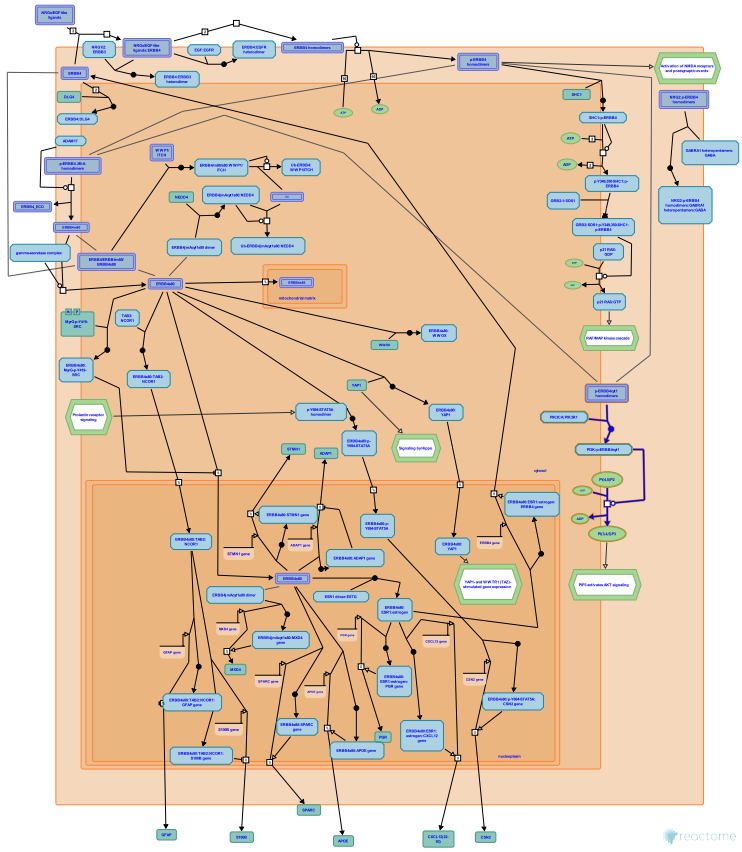
PI3K events in ERBB4 signaling



Earp HS, 3rd., Harris, RC., Matthews, L., Misior, AM., Orlic-Milacic, M., Stern, DF., Zeng, F.

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06/05/2024

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. ↗

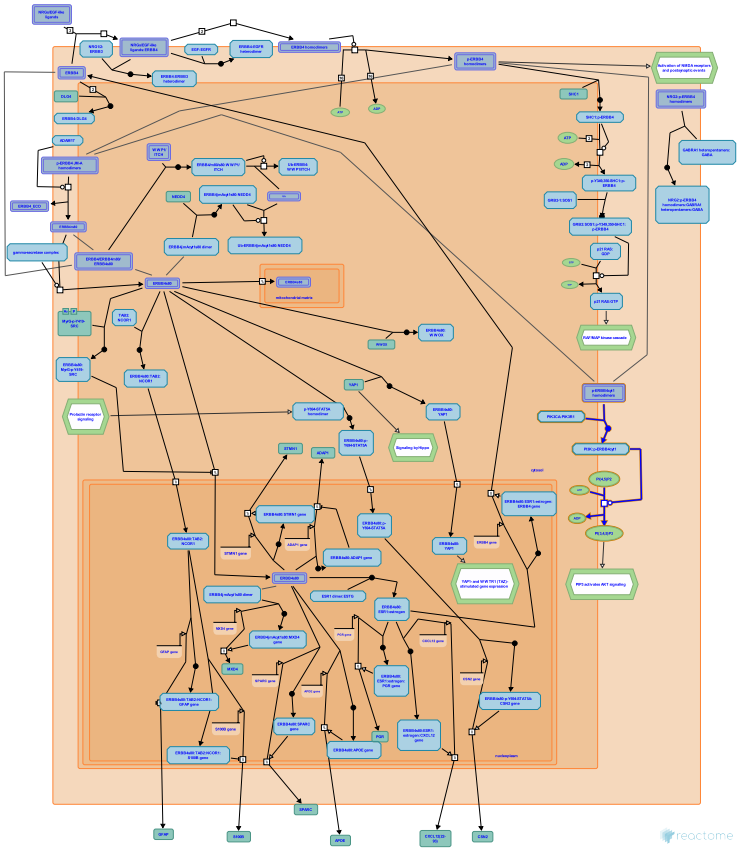
Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

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. ↗

PI3K events in ERBB4 signaling ↗

Stable identifier: R-HSA-1250342



The CYT1 isoforms of ERBB4 possess a C-tail tyrosine residue that, upon trans-autophosphorylation, serves as a docking site for the p85 alpha subunit of PI3K - PIK3R1 (Kaushansky et al. 2008, Cohen et al. 1996). Binding of PIK3R1 to CYT1 isoforms of ERBB4 is followed by recruitment of the p110 catalytic subunit of PI3K (PIK3CA), leading to assembly of an active PI3K complex that converts PIP2 to PIP3 and activates AKT signaling (Kainulainen et al. 2000).

Editions

2011-11-04	Authored	Orlic-Milacic, M.
2011-11-07	Edited	Matthews, L.
2011-11-11	Reviewed	Harris, RC., Zeng, F.
2012-02-20	Reviewed	Earp HS, 3rd., Misior, AM.
2019-02-21	Authored	Stern, DF.
2019-03-06	Edited	Orlic-Milacic, M.

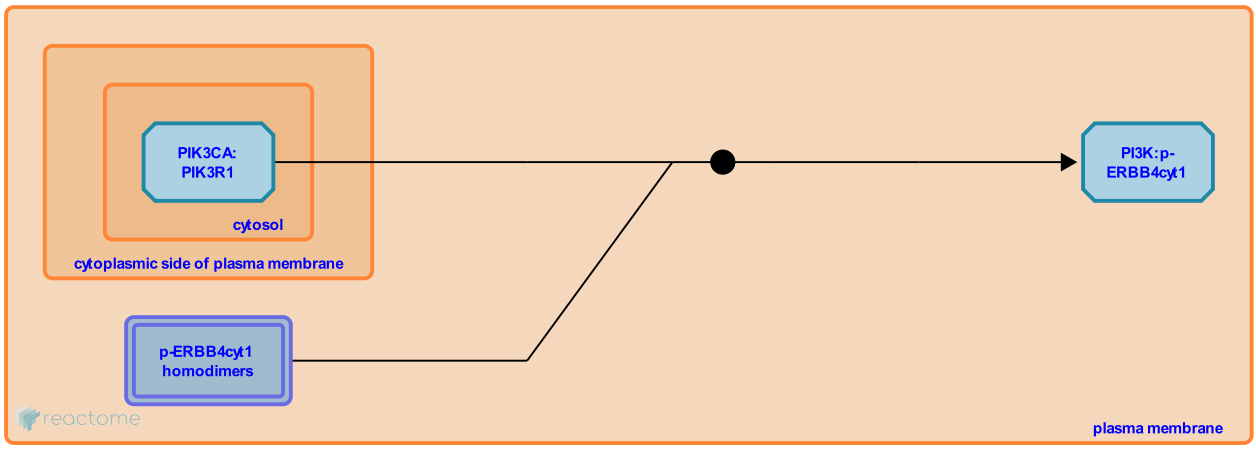
Binding of p85 subunit of PI3K (PIK3R1) to p-ERBB4cyt1 homodimers

Location: PI3K events in ERBB4 signaling

Stable identifier: R-HSA-1250353

Type: binding

Compartments: plasma membrane, extracellular region



p85 subunit of PI3K (PIK3R1) directly binds to phosphorylated ERBB4 CYT1 homodimers through docking tyrosine residues on either ERBB4 JM A CYT1 (tyrosine Y1056) or ERBB4 JM B CYT1 (tyrosine Y1046) isoform (Cohen et al. 1996, Kainulainen et al. 2000, Kaushansky et al. 2008).

Followed by: Conversion of PIP2 into PIP3 by PI3K bound to p-ERBB4cyt1 homodimers

Literature references

Lane, WS., MacBeath, G., Budnik, BA., Rush, J., Kaushansky, A., Gordus, A. (2008). System-wide investigation of ErbB4 reveals 19 sites of Tyr phosphorylation that are unusually selective in their recruitment properties. *Chem Biol, 15*, 808-17.

Santiestevan, E., Sundvall, M., Kainulainen, V., Määttä, JA., Elenius, K., Klagsbrun, M. (2000). A natural ErbB4 isoform that does not activate phosphoinositide 3-kinase mediates proliferation but not survival or chemotaxis. *J Biol Chem, 275*, 8641-9.

Fell, HP., Foy, L., Green, JM., Cohen, BD. (1996). HER4-mediated biological and biochemical properties in NIH 3T3 cells. Evidence for HER1-HER4 heterodimers. *J Biol Chem, 271*, 4813-8.

Editions

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2019-02-21	Authored	Stern, DF.
2019-03-06	Edited	Orlic-Milacic, M.

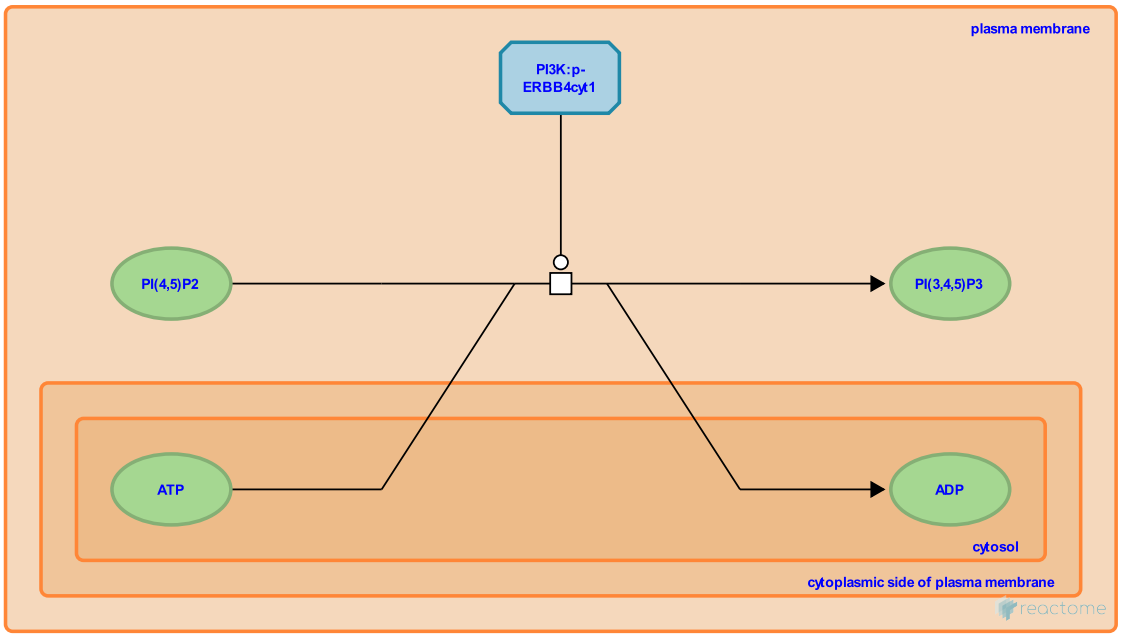
Conversion of PIP2 into PIP3 by PI3K bound to p-ERBB4cyt1 homodimers ↗

Location: PI3K events in ERBB4 signaling

Stable identifier: R-HSA-1250370

Type: transition

Compartments: plasma membrane, extracellular region, cytosol



Activated PI3K bound to phosphorylated ERBB4 CYT-1 homodimers converts PIP2 into PIP3, which leads to activation of AKT signaling (Kainulainen et al. 2000).

Preceded by: Binding of p85 subunit of PI3K (PIK3R1) to p-ERBB4cyt1 homodimers

Literature references

Santiestevan, E., Sundvall, M., Kainulainen, V., Määttä, JA., Elenius, K., Klagsbrun, M. (2000). A natural ErbB4 isoform that does not activate phosphoinositide 3-kinase mediates proliferation but not survival or chemotaxis. *J Biol Chem, 275*, 8641-9. ↗

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