Calmodulin binds CAMK4

Castagnoli, L., Hansen, KB., Jassal, B., Le Novere, N., Orlic-Milacic, M., Yi, F.

European Bioinformatics Institute, New York University Langone Medical Center, Ontario Institute for Cancer Research, Oregon Health and Science University.

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

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. ↗

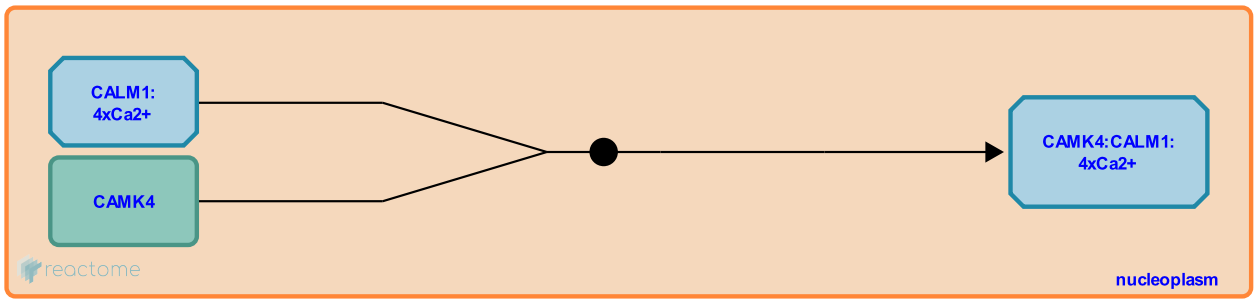
Calmodulin binds CAMK4 ↗

Stable identifier: R-HSA-111913

Type: binding

Compartments: nucleoplasm

Inferred from: Calmodulin binds CaMK IV (Rattus norvegicus)



CaMKIV (CAMK4) becomes fully activated after a three-step mechanism. In the first step, upon a transient increase in intracellular calcium, calcium-bound calmodulin (Ca2+/CaM) binds to its autoregulatory domain, which relieves intersteric inhibition (Chatila et al. 1996, Tokumitsu et al. 2004). In the second step, an activating protein kinase, calcium/calmodulin-dependent protein kinase kinase (CaMKK), binds to the Ca2+/CaM:CaMKIV complex and phosphorylates CaMKIV on a threonine residue in the activation loop (Chatila et al. 1996, Anderson et al. 1998, Tokumitsu et al. 2004). In the third step, CaMKK-phosphorylated CAMK4 autophosphorylates on two serine residues at the N-terminus (Chatila et al. 1996). After full activation by the three-step mechanism mentioned above, the activity of CaMKIV becomes autonomous and no longer requires bound Ca2+/CaM. This activity is required for CaMKIV-mediated transcriptional regulation. The CaMKIV-associated PP2A then dephosphorylates CaMKIV, thereby terminating autonomous activity and CaMKIV-mediated gene transcription.

Editions

2004-03-31	Authored	Jassal, B., Le Novere, N.
2008-11-06	Reviewed	Castagnoli, L.
2008-11-06	Edited	Jassal, B.
2018-11-02	Reviewed	Hansen, KB., Yi, F.
2018-11-07	Edited	Orlic-Milacic, M.