NEK9 phosphorylates NEK6/NEK7

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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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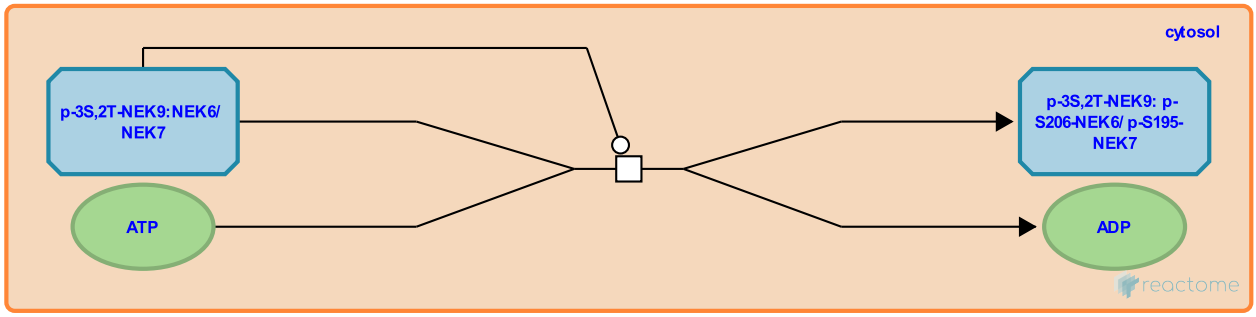
Stable identifier: R-HSA-2984258

Type: transition

Compartments: cytosol



NEK9, activated by CDK1- and PLK1-mediated phosphorylation, phosphorylates NEK6 on serine residue S206, and NEK7 on serine residue S195. S206 and S195 are located in the activation loop of NEK6 and NEK7, respectively. NEK6 activation is dependent on S206 phosphorylation, although phosphorylation at threonine T202 may augment NEK6 kinase activity. NEK7 activity also depends on phosphorylation of S195. NEK9 remains tightly associated with NEK6 (as well as NEK7) after phosphorylation, and may direct NEK6/NEK7 to specific target (Belham et al. 2003). In addition, irrespective of phosphorylation, binding of the non-catalytic C-terminus of NEK9 to NEK7 (as well as NEK6), relieves autoinhibitory conformation of NEK7/NEK6. The autoinhibitory conformation of NEK7 depends on the formation of a hydrogen bond between tyrosine Y97 (tyrosine Y108 in NEK6) and leucine L180. This Y97-involving hydrogen bond prevents the formation of a salt bridge between lysine K63 and glutamate E82 of NEK7, which is essential for catalysis. Binding of NEK9 is thought to disrupt the hydrogen bond between Y97 and L180 of NEK7 (Y108 and L191 of NEK6) and allow NEK7/NEK6 to achieve active conformation (Richards et al. 2009).

Literature references

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Editions

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