PKC phosphorylates NCF1

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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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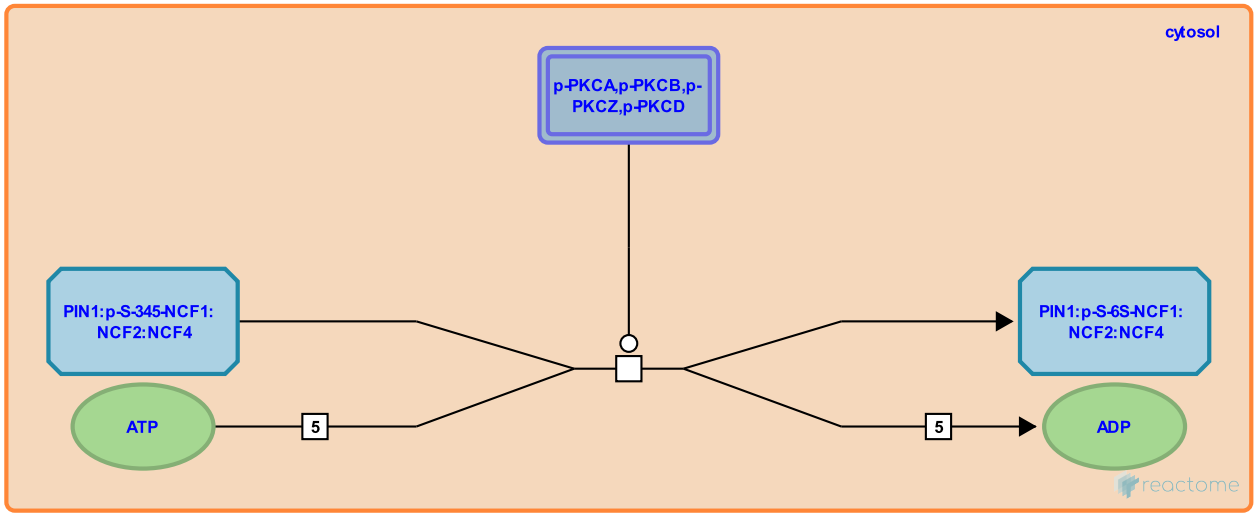
Stable identifier: R-HSA-9626817

Type: transition

Compartments: cytosol



Neutrophil cytosolic factor 1 (NCF1, also known as p47phox) is a component of the NADPH oxidase (NOX2) complex, which consists of six subunits (Groemping Y et al. 2003; El-Benna J et al. 2005). Two of these subunits, p22phox and gp91phox, are integral membrane proteins and form a heterodimeric flavocytochrome that constitutes the catalytic core of the enzyme. The remaining oxidase components reside in the cytosol and include the small GTPase Rac, as well as a complex of NCF4 (p40phox), NCF1, and NCF2 (p67phox) (Groemping Y et al. 2003; El-Benna J et al. 2005). In the resting state, the interaction of NCF1 (p47phox) with p22phox, and thereby translocation and NADPH oxidase activation, is prevented by an auto-inhibited conformation of NCF1 (Groemping Y et al. 2003; Yuzawa S et al. 2004). This is believed to arise from an intramolecular interaction of the SH3 domains with the C-terminal auto-inhibitory region (AIR) (amino acids 292-340) of NCF1 to keep the protein 'locked' (Groemping Y et al. 2003; El Benna J et al. 2016). Priming induced by TNF-α or GM-CSF induces NCF1 phosphorylation on Ser345, activation of the proline isomerase PIN1, which binds to NCF1 to induce conformational changes (Boussetta T et al. 2010). This process facilitates extensive phosphorylation of NCF1 by PKC on other sites and induces full opening of NCF1 (Boussetta T et al. 2010). Phosphorylation studies showed that p47phox is phosphorylated on serines located between Ser303 and Ser379 (El Benna J et al. 1994; 2009). Most of these sites correspond to PKC consensus phosphorylation sites, and PKCα, -β, -δ and -ζ were all shown to phosphorylate NCF1 (p47phox) in vitro or in human neutrophil-like HL-60 cells (Dang PM et al. 2001; Fontayne A et al. 2002; Belambri SA et al. 2018). In vitro studies also showed that phosphorylation of p47phox induced its binding to the proline rich region (PRR) of p22phox and enhanced the binding of NCF2 (p67phox) to gp91phox (Fontayne A et al. 2002; Dang PMC et al. 2002; Boussetta T et al. 2010).

The Reactome event depicts the PKC-mediated phosphorylation of NCF1 on Ser303, Ser304, Ser320, Ser328, Ser348. However, NCF1 becomes phosphorylated by PKCs on multiple sites and the number of sites is not defined.

Literature references

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Editions

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