PKC-delta phosphorylates CARD9

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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

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. ↗

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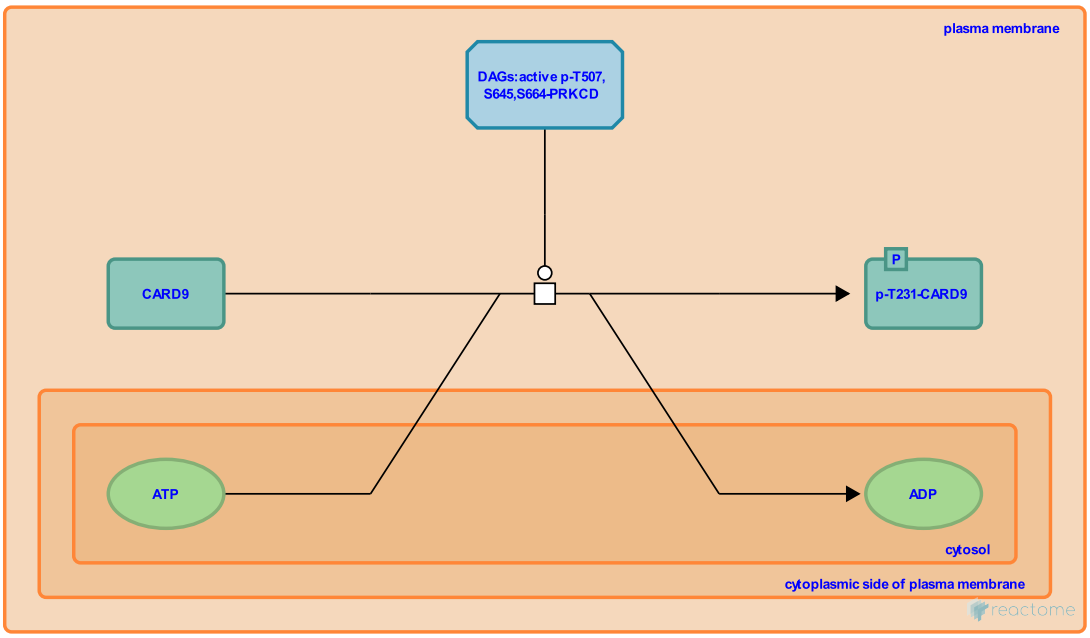
Stable identifier: R-HSA-5607740

Type: transition

Compartments: plasma membrane, cytosol



Activation of NF-kB signaling is a critical event downstream of CLEC7A (Dectin-1), CLEC6A (Dectin-2) (Bi et al. 2010) and CLEC4E (Mincle) (Yamasaki et al. 2008), requiring the adapter protein Caspase recruitment domain (CARD)-containing protein 9 (CARD9) in dendritic cells and in macrophages (Gross et al. 2006, Hara et al. 2007). CARD9 is analogous to CARD-containing MAGUK protein 1 (CARMA1), which mediates T-cell receptor (TCR) activation of NF-kB in lymphocytes. CARD9 is downstream of SYK and becomes phosphorylated by PRKCD (Protein kinase C-delta) phosphorylates CARD9 on Thr-231 (T231), which is required for the signal-induced association of CARD9 with B-cell lymphoma 10 (BCL10) and Mucosa-associated lymphoid tissue 1 (MALT1) and the subsequent recruitment of MAP3K transforming growth factor beta activated kinase 1 (TAK1), leading to activation of the NF-kB pathway (Strasser et al. 2012). A homozygous loss-of-function mutation in human CARD9 results in a premature termination codon (Gln295*). Patients with this mutation are highly susceptible to fungal infections (Glocker et al. 2009).

Literature references

Baier, G., Rojowska, A., Ruland, J., Leitges, M., Neumann, K., Urlaub, H. et al. (2012). Syk kinase-coupled C-type lectin receptors engage protein kinase C-? to elicit Card9 adaptor-mediated innate immunity. *Immunity, 36*, 32-42. ↗

Editions

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