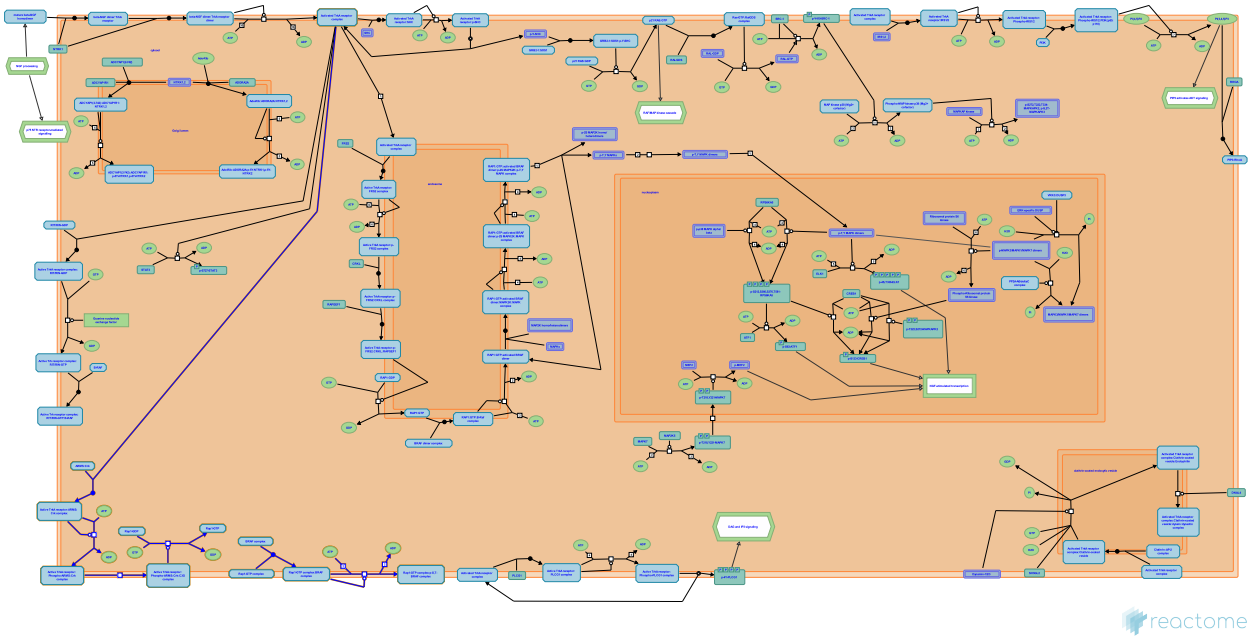
ARMS-mediated activation



Annibali, D., Greene, LA., Jassal, B., Nasi, S.

European Bioinformatics Institute, New York University Langone Medical Center, Ontario Institute for Cancer Research, Oregon Health and Science University.

14/10/2024

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. ↗

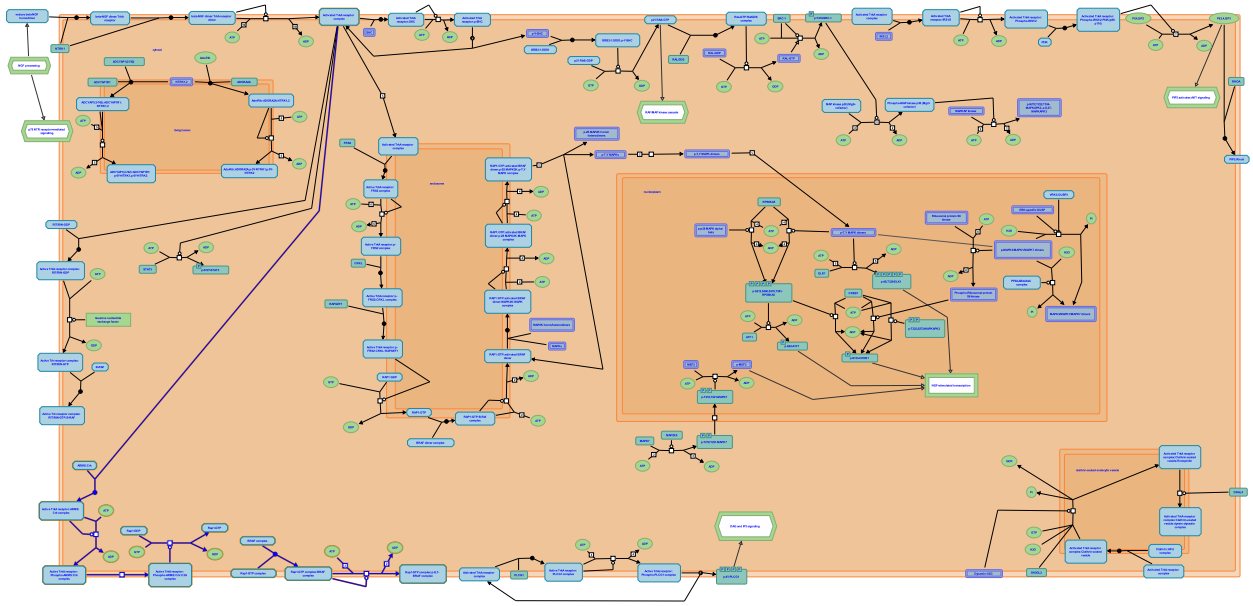
Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

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. ↗

ARMS-mediated activation ↗

Stable identifier: R-HSA-170984



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

ARMS:Crk complex binds to active TrkA receptor ↗

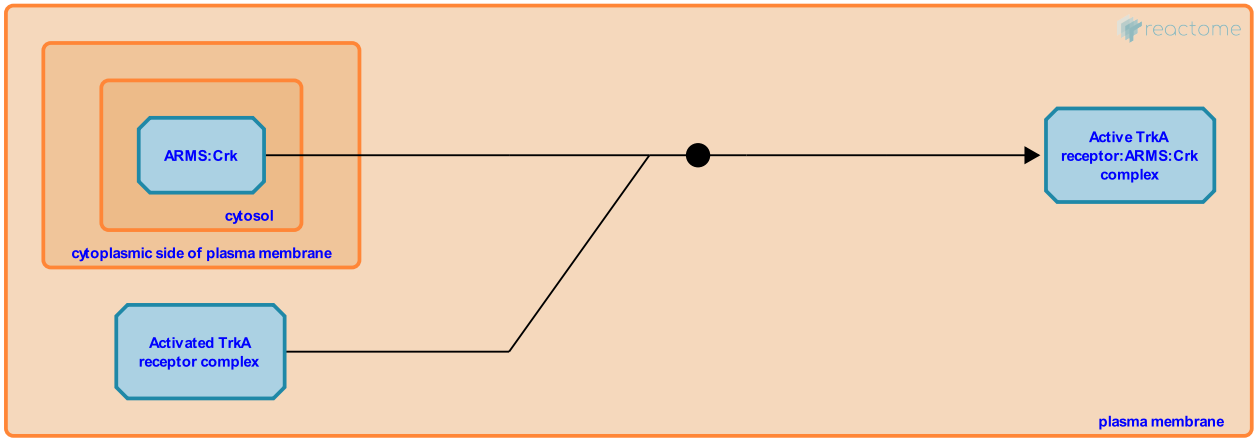
Location: ARMS-mediated activation

Stable identifier: R-HSA-169891

Type: binding

Compartments: plasma membrane, extracellular region, cytosol

Inferred from: ARMS:Crk binds to active Trk receptor (Rattus norvegicus)



Ankyrin-Rich Membrane Spanning protein (ARMS or Kidins220) is a specific target of Trk receptor tyrosine phosphorylation. The ARMS/Kidins220:Crk complex is an upstream component of the C3G-Rap1-MAP kinase cascade and is SH3 dependent.

Followed by: ARMS is phosphorylated by active TrkA receptor

Editions

2006-10-10	Edited	Jassal, B.
2006-10-10	Authored	Annibali, D., Nasi, S.
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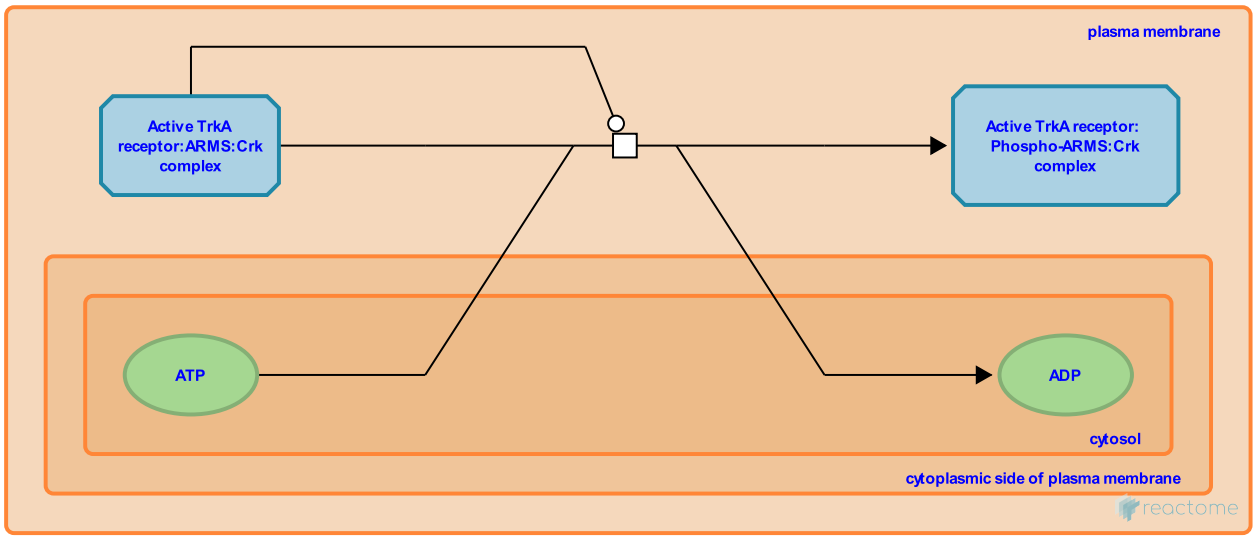
ARMS is phosphorylated by active TrkA receptor ↗

Location: ARMS-mediated activation

Stable identifier: R-HSA-169905

Type: transition

Compartments: plasma membrane, cytosol



Phosphorylation of ARMS by Trk receptor (on tyrosine 1096) enables ARMS to recruit Crk via it's SH2 domain and freeing the SH3 domain. The SH3 domain of Crk is then free to bind C3G for MAP kinase activation.

Preceded by: ARMS:Crk complex binds to active TrkA receptor

Followed by: Crk's SH3 domain engages C3G

Literature references

Arevalo, JC., Teng, KK., Pereira, DB., Yano, H., Chao, MV. (2006). Identification of a switch in neurotrophin signaling by selective tyrosine phosphorylation. *J Biol Chem, 281*, 1001-7. ↗

Editions

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

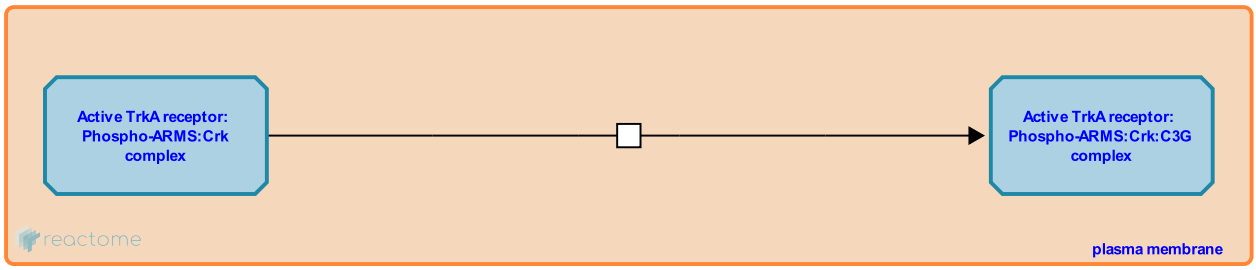
Crk's SH3 domain engages C3G ↗

Location: ARMS-mediated activation

Stable identifier: R-HSA-169895

Type: transition

Compartments: plasma membrane, extracellular region, cytosol



Rap guanine nucleotide exchange factor 1 (RAPGEF1, C3G) is a guanine nucleotide exchange factor for Rap1, which is recruited by Crk adaptor proteins (Knudsen et al. 1994; York, 1998).

Preceded by: ARMS is phosphorylated by active TrkA receptor

Followed by: C3G stimulates nucleotide exchange on Rap1

Literature references

Arevalo, JC., Teng, KK., Pereira, DB., Yano, H., Chao, MV. (2006). Identification of a switch in neurotrophin signaling by selective tyrosine phosphorylation. *J Biol Chem, 281*, 1001-7. ↗

Editions

2006-10-10	Edited	Jassal, B.
2006-10-10	Authored	Annibali, D., Nasi, S.
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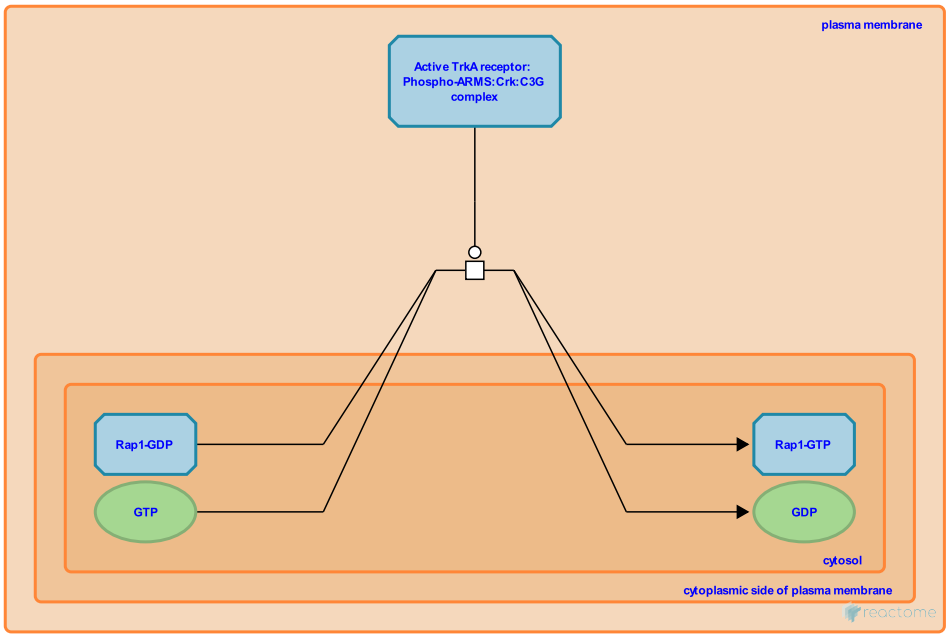
C3G stimulates nucleotide exchange on Rap1 ↗

Location: ARMS-mediated activation

Stable identifier: R-HSA-169904

Type: transition

Compartments: plasma membrane, cytosol



Rap1 is a small G protein, necessary for prolonged ERK activity in PC12 cells. In such cells, NGF triggers a program of neuronal differentiation through the activation of a Rap1:B-RAF:ERK module Rap1 is activated by NGF, but not by epidermal growth factor (EGF), although both growth factors cause transient activation of RAS. Activation of Rap1 by NGF requires internalization of TRKA to intracellular vesicles, mostly endosomes, containing Rap1, B-RAF, MEK and ERKs. Rap1 does not co-localize with RAS. Therefore, the ability of Rap1 to bind RAF-1 without activating it might sequester RAF-1 from RAS. Activation of GEFs that couple to Rap1 as well as RAS might provide a mechanism to limit signals to RAS.

Preceded by: Crk's SH3 domain engages C3G

Followed by: Rap1-GTP complex binds BRAF complex

Literature references

Arevalo, JC., Teng, KK., Pereira, DB., Yano, H., Chao, MV. (2006). Identification of a switch in neurotrophin signaling by selective tyrosine phosphorylation. *J Biol Chem, 281*, 1001-7. ↗

Editions

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

Rap1-GTP complex binds BRAF complex ↗

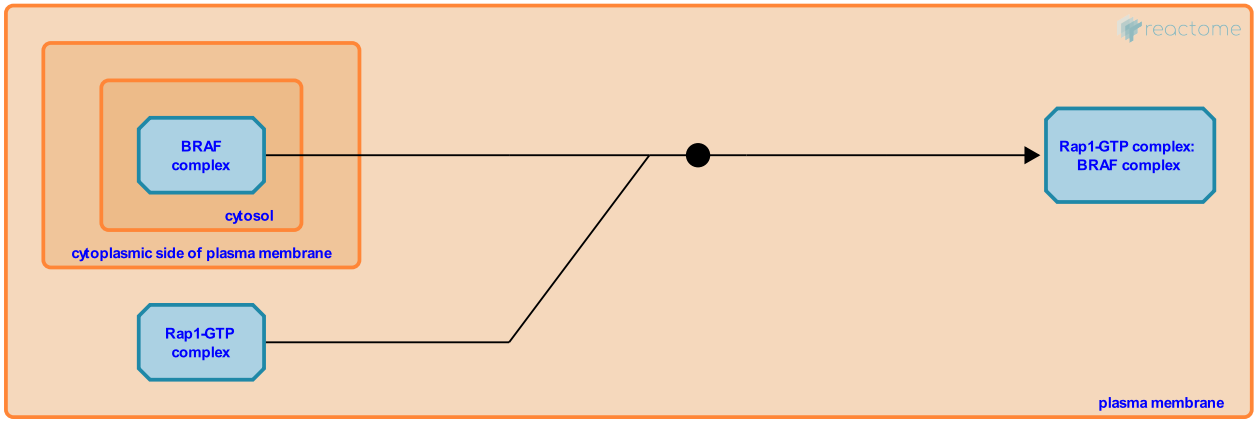
Location: ARMS-mediated activation

Stable identifier: R-HSA-169901

Type: binding

Compartments: plasma membrane, cytosol

Inferred from: Rap1-GTP binds Raf1 (Rattus norvegicus)



Rap1 binds to B-RAF; as a consequence, B-RAF is recruited to endosomes. The binding event of Rap1 to B-RAF is thought to be very similar to the binding of RAS to RAF-1. In neuronal cells that express B-Raf, NGF induced activation of Rap1 promotes a sustained activation of ERKs and is required for the induction of electrical excitability and a subset of neuron-specific genes. As regards morphological differentiation (e. g. neurite outgrowth in PC12 cells), things are more complex. The transient activation of ERKs via RAS is not sufficient for neurite outgrowth in the absence of additional signals. On the contrary, constitutive activation of Rap1 is sufficient to trigger neurite outgrowth, but it is not necessary for this response.
Clearly, morphological differentiation of PC12 cells involves the activation of multiple pathways by NGF. Rap1 activates B-Raf, but inhibits RAF-1. Consequently, Rap1 could have two opposing functions: to limit ERK activation in B-RAF-negative cells and to increase ERK activation in B-Raf-positive cells.

Preceded by: C3G stimulates nucleotide exchange on Rap1

Followed by: BRAF in Rap1-GTP complex:BRAF complex autophosphorylates

Editions

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

BRAF in Rap1-GTP complex:BRAF complex autophosphorylates ↗

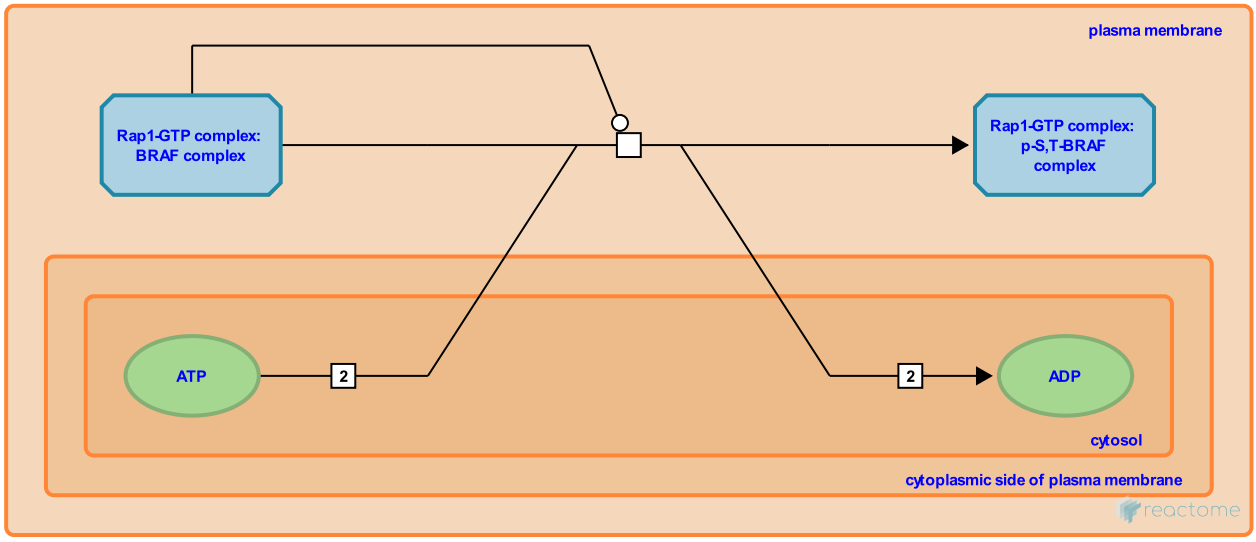
Location: ARMS-mediated activation

Stable identifier: R-HSA-9612980

Type: transition

Compartments: plasma membrane, cytosol

Inferred from: Rap1-GTP phosphorylates Raf1 (Rattus norvegicus)



Rap1 binds to B-RAF; as a consequence, B-RAF is recruited to endosomes. The binding event of Rap1 to B-RAF is thought to be very similar to the binding of RAS to RAF-1. In neuronal cells that express B-Raf, NGF induced activation of Rap1 promotes a sustained activation of ERKs and is required for the induction of electrical excitability and a subset of neuron-specific genes. As regards morphological differentiation (e. g. neurite outgrowth in PC12 cells), things are more complex. The transient activation of ERKs via RAS is not sufficient for neurite outgrowth in the absence of additional signals. On the contrary, constitutive activation of Rap1 is sufficient to trigger neurite outgrowth, but it is not necessary for this response.
Clearly, morphological differentiation of PC12 cells involves the activation of multiple pathways by NGF. Rap1 activates B-Raf, but inhibits RAF-1. Consequently, Rap1 could have two opposing functions: to limit ERK activation in B-RAF-negative cells and to increase ERK activation in B-Raf-positive cells.

Preceded by: Rap1-GTP complex binds BRAF complex

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

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