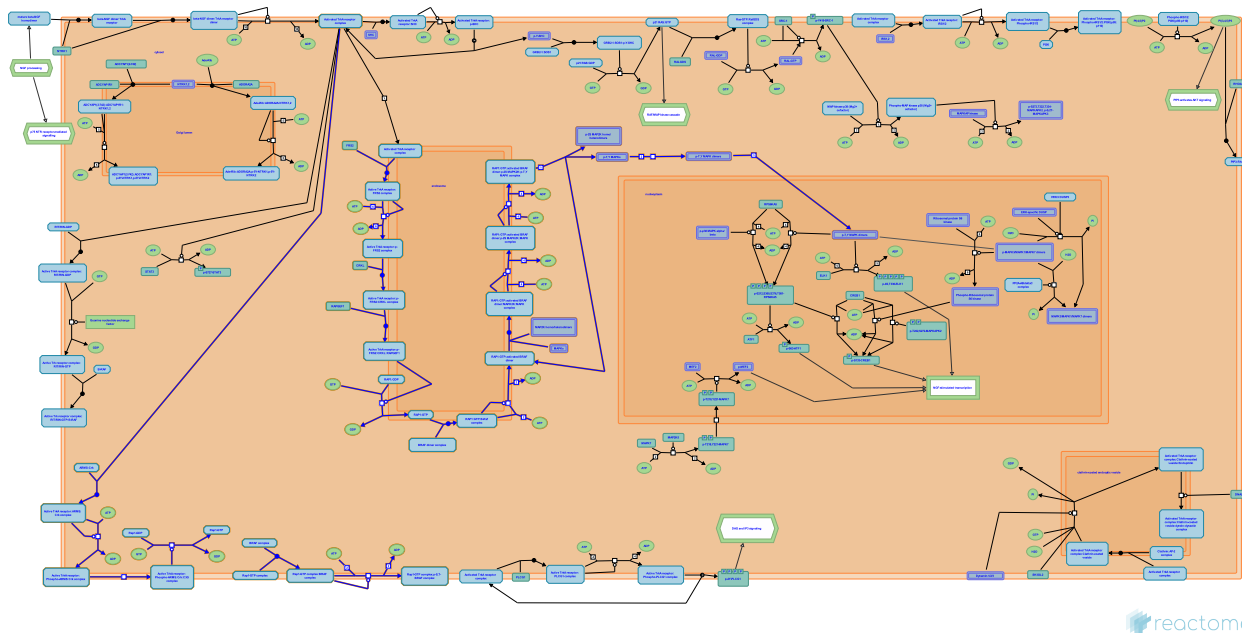


Prolonged ERK activation events



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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](https://reactome.org/about/reactome-textbook/).

19/05/2024

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. [↗](#)

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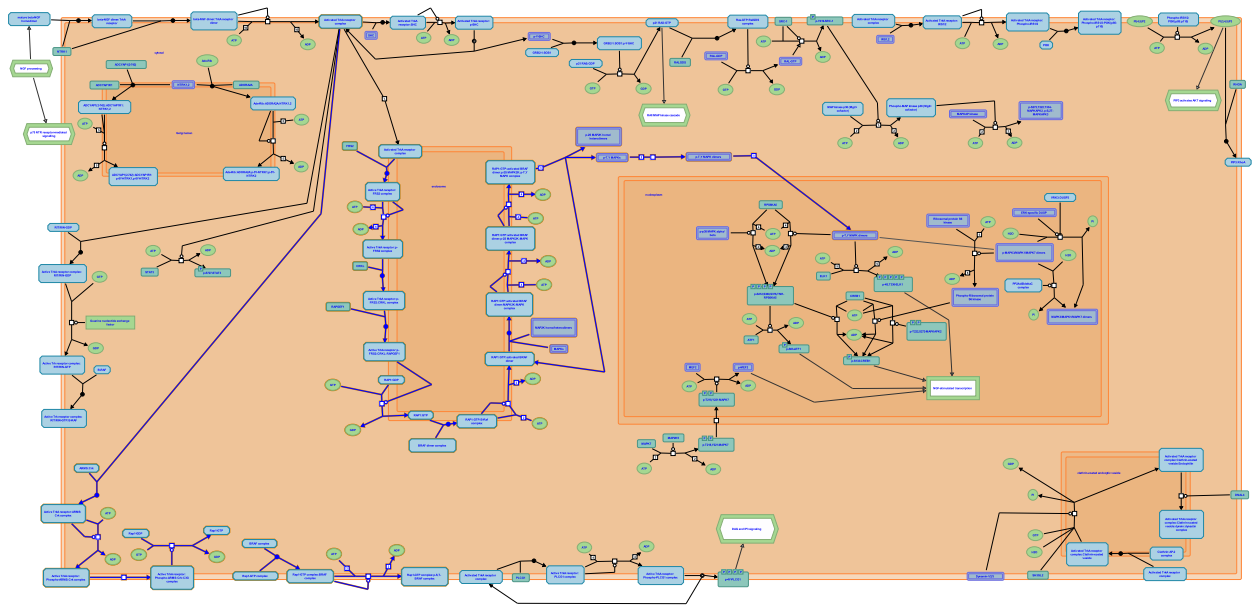
Fabregat, A., Korninger, F., Viteri, G., Sidiropoulos, K., Marin-Garcia, P., Ping, P. et al. (2018). Reactome graph database: Efficient access to complex pathway data. *PLoS computational biology*, 14, e1005968. [↗](#)

Reactome database release: 88

This document contains 3 pathways ([see Table of Contents](#))

Prolonged ERK activation events ↗

Stable identifier: R-HSA-169893



After NGF binding, activated Trk receptors provide multiple docking sites for adaptor proteins and enzymes. Two docking proteins, the Ankyrin-Rich Membrane Spanning protein (ARMS/Kidins220) and Fibroblast growth factor receptor substrate 2 (Frs2), target signaling molecules in response to NGF stimulation and link receptor activation with the MAP kinase (also called the Extracellular signal-Regulated Kinase cascade, ERK) cascade, an essential process for growth factor-induced cell proliferation and differentiation.

A feature of NGF signaling is the sustained activation of the MAPK cascade. This is achieved by the small G protein, Rap1 which binds to and activates B-Raf, an activator of the MAPK cascade. Rap1 is a member of the Ras family of G proteins and like all G proteins, Rap1 is in an inactive state when bound to GDP and is active when bound to GTP. A specific GEF (guanine nucleotide exchange factor) called C3G can activate Rap1 by exchanging GDP for GTP.

Literature references

Stork, PJ. (2003). Does Rap1 deserve a bad Rap?. *Trends Biochem Sci*, 28, 267-75. ↗

Miller, FD., Kaplan, DR. (1997). Signal transduction by the neurotrophin receptors. *Curr Opin Cell Biol*, 9, 213-21. ↗

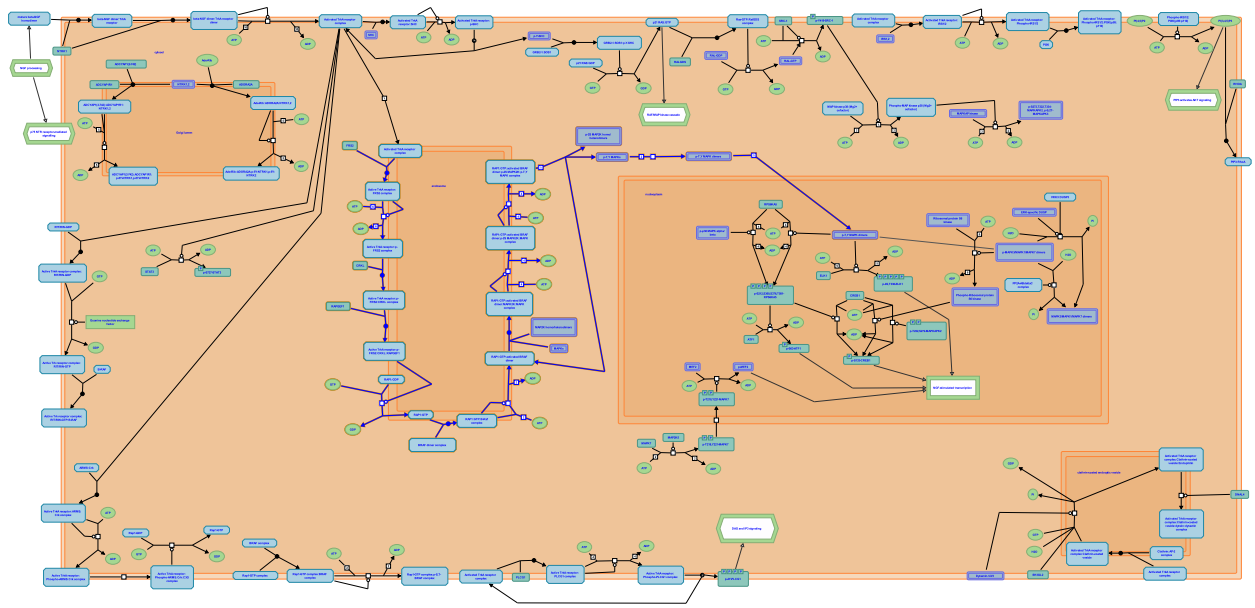
Editions

2006-10-10	Edited	Jassal, B.
2006-10-10	Authored	Annibali, D., Nasi, S.
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Frs2-mediated activation

Location: Prolonged ERK activation events

Stable identifier: R-HSA-170968



reactome

The adaptor protein Frs2 (Fibroblast growth factor receptor substrate 2) can mediate the prolonged activation of the MAPK (ERK) cascade.

Literature references

Miller, FD., Kaplan, DR. (1997). Signal transduction by the neurotrophin receptors. *Curr Opin Cell Biol*, 9, 213-21. ↗

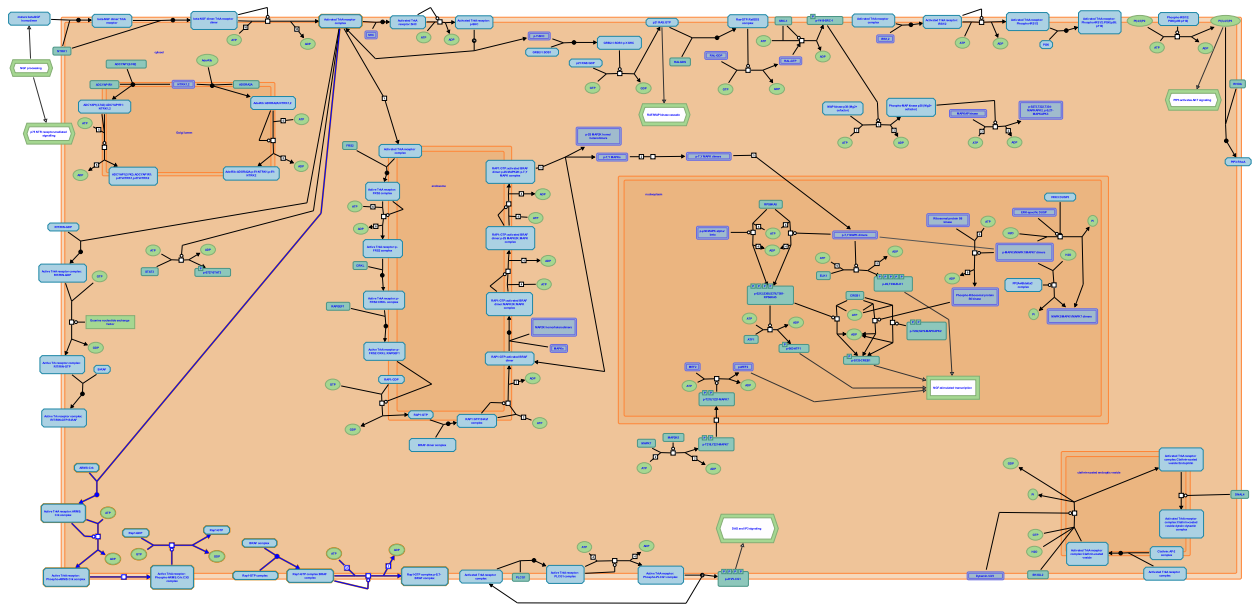
Editions

2006-10-10	Edited	Jassal, B.
2006-10-10	Authored	Annibali, D., Nasi, S.
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ARMS-mediated activation ↗

Location: Prolonged ERK activation events

Stable identifier: R-HSA-170984



reactome

ARMS (Ankyrin-Rich Membrane Spanning/Kidins 220) is a 220kD tetraspanning adaptor protein which becomes rapidly tyrosine phosphorylated by active Trk receptors. ARMS is another adaptor protein which is involved in the activation of Rap1 and the subsequent prolonged activation of the MAPK cascade.

Literature references

Miller, FD., Kaplan, DR. (1997). Signal transduction by the neurotrophin receptors. *Curr Opin Cell Biol*, 9, 213-21. ↗

Editions

2006-10-10	Edited	Jassal, B.
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