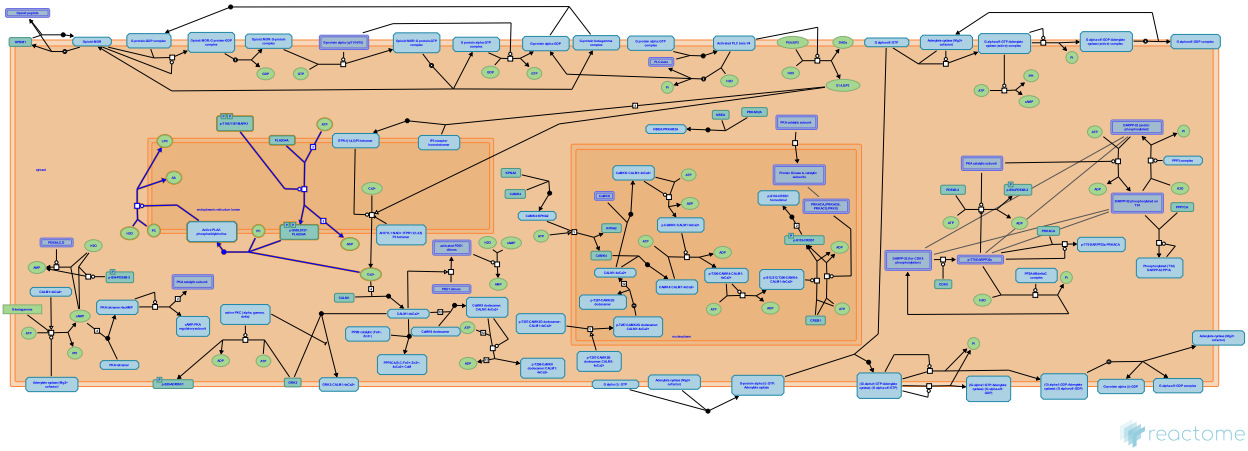
phospho-PLA2 pathway



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This is just an excerpt of a full-length report for this pathway. To access the complete report, please download it at the Reactome Textbook.

04/05/2024

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. ↗

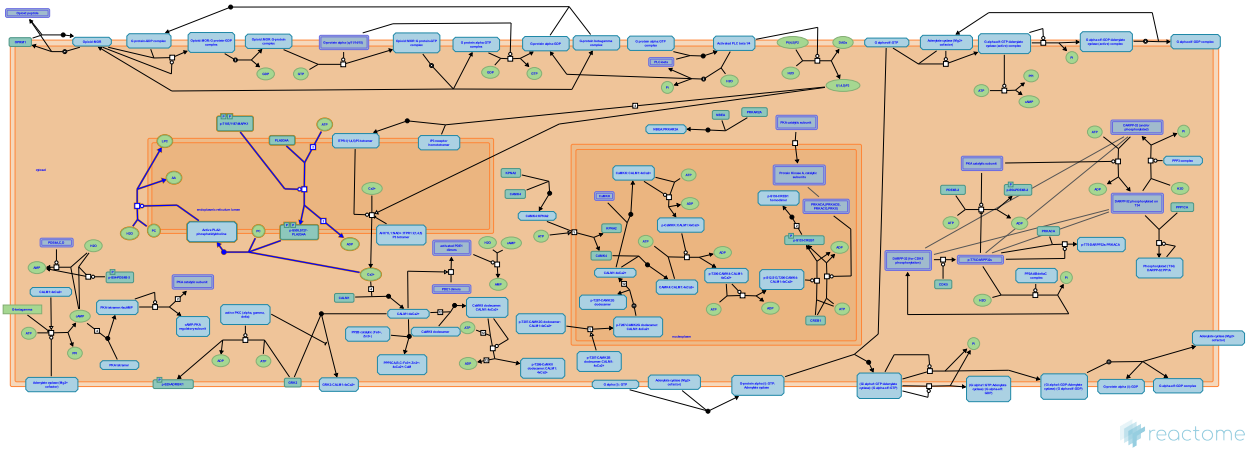
Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

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. ↗

phospho-PLA2 pathway ↗

Stable identifier: R-HSA-111995

Compartments: endoplasmic reticulum membrane, endoplasmic reticulum lumen, cytosol



Phospholipase A2 (PLA2) enzymes hydrolyze arachidonic acid (AA) from the sn-2 position of phospholipids. AA is a precursor of eicosanoids, lipid mediators involved in inflammtory responses. PLA2 enzymes function as regulators of phospholipid acyl turnover, either as housekeepers for membrane repair or for the production of imflammatory lipid mediators. There are diverse forms of PLA2 enyzmes including secretory (sPLA2), calcium-independent and cytosolic (cPLA2). The cPLA2 form which mediates arachidonic acid release is annotated here.

Literature references

Leslie, CC. (1997). Properties and regulation of cytosolic phospholipase A2. *J Biol Chem, 272*, 16709-12. ↗

Editions

2004-03-31	Authored	Jassal, B., Le Novere, N.
2008-11-06	Reviewed	Castagnoli, L.
2008-11-06	Edited	Jassal, B.

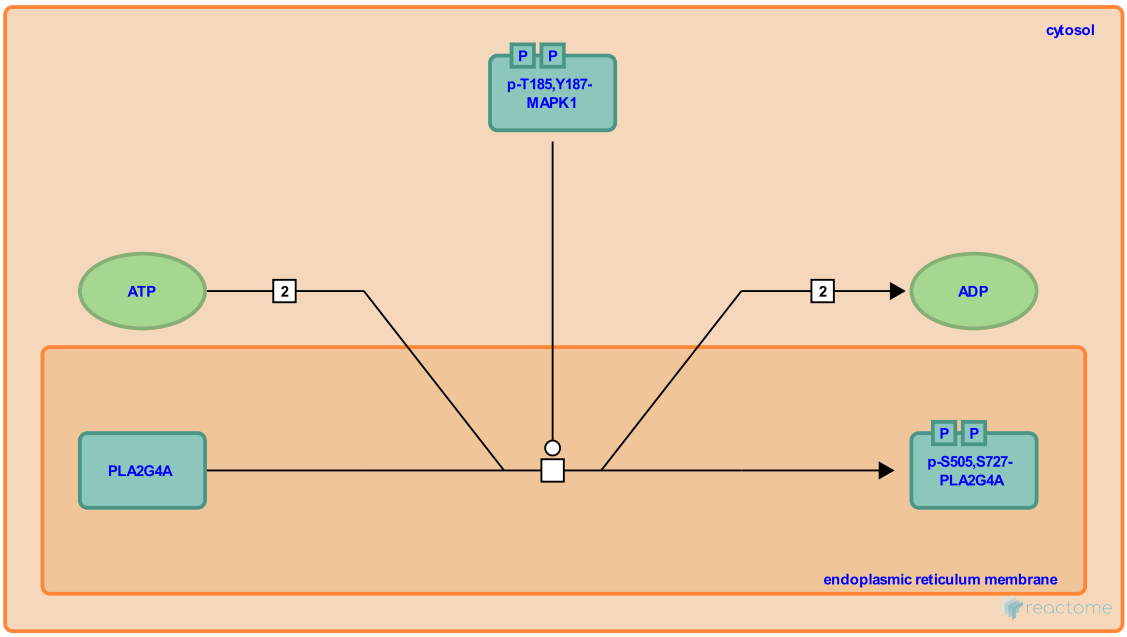
Phosphorylation of cPLA2 by ERK-2 ↗

Location: phospho-PLA2 pathway

Stable identifier: R-HSA-111898

Type: transition

Compartments: endoplasmic reticulum membrane, cytosol



ERK2 phosphorylates cPLA2, increasing enzymatic activity. The site of cPLA2 phosphorylation by ERK2 is Ser-505, the major site of cPLA2 phosphorylation observed in phorbol ester-treated cells.

Followed by: Phospho-cPLA2 translocates to membranes when intracellular calcium levels increase

Literature references

Davis, RJ., Knopf, JL., Seth, A., Wartmann, M., Lin, AY., Lin, LL. (1993). cPLA2 is phosphorylated and activated by MAP kinase. *Cell, 72*, 269-78. ↗

Editions

2004-03-31	Authored	Jassal, B., Le Novere, N.
2008-11-06	Reviewed	Castagnoli, L.
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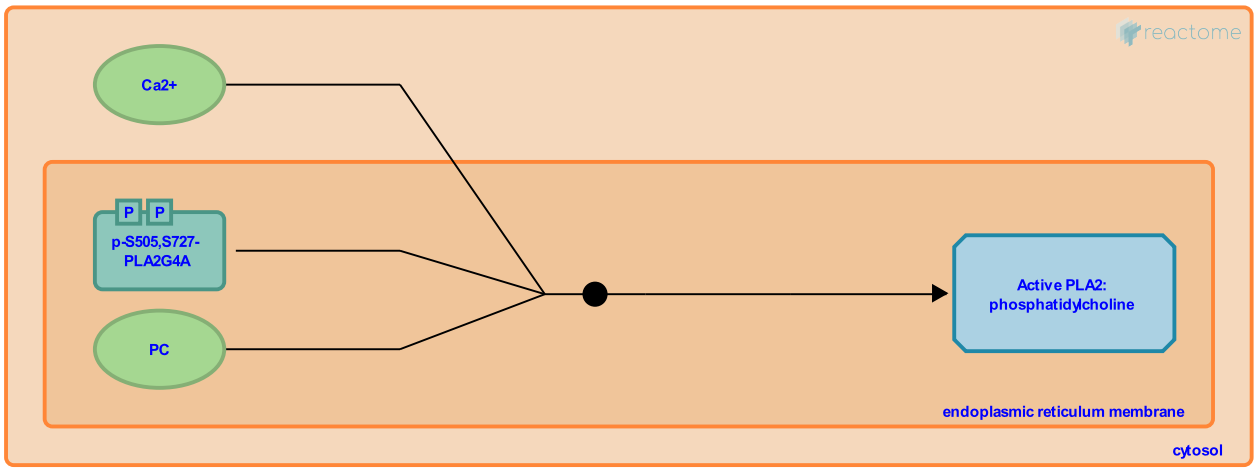
Phospho-cPLA2 translocates to membranes when intracellular calcium levels increase ↗

Location: phospho-PLA2 pathway

Stable identifier: R-HSA-111881

Type: binding

Compartments: endoplasmic reticulum membrane, cytosol



The 85kDa cytosolic phospholipase A2 (cPLA2 - PLA2G4A) is involved in cell signalling processes and inflammatory response and is regulated by phosphorylation and calcium concentrations. cPLA2 is phosphorylated at Ser727 and by a MAPK at Ser505. When phosphorylation is coupled with an influx of calcium ions, PLA2 becomes stimulated and translocates to the membrane where it releases arachidonic acid (AA) from membrane phospholipids. Calcium does not itself activate cPLA2. cPLA2 contains an N-terminal calcium-dependent phospholipid binding domain (CaLB) which shares homology with C2 domains (plays roles in signal transduction and membrane trafficking) and binds it to the membrane. Arachidonic acid is both a signalling molecule and the precursor for other signalling molecules termed eicosanoids (e.g., prostaglandins, leukotrienes and platelet-activating factor). A strict regulation of the activity of phospholipase enzyme is essential.

Preceded by: Phosphorylation of cPLA2 by ERK-2

Followed by: Hydrolysis of phosphatidylcholine

Literature references

Ramesha, CS., Kriz, RW., Knopf, JL., Lin, AY., Lin, LL., Clark, JD. et al. (1991). A novel arachidonic acid-selective cytosolic PLA2 contains a Ca(2+)-dependent translocation domain with homology to PKC and GAP. *Cell, 65*, 1043-51. ↗

Dudler, T., Bartoli, F., Gelb, MH., Watson, SP., Kramer, RM., Apitz-Castro, R. et al. (1998). Identification of the phosphorylation sites of cytosolic phospholipase A2 in agonist-stimulated human platelets and HeLa cells. *J Biol Chem , 273*, 4449-58. ↗

Spencer, DM., Evans, JH., Zweifach, A., Leslie, CC. (2001). Intracellular calcium signals regulating cytosolic phospholipase A2 translocation to internal membranes. *J Biol Chem, 276*, 30150-60. ↗

Editions

2004-03-31	Authored	Jassal, B., Le Novere, N.
2008-11-06	Reviewed	Castagnoli, L.
2008-11-06	Edited	Jassal, B.

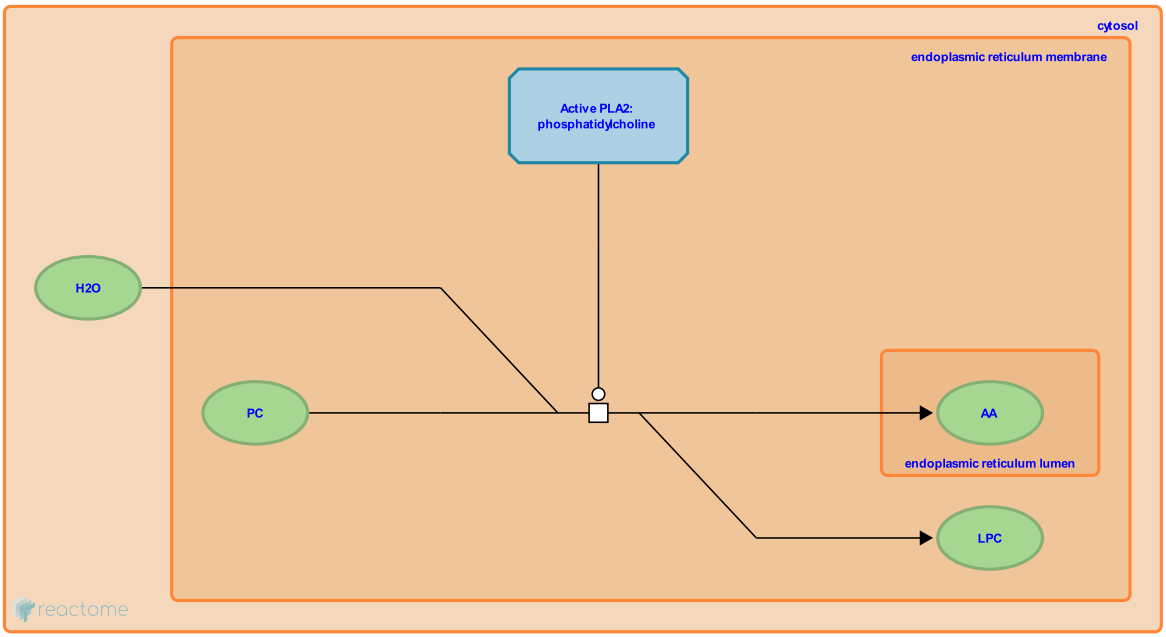
Hydrolysis of phosphatidylcholine ↗

Location: phospho-PLA2 pathway

Stable identifier: R-HSA-111883

Type: transition

Compartments: endoplasmic reticulum membrane, endoplasmic reticulum lumen, cytosol



Once bound to the membrane, cPLA2 hydrolyzes phosphatidylcholine to produce arachidonic acid (AA), a precursor to inflammatory mediators. While several phospholipases can catalyze this reaction in cells overexpressing the enzymes, PLA2G4A is the major enzyme that catalyzes this reaction in vivo (Reed et al. 2011). At the same time, possible physiological roles have been described for soluble phospholipases (sPLA) in the mobilization of arachidonic acid in some cell types or under some physiological conditions (Murakami et al. 2011). Here, the major role of PLA2G4A has been annotated.

Preceded by: Phospho-cPLA2 translocates to membranes when intracellular calcium levels increase

Literature references

Taketomi, Y., Yamamoto, K., Sato, H., Murakami, M. (2011). Secreted phospholipase A2 revisited. *J. Biochem., 150*, 233-55. ↗

Gelb, MH., Aloulou, A., Adler, D., Leslie, CC., Ghomashchi, F., Boutaud, O. et al. (2011). Functional characterization of mutations in inherited human cPLA? deficiency. *Biochemistry, 50*, 1731-8. ↗

Editions

2004-03-31	Authored	Jassal, B., Le Novere, N.
2008-11-06	Edited	Jassal, B.
2012-11-10	Reviewed	Rush, MG.

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