Activation of conventional Protein Kinase C

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

06/10/2022

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. ↗

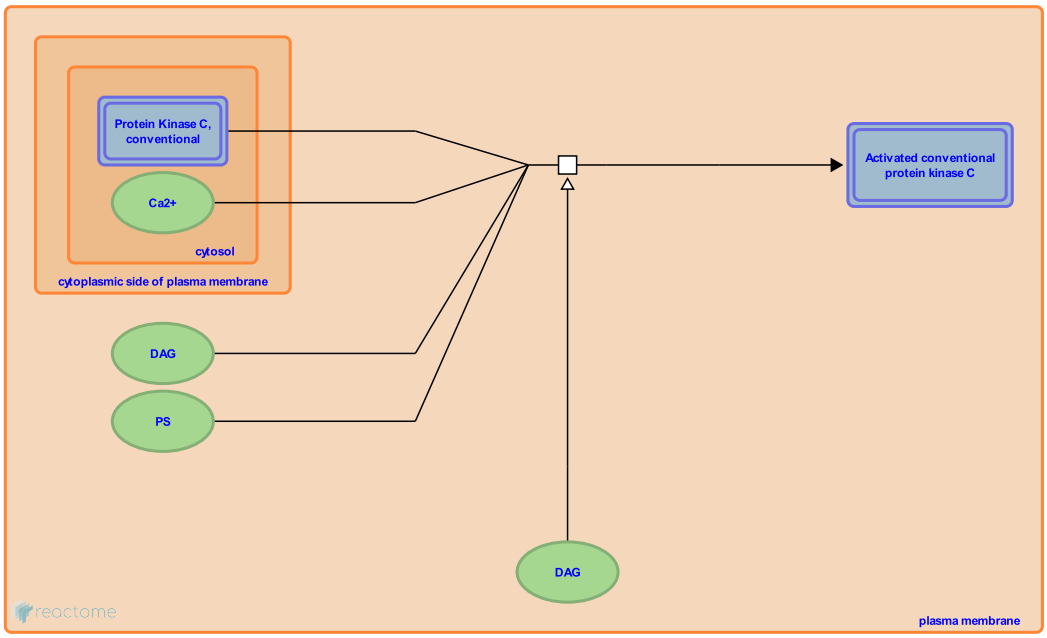
Fabregat, A., Korninger, F., Viteri, G., Sidiropoulos, K., Marin-Garcia, P., Ping, P. et al. (2018). Reactome graph database: Efficient access to complex pathway data. *PLoS computational biology, 14*, e1005968. ↗

Activation of conventional Protein Kinase C ↗

Stable identifier: R-HSA-114553

Type: transition

Compartments: cytosol, plasma membrane



Protein Kinase C (PKC) is positively regulated by events that increase the plasma membrane concentration of diacylglycerol (DAG). Activation of PKC requires the coordinated binding of two membrane-targeting domains. The C1 domain binds diacylglycerol, the C2 domain binds phosphatidylserine. Each can bind the membrane independently, but with insufficient affinity for membrane recruitment and activation.

The conventional Protein Kinase C (cPKC) isoforms have two membrane-targetting domains, a C1 domain which binds to the membrane lipid diacylglycerol (DAG) and a C2 domain which binds membrane phospholipids such as phosphatidylserine, in a calcium-dependent manner. Association of both domains with the plasma membrane produces a conformational change that releases an autoinhibitory pseudosubstrate segment from the substrate-binding cavity, allowing substrate binding and downstream signaling.

Literature references

Meyer, T., Oancea, E. (1998). Protein kinase C as a molecular machine for decoding calcium and diacylglycerol signals. *Cell, 95*, 307-18. ↗