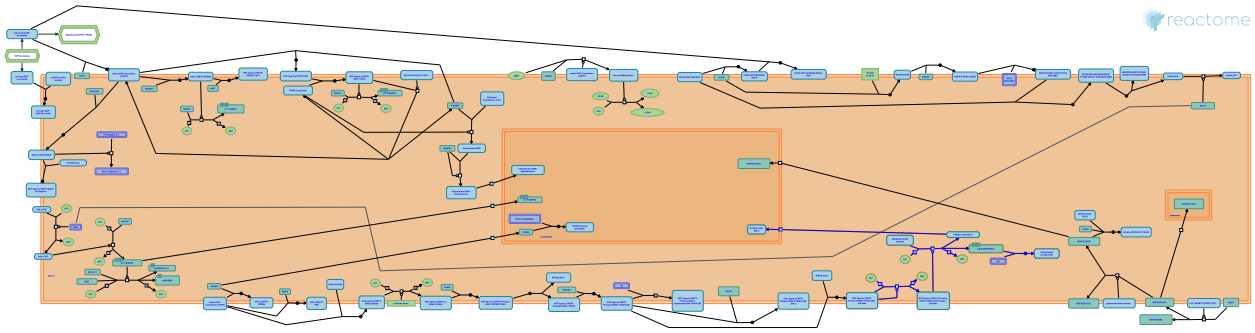
NF-kB is activated and signals survival



Annibali, D., Chao, MV., Friedman, WJ., Jassal, B., Nasi, S.

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

27/04/2024

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. ↗

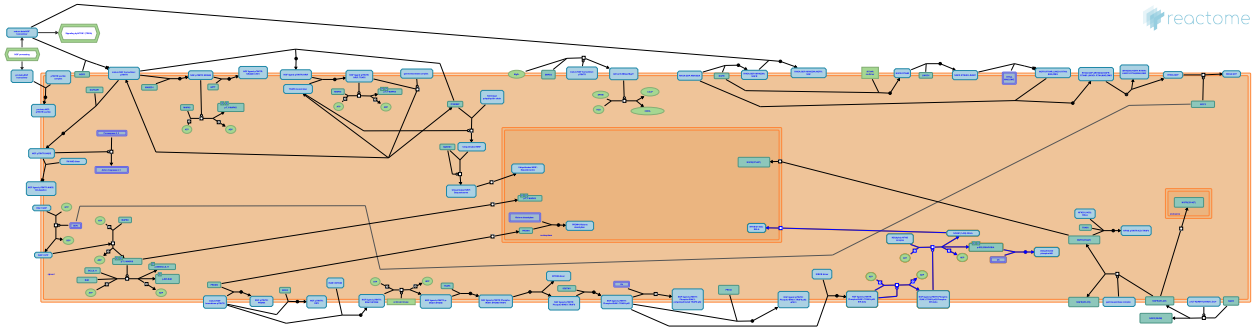
Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

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. ↗

NF-kB is activated and signals survival ↗

Stable identifier: R-HSA-209560



Upon activation in response to NGF, NF-kB moves to the nucleus, where it turns on genes that promote survival, and triggers the expression of HES1/5 to modulate dendritic growth.

Literature references

Mattson, MP. (2005). NF-kappaB in the survival and plasticity of neurons. *Neurochem Res, 30*, 883-93. ↗

Editions

2006-10-10	Authored	Annibali, D., Nasi, S.
2008-05-20	Reviewed	Friedman, WJ.
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2008-05-28	Reviewed	Chao, MV.

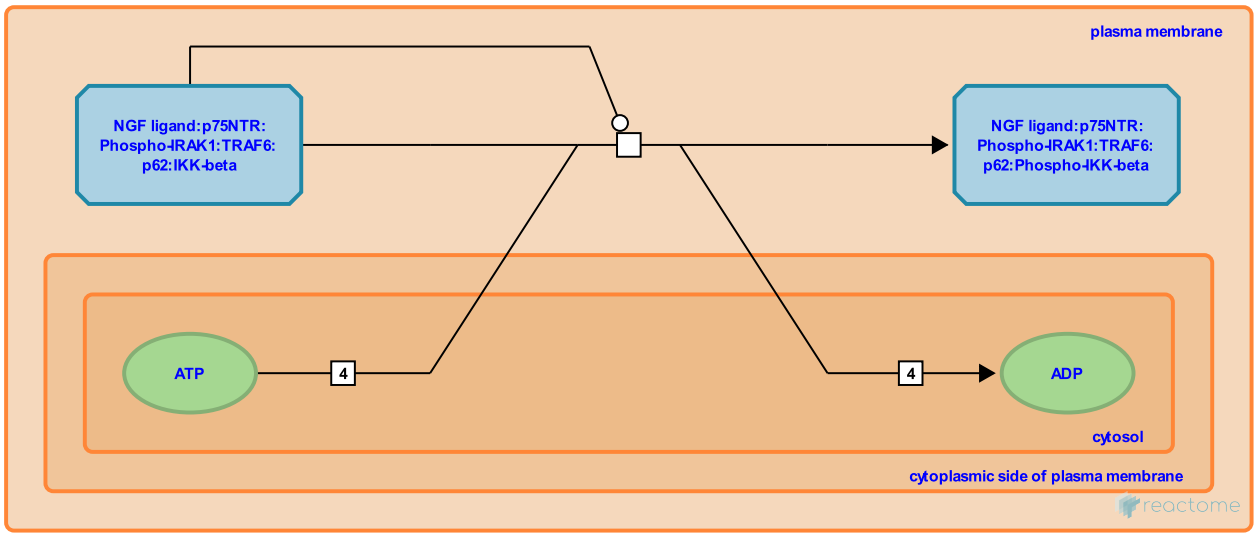
IKKbeta is activated ↗

Location: NF-kB is activated and signals survival

Stable identifier: R-HSA-193703

Type: transition

Compartments: plasma membrane, cytosol



Atypical PKC isoforms phosphorylate the beta subunit of the IKK complex (on Serines 177 and 181) thereby serving as an IKK kinase. TRAF6 and p62 as well appear to have a role in IKK activation. TRAF6 mediates the assembly of K63-linked poly-Ub chains required for IKK activation. The ubiquitin binding property of p62 may also be relevant in regulating IKK activation.

Followed by: IKKbeta phosphorylates IkB causing NF-kB to dissociate

Literature references

Bren, G., Moscat, J., Diaz-Meco, MT., Paya, CV., Lallena, MJ. (1999). Activation of IkappaB kinase beta by protein kinase C isoforms. *Mol Cell Biol, 19*, 2180-8. ↗

Editions

2006-10-10	Authored	Annibali, D., Nasi, S.
2008-05-20	Reviewed	Friedman, WJ.
2008-05-20	Edited	Jassal, B.
2008-05-28	Reviewed	Chao, MV.

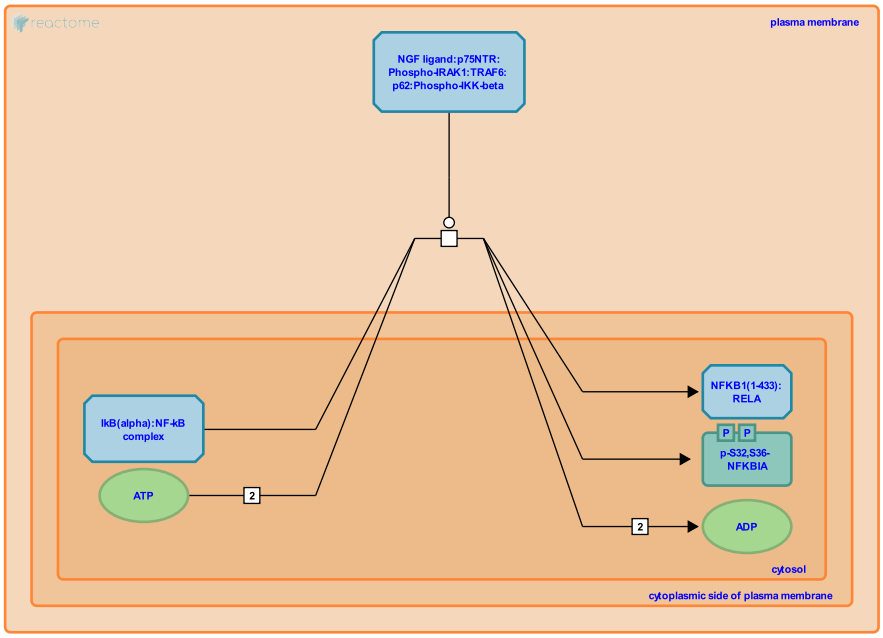
IKKbeta phosphorylates IkB causing NF-kB to dissociate ↗

Location: NF-kB is activated and signals survival

Stable identifier: R-HSA-193705

Type: transition

Compartments: plasma membrane, cytosol



IkB is an inhibitory protein that sequesters NF-kB in the cytoplasm, by masking a nuclear localization signal, located just at the C-terminal end in each of the NF-kB subunits. A key event in NF-kB activation involves phosphorylation of IkB by an IkB kinase (IKK). NGF stimulates the activity of the IkB kinase IKK-beta, and, possibly, IKK-alpha as well. Once IkB is phosphorylated, the IkB:NF-kB complex dissociates.

Preceded by: IKKbeta is activated

Followed by: NF-kB migrates to the nucleus and turns on transcription, IkB is ubiquitinated and degraded

Literature references

Rothwarf, DM., Karin, M., Zandi, E., DiDonato, JA., Hayakawa, M. (1997). A cytokine-responsive IkappaB kinase that activates the transcription factor NF-kappaB. *Nature, 388*, 548-54. ↗

Editions

2006-10-10	Authored	Annibali, D., Nasi, S.
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2008-05-20	Edited	Jassal, B.
2008-05-28	Reviewed	Chao, MV.

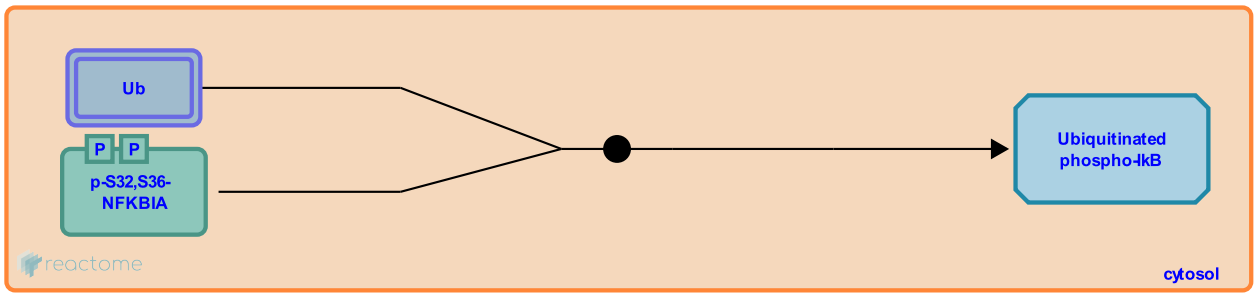
IkB is ubiquitinated and degraded ↗

Location: NF-kB is activated and signals survival

Stable identifier: R-HSA-209536

Type: binding

Compartments: cytosol



Once dissociated from NF-kB, the phosphorylated IkB protein is ubiquitinated at lysines 21 and 22, and degraded by the proteosome (Baldi et al 1996).

Preceded by: IKKbeta phosphorylates IkB causing NF-kB to dissociate

Editions

2006-10-10	Authored	Annibali, D., Nasi, S.
2008-05-20	Reviewed	Friedman, WJ.
2008-05-20	Edited	Jassal, B.
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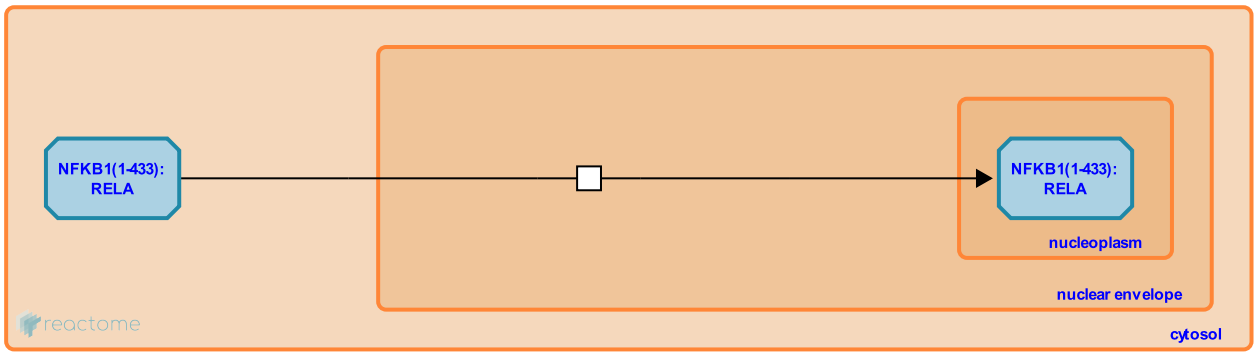
NF-kB migrates to the nucleus and turns on transcription ↗

Location: NF-kB is activated and signals survival

Stable identifier: R-HSA-193691

Type: transition

Compartments: nuclear envelope



Once dissociated from IkB, NF-kB moves to the nucleus. Once in the nucleus, NF-kB binds DNA at promoters of target genes. This entails transcription of several genes including the two HLH transcriptional regulators HES1 and HES5. HES1 and HES5 transcription can also be activated via NOTCH signalling. Increased production of HES1 and HES5 reduces the number of primary dendrites and promotes dendrite elongation.

Preceded by: IKKbeta phosphorylates IkB causing NF-kB to dissociate

Literature references

Arévalo, MA., Grantyn, R., Rodriguez-Tébar, A., Salama-Cohen, P., Meier, J. (2005). NGF controls dendrite development in hippocampal neurons by binding to p75NTR and modulating the cellular targets of Notch. *Mol Biol Cell, 16*, 339-47. ↗

Editions

2006-10-10	Authored	Annibali, D., Nasi, S.
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2008-05-20	Edited	Jassal, B.
2008-05-28	Reviewed	Chao, MV.

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