RAC1 and CDC42 activate PAK1

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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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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. ↗

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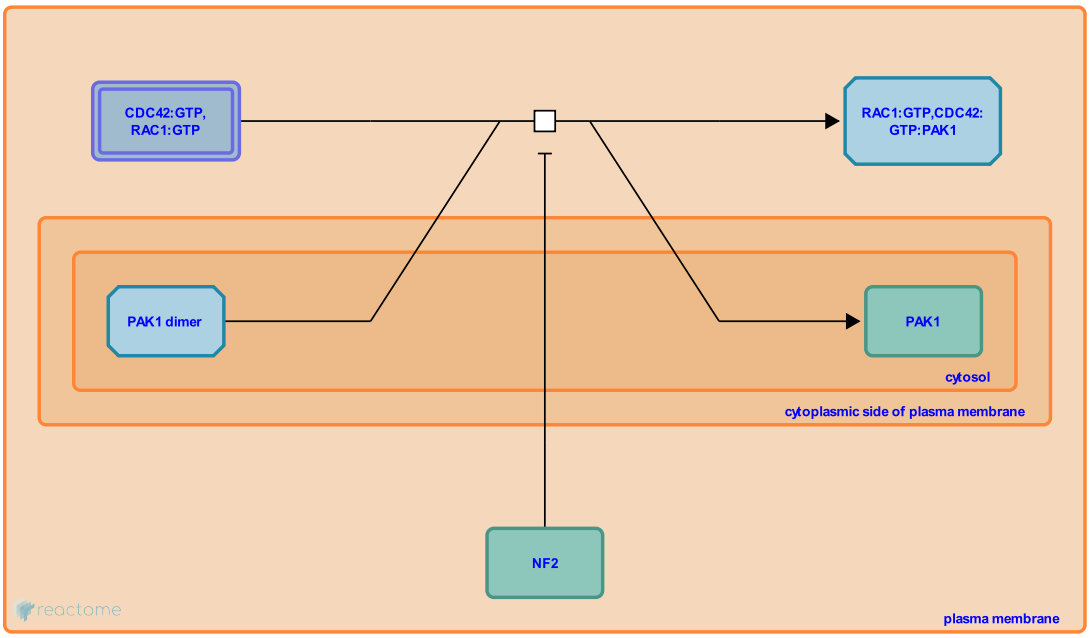
Stable identifier: R-HSA-2029456

Type: transition

Compartments: cytosol, plasma membrane



PAK1, a downstream effector of CDC42 and RAC1, is found localized in phagosomes. Upon activation, PAK1 phosphorylates LIMK, which directly phosphorylates and inactivates cofilin, a protein that mediates depolymerization of actin filaments. Thus, RAC and CDC42 coordinate actin dynamics by inducing actin polymerization via ARP2/3 on one hand, and inhibiting actin depolyerization via LIMK and cofilin on the other (Garcia-Garcia & Rosales 2002).
PAK1 exists as homodimer in a trans-inhibited conformation. The kinase inhibitory (KI) domain of one PAK1 molecule binds to the C-terminal catalytic domain of the other and inhibits catalytic activity. GTPases RAC1/CDC42 bind the GBD domain of PAK1 thereby altering the conformation of the KI domain, relieving inhibition of its catalytic domain, and allowing PAK1 autophosphorylation that is required for full kinase activity (Parrini et al. 2002, Zhao & Manser 2005).

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Editions

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