MAPK1 or MAPK3 phosphorylates NCF1 at Ser345

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03/05/2024

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

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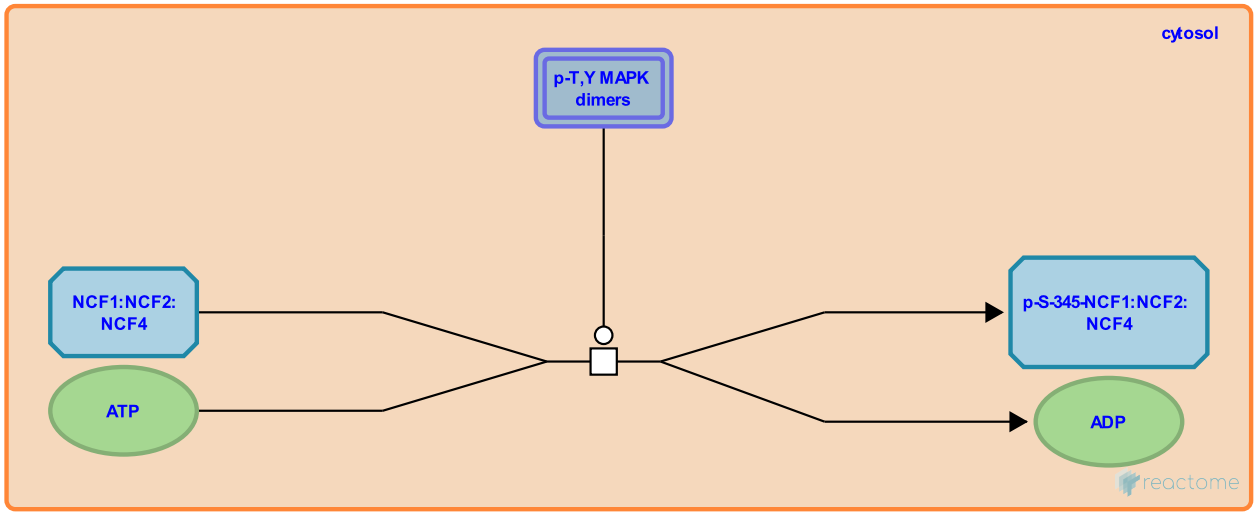
Stable identifier: R-HSA-9626832

Type: transition

Compartments: cytosol



In resting cells, the NADPH oxidase components, NCF1 (p47phox), NCF2 (p67phox), and NCF4 (p40phox) are located in the cytosol where they associate in a trimer complex with a 1:1:1 stoichiometry through specific domains (Groemping Y & Rittinger K 2005; El-Benna J et al. 2005; Park JW et al. 1994; Lapouge K et al. 2002; El-Benna J et al. 2016). However, NCF1 may also exist separately from the trimer (El-Benna J et al. 2016). In the resting state, two SH3 domains of NCF1 (p47phox) bind the auto-inhibitory region (AIR; amino acids 292-340) to keep NCF1 in a closed auto-inhibited state, preventing its binding to p22phox and therefore NOX2 activation (Groemping Y et al. 2003; Yuzawa S et al. 2004; El-Benna J et al. 2016). Priming of neutrophils by several agents such as GM-CSF, TNFα, PAF, LPS and CL097, a TLR7/8 agonist, induces partial phosphorylation of NCF1 (Makni-Maalej K et al. 2015; Dang PM et al. 1999; Dewas C et al. 2003; DeLeo FR et al. 1998). Mass spectrometry analysis of NCF1 identified Ser345 as the phosphorylated site in neutrophils primed by TNFα and GM-CSF, and site-directed mutagenesis of Ser345 and use of a competitive inhibitory peptide containing the Ser345 sequence have demonstrated that this step is critical for the priming of ROS production in human neutrophils (Dang PMC et al. 2006). Further, inhibitors of the MAPK1 and MAPK3 (ERK1/2) pathway abrogated GM-CSF-induced phosphorylation of Ser345 (Dang PMC et al. 2006).

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Editions

2018-10-30	Authored, Edited	Shamovsky, V.
2018-11-07	Reviewed	Nüsse, O.