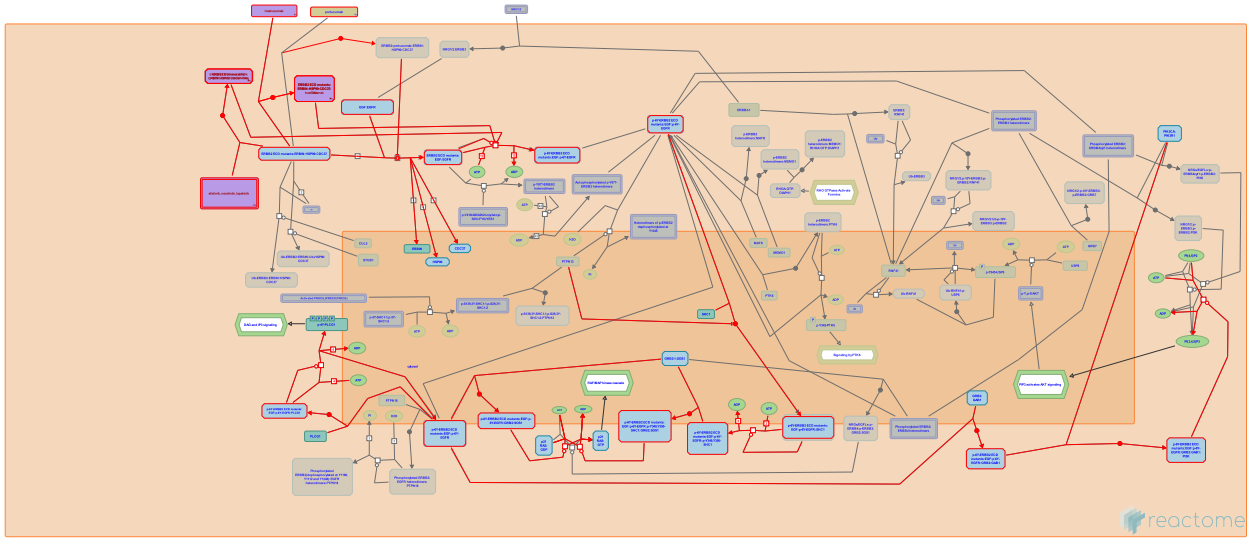
Signaling by ERBB2 ECD mutants



Bose, R., Kancha, RK., Krishna, A., Orlic-Milacic, M.

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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.

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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. ↗

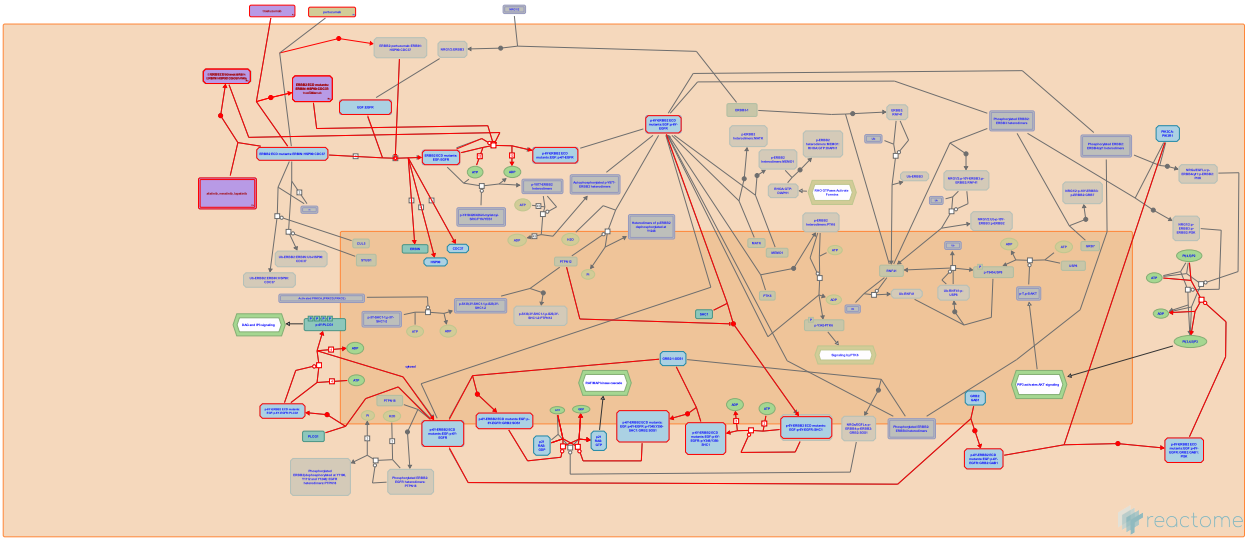
Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

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. ↗

Signaling by ERBB2 ECD mutants ↗

Stable identifier: R-HSA-9665348

Diseases: cancer



ERBB2 extracellular domain (ECD) mutants harbor missense mutations that lead to substitutions of amino acid residues in the heterodimerization arm contact surface, involved in formation of ERBB2 heterodimers. The functionally studied ERBB2 ECD mutants, ERBB2 G309A (Bose et al. 2013), ERBB2 G309E (Greulich et al. 2012) and ERBB2 S310F (Greulich et al. 2012) seem to preferntially heterodimerize with EGFR. Heterodimerization of ERBB2 G309E involves formation of disulfide bonds (Greulich et al. 2012). ERBB2 S310F shows stronger activation of downstream signaling than ERBB2 G309A and ERBB2 G309E, and is hyperphosphorylated on tyrosine residues in the C-tail (Greulich et al. 2012), while the C-tail phosphorylation of ERBB2 G309A (Bose et al. 2013) and ERBB2 G309E (Greulich et al. 2012) is comparable to the wild type ERBB2.
RAS signaling and PLCgamma1 signaling are activated dowsntream of all three ERBB2 ECD mutants, ERBB2 G309A (Bose et al. 2013), ERBB2 G309E (Greulich et al. 2012) and ERBB2 S310F (Greulich et al. 2012), as evidenced by activating phosphorylation on ERKs (MAPK1 and MAPK3) and PLCG1, respectively. ERBB2 G309E and ERBB2 S310F also activate PI3K/AKT signaling, demonstrated by activating phosphorylation of AKT1 (Greulich et al. 2012). Activation of PI3K/AKT signaling downstream of ERBB2 G309A has not been tested. Signaling downstream of ERBB2 S310Y has been poorly characterized and it is annotated as a candidate. Many regulators of cell migration show increased phosphorylation in cells expressing ERBB2 G309E and ERBB2 S310F (Greulich et al. 2012).
Comapred with the wild type ERBB2, ERBB2 G309E, ERBB2 S310F and ERBB2 S310Y are more sensitive to the ERBB2-directed therapeutic antibody trastuzumab (herceptin) and to tyrosine kinase inhibitors lapatinib, neratinib and afatinib (Greulich et al. 2012). ERBB2 G309A was also responsive to trastuzumab, lapatinib and neratinib (Bose et al. 2013).

Literature references

Walker, SR., Greulich, H., Pho, NH., Banerji, S., Berger, AH., Lawrence, MS. et al. (2012). Functional analysis of receptor tyrosine kinase mutations in lung cancer identifies oncogenic extracellular domain mutations of ERBB2. *Proc. Natl. Acad. Sci. U.S.A., 109*, 14476-81. ↗

Bose, R., Shen, W., Aronson, AB., Goel, N., Koboldt, DC., Li, S. et al. (2013). Activating HER2 mutations in HER2 gene amplification negative breast cancer. *Cancer Discov, 3*, 224-37. ↗

Editions

2019-10-25	Reviewed	Bose, R., Krishna, A.
2019-10-30	Authored	Orlic-Milacic, M.
2019-11-01	Edited	Orlic-Milacic, M.
2019-11-03	Reviewed	Kancha, RK.

ERBB2 ECD mutants heterodimerize with EGFR ↗

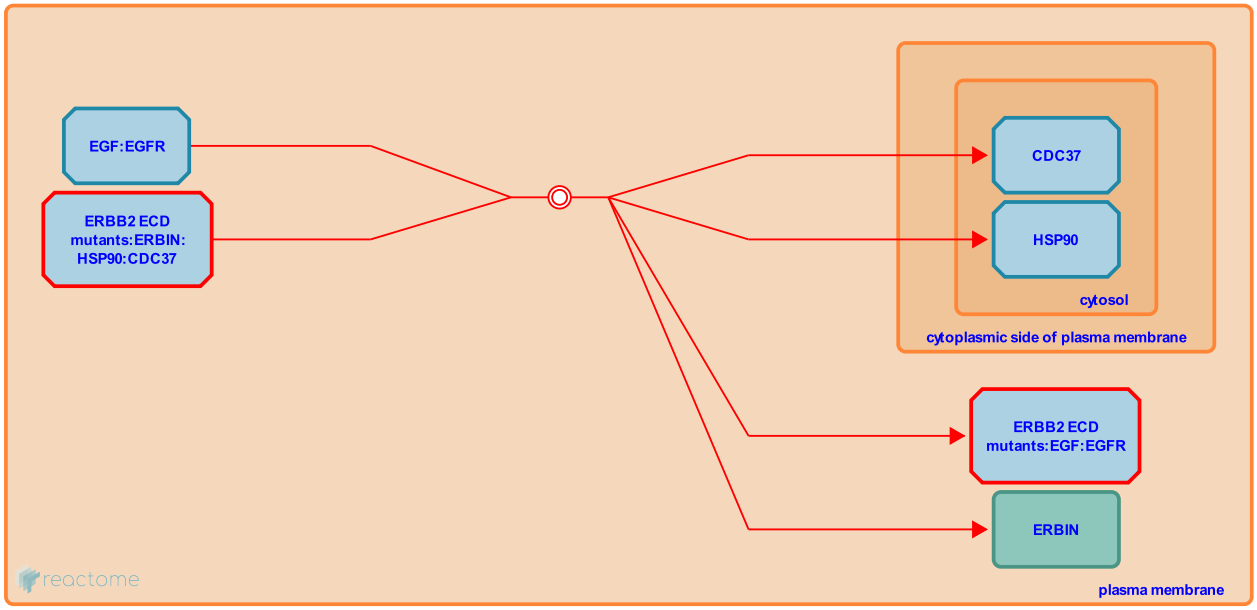
Location: Signaling by ERBB2 ECD mutants

Stable identifier: R-HSA-9665388

Type: dissociation

Compartments: plasma membrane

Diseases: cancer



ERBB2 extracellular domain (ECD) mutants harbor missense mutations that lead to substitutions of amino acid residues in the heterodimerization arm contact surface, involved in formation of ERBB2 heterodimers. The functionally studied ERBB2 ECD mutants, ERBB2 G309A (Bose et al. 2013), ERBB2 G309E (Greulich et al. 2012) and ERBB2 S310F (Greulich et al. 2012) seem to preferntially heterodimerize with EGFR. Heterodimerization of ERBB2 G309E involves formation of disulfide bonds (Greulich et al. 2012).

Followed by: Heterodimers of ERBB2 ECD mutants and EGFR trans-autophosphorylate

Literature references

Walker, SR., Greulich, H., Pho, NH., Banerji, S., Berger, AH., Lawrence, MS. et al. (2012). Functional analysis of receptor tyrosine kinase mutations in lung cancer identifies oncogenic extracellular domain mutations of ERBB2. *Proc. Natl. Acad. Sci. U.S.A., 109*, 14476-81. ↗

Bose, R., Shen, W., Aronson, AB., Goel, N., Koboldt, DC., Li, S. et al. (2013). Activating HER2 mutations in HER2 gene amplification negative breast cancer. *Cancer Discov, 3*, 224-37. ↗

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Heterodimers of ERBB2 ECD mutants and EGFR trans-autophosphorylate ↗

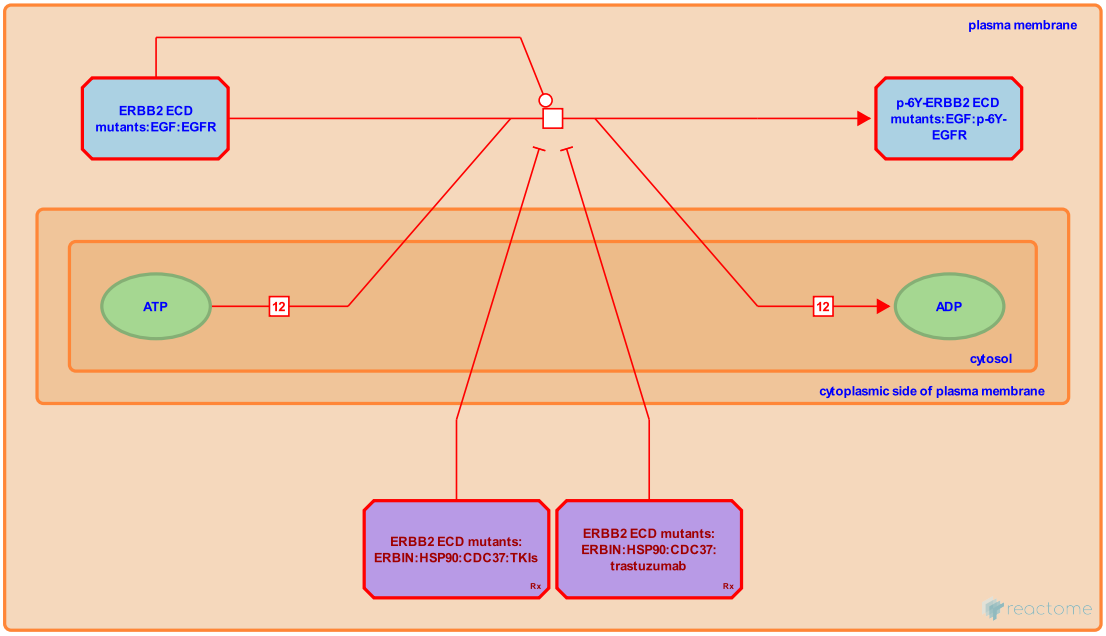
Location: Signaling by ERBB2 ECD mutants

Stable identifier: R-HSA-9665389

Type: transition

Compartments: plasma membrane, cytosol

Diseases: cancer



ERBB2 S310F shows stronger activation of downstream signaling than ERBB2 G309A and ERBB2 G309E, and is hyperphosphorylated on tyrosine residues in the C-tail (Greulich et al. 2012), while the C-tail phosphorylation of ERBB2 G309A (Bose et al. 2013) and ERBB2 G309E (Greulich et al. 2012) is comparable to the wild type ERBB2. Phosphorylation of EGFR was demonstrated in the presence of ERBB2 G309A (Bose et al. 2013). Except for ERBB2 C-tail tyrosine residues Y1221 and Y1222, which were shown to undergo trans-autophosphorylation in ERBB2 G309E, ERBB2 S310F and ERBB2 S310Y (Greulich et al. 2012), phosphorylation of specific tyrosine residues in ERBB2 and EGFR has not been examined and they are assumed to be the same as in the wild type ERBB2 heterodimers with EGFR.

Preceded by: ERBB2 ECD mutants heterodimerize with EGFR

Followed by: GRB2:SOS1 binds to phosphorylated heterodimers of ERBB2 ECD mutants and EGFR, Phosphorylated heterodimers of ERBB2 ECD mutants and EGFR bind PLCG1, Phosphorylated heterodimers of ERBB2 ECD mutants and EGFR bind SHC1, Phosphorylated heterodimers of ERBB2 ECD mutants and EGFR bind GRB2:GAB1

Literature references

Walker, SR., Greulich, H., Pho, NH., Banerji, S., Berger, AH., Lawrence, MS. et al. (2012). Functional analysis of receptor tyrosine kinase mutations in lung cancer identifies oncogenic extracellular domain mutations of ERBB2. *Proc. Natl. Acad. Sci. U.S.A., 109*, 14476-81. ↗

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Phosphorylated heterodimers of ERBB2 ECD mutants and EGFR bind SHC1 ↗

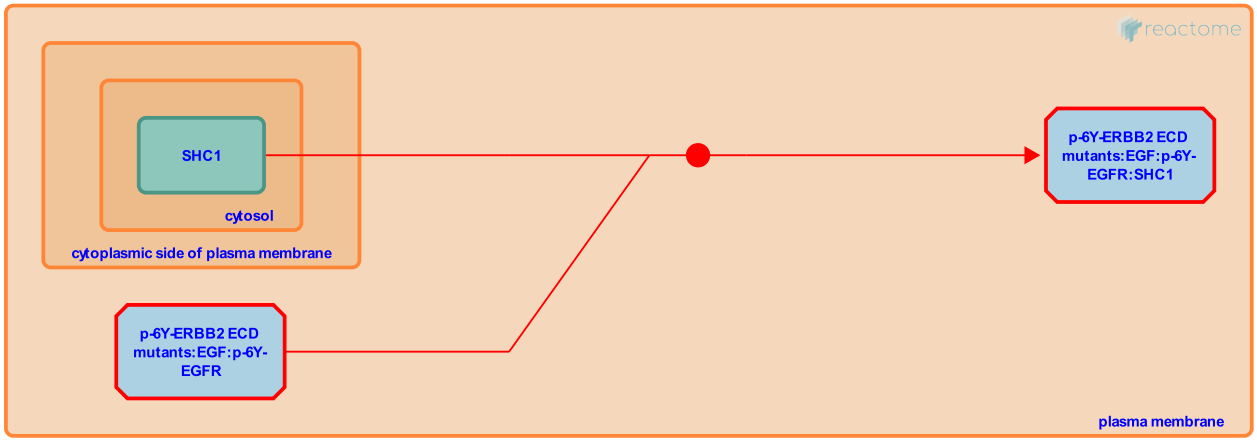
Location: Signaling by ERBB2 ECD mutants

Stable identifier: R-HSA-9665416

Type: binding

Compartments: plasma membrane, cytosol

Diseases: cancer



RAS signaling is activated dowsntream of ERBB2 ECD mutants ERBB2 G309A (Bose et al. 2013), ERBB2 G309E (Greulich et al. 2012) and ERBB2 S310F (Greulich et al. 2012), as evidenced by activating phosphorylation of ERKs (MAPK1 and MAPK3). It is assumed that phosphorylated heterodimers of ERBB2 ECD mutants and EGFR, like phosphorylated heterodimers of the wild type ERBB2, bind to SHC1.

Preceded by: Heterodimers of ERBB2 ECD mutants and EGFR trans-autophosphorylate

Followed by: Phosphorylated heterodimers of ERBB2 ECD mutants and EGFR phosphorylate SHC1

Literature references

Walker, SR., Greulich, H., Pho, NH., Banerji, S., Berger, AH., Lawrence, MS. et al. (2012). Functional analysis of receptor tyrosine kinase mutations in lung cancer identifies oncogenic extracellular domain mutations of ERBB2. *Proc. Natl. Acad. Sci. U.S.A., 109*, 14476-81. ↗

Bose, R., Shen, W., Aronson, AB., Goel, N., Koboldt, DC., Li, S. et al. (2013). Activating HER2 mutations in HER2 gene amplification negative breast cancer. *Cancer Discov, 3*, 224-37. ↗

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Phosphorylated heterodimers of ERBB2 ECD mutants and EGFR phosphorylate SHC1

↗

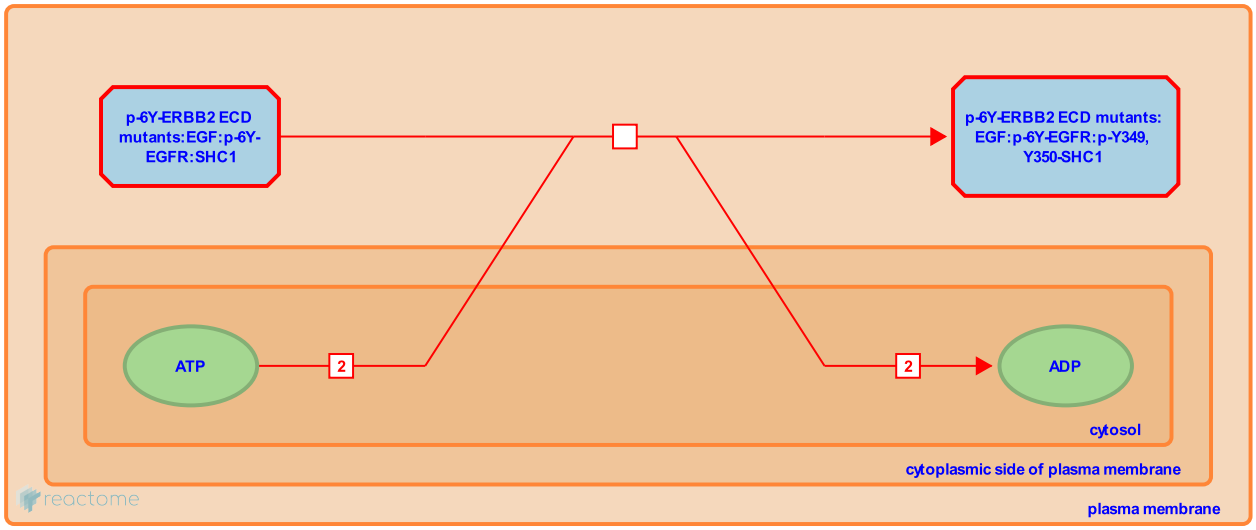
Location: Signaling by ERBB2 ECD mutants

Stable identifier: R-HSA-9665406

Type: transition

Compartments: plasma membrane, cytosol

Diseases: cancer



RAS signaling is activated dowsntream of ERBB2 ECD mutants ERBB2 G309A (Bose et al. 2013), ERBB2 G309E (Greulich et al. 2012) and ERBB2 S310F (Greulich et al. 2012), as evidenced by activating phosphorylation of ERKs (MAPK1 and MAPK3). It is assumed that phosphorylated heterodimers of ERBB2 ECD mutants and EGFR, like phosphorylated heterodimers of the wild type ERBB2, can bind to and phosphorylate SHC1.

Preceded by: Phosphorylated heterodimers of ERBB2 ECD mutants and EGFR bind SHC1

Followed by: Phosphorylated heterodimers of ERBB2 ECD mutants and EGFR recruit GRB2:SOS1 through SHC1

Literature references

Walker, SR., Greulich, H., Pho, NH., Banerji, S., Berger, AH., Lawrence, MS. et al. (2012). Functional analysis of receptor tyrosine kinase mutations in lung cancer identifies oncogenic extracellular domain mutations of ERBB2. *Proc. Natl. Acad. Sci. U.S.A., 109*, 14476-81. ↗

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Phosphorylated heterodimers of ERBB2 ECD mutants and EGFR recruit GRB2:SOS1 through SHC1

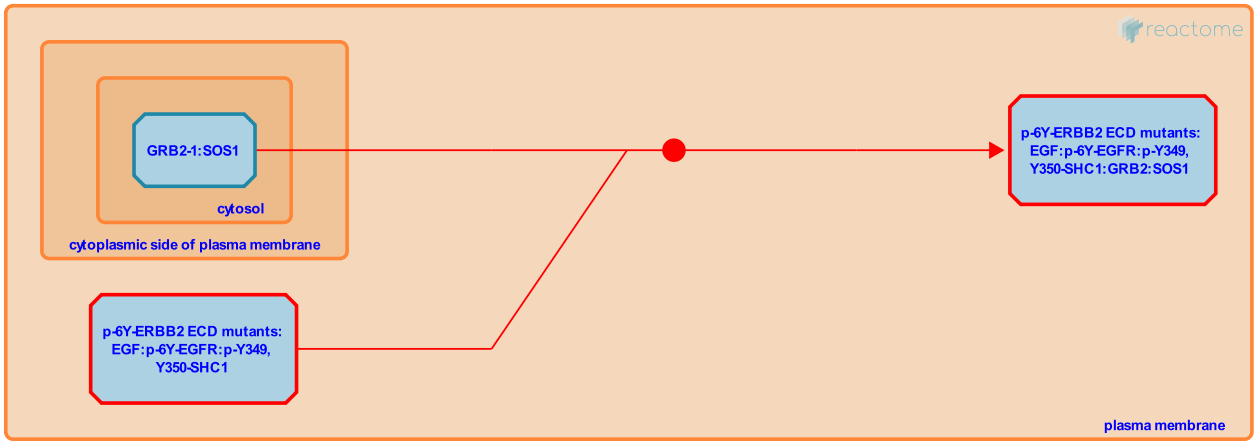
Location: Signaling by ERBB2 ECD mutants

Stable identifier: R-HSA-9665413

Type: binding

Compartments: plasma membrane, cytosol

Diseases: cancer



RAS signaling is activated dowsntream of ERBB2 ECD mutants ERBB2 G309A (Bose et al. 2013), ERBB2 G309E (Greulich et al. 2012) and ERBB2 S310F (Greulich et al. 2012), as evidenced by activating phosphorylation of ERKs (MAPK1 and MAPK3). It is assumed that phosphorylated heterodimers of ERBB2 ECD mutants and EGFR, like phosphorylated heterodimers of the wild type ERBB2, can recruit the GRB2:SOS1 complex through phosphorylated SHC1.

Preceded by: Phosphorylated heterodimers of ERBB2 ECD mutants and EGFR phosphorylate SHC1

Followed by: RAS guanyl nucleotide exchange mediated by the p-6Y- ERBB2 ECD mutants:EGF:p-6Y-EGFR:p-SHC1:GRB2:SOS1

Literature references

Walker, SR., Greulich, H., Pho, NH., Banerji, S., Berger, AH., Lawrence, MS. et al. (2012). Functional analysis of receptor tyrosine kinase mutations in lung cancer identifies oncogenic extracellular domain mutations of ERBB2. *Proc. Natl. Acad. Sci. U.S.A., 109*, 14476-81.

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RAS guanyl nucleotide exchange mediated by the p-6Y- ERBB2 ECD mutants:EGF:p-6Y-EGFR:p-SHC1:GRB2:SOS1 ↗

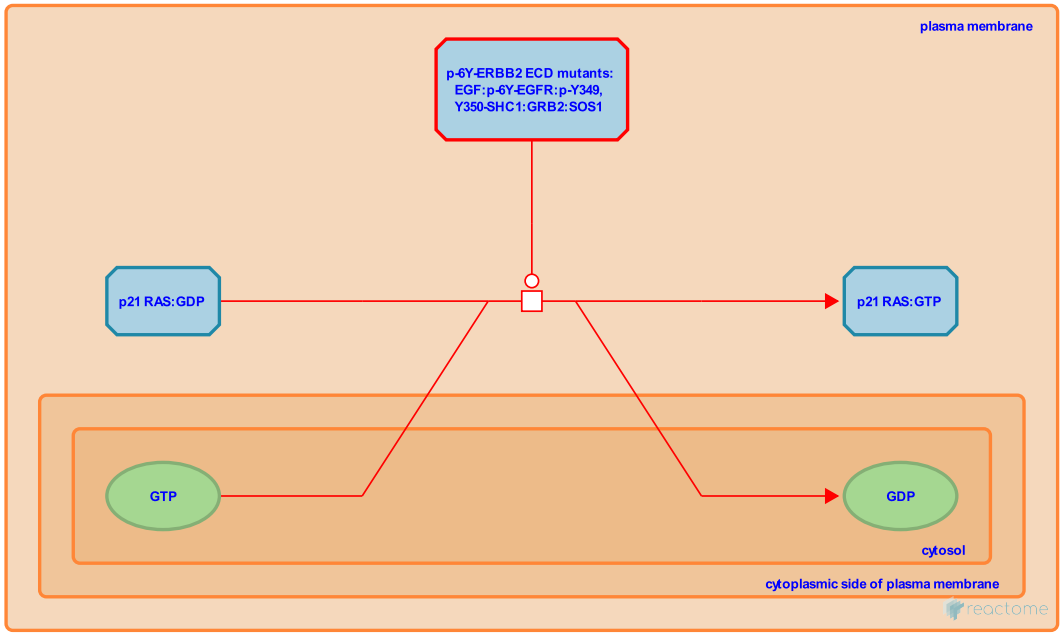
Location: Signaling by ERBB2 ECD mutants

Stable identifier: R-HSA-9665404

Type: transition

Compartments: plasma membrane, cytosol

Diseases: cancer



RAS signaling is activated dowsntream of ERBB2 ECD mutants ERBB2 G309A (Bose et al. 2013), ERBB2 G309E (Greulich et al. 2012) and ERBB2 S310F (Greulich et al. 2012), as evidenced by activating phosphorylation of ERKs (MAPK1 and MAPK3). It is assumed that phosphorylated heterodimers of ERBB2 ECD mutants and EGFR, like phosphorylated heterodimers of the wild type ERBB2, can recruit the GRB2:SOS1 complex through phosphorylated SHC1, leading to guanyl nucleotide exchange on RAS and activation of RAS signaling.

Preceded by: Phosphorylated heterodimers of ERBB2 ECD mutants and EGFR recruit GRB2:SOS1 through SHC1

Literature references

Walker, SR., Greulich, H., Pho, NH., Banerji, S., Berger, AH., Lawrence, MS. et al. (2012). Functional analysis of receptor tyrosine kinase mutations in lung cancer identifies oncogenic extracellular domain mutations of ERBB2. *Proc. Natl. Acad. Sci. U.S.A., 109*, 14476-81. ↗

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GRB2:SOS1 binds to phosphorylated heterodimers of ERBB2 ECD mutants and EGFR

↗

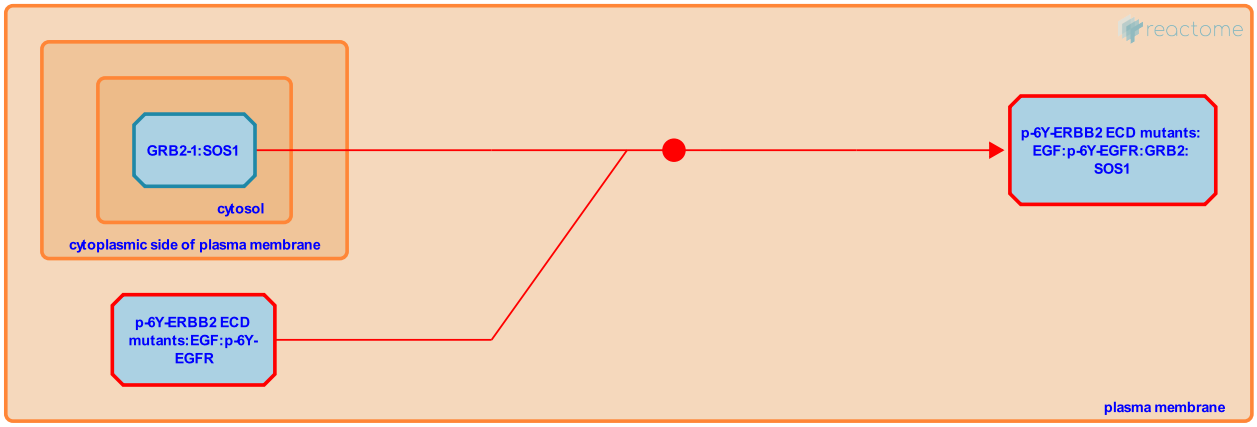
Location: Signaling by ERBB2 ECD mutants

Stable identifier: R-HSA-9665409

Type: binding

Compartments: plasma membrane, cytosol

Diseases: cancer



RAS signaling is activated dowsntream of ERBB2 ECD mutants ERBB2 G309A (Bose et al. 2013), ERBB2 G309E (Greulich et al. 2012) and ERBB2 S310F (Greulich et al. 2012), as evidenced by activating phosphorylation of ERKs (MAPK1 and MAPK3). It is assumed that phosphorylated heterodimers of ERBB2 ECD mutants and EGFR, like phosphorylated heterodimers of the wild type ERBB2, can directly recruit the GRB2:SOS1 complex.

Preceded by: Heterodimers of ERBB2 ECD mutants and EGFR trans-autophosphorylate

Followed by: RAS activation by SOS1 bound to phosphorylated heterodimers of ERBB2 ECD mutants and EGFR through GRB2

Literature references

Walker, SR., Greulich, H., Pho, NH., Banerji, S., Berger, AH., Lawrence, MS. et al. (2012). Functional analysis of receptor tyrosine kinase mutations in lung cancer identifies oncogenic extracellular domain mutations of ERBB2. *Proc. Natl. Acad. Sci. U.S.A., 109*, 14476-81. ↗

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2019-11-03	Reviewed	Kancha, RK.

RAS activation by SOS1 bound to phosphorylated heterodimers of ERBB2 ECD mutants and EGFR through GRB2 ↗

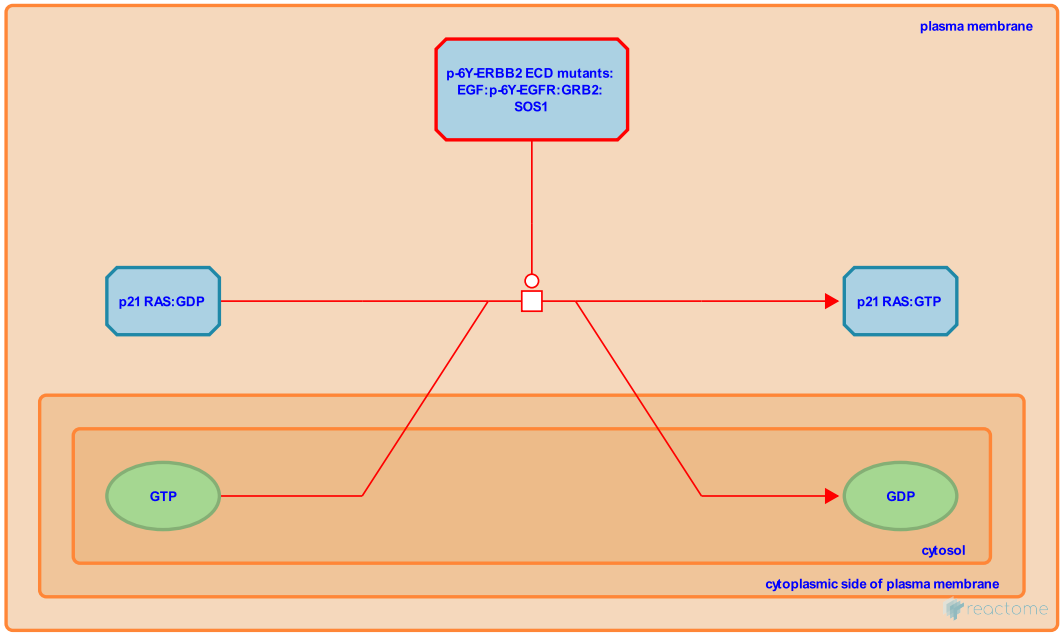
Location: Signaling by ERBB2 ECD mutants

Stable identifier: R-HSA-9665408

Type: transition

Compartments: plasma membrane, cytosol

Diseases: cancer



RAS signaling is activated dowsntream of ERBB2 ECD mutants ERBB2 G309A (Bose et al. 2013), ERBB2 G309E (Greulich et al. 2012) and ERBB2 S310F (Greulich et al. 2012), as evidenced by activating phosphorylation of ERKs (MAPK1 and MAPK3). It is assumed that phosphorylated heterodimers of ERBB2 ECD mutants and EGFR, like phosphorylated heterodimers of the wild type ERBB2, can directly recruit the GRB2:SOS1 complex, leading to guanyl nucleotide exchange on RAS and activation of RAS signaling.

Preceded by: GRB2:SOS1 binds to phosphorylated heterodimers of ERBB2 ECD mutants and EGFR

Literature references

Walker, SR., Greulich, H., Pho, NH., Banerji, S., Berger, AH., Lawrence, MS. et al. (2012). Functional analysis of receptor tyrosine kinase mutations in lung cancer identifies oncogenic extracellular domain mutations of ERBB2. *Proc. Natl. Acad. Sci. U.S.A., 109*, 14476-81. ↗

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Phosphorylated heterodimers of ERBB2 ECD mutants and EGFR bind GRB2:GAB1 ↗

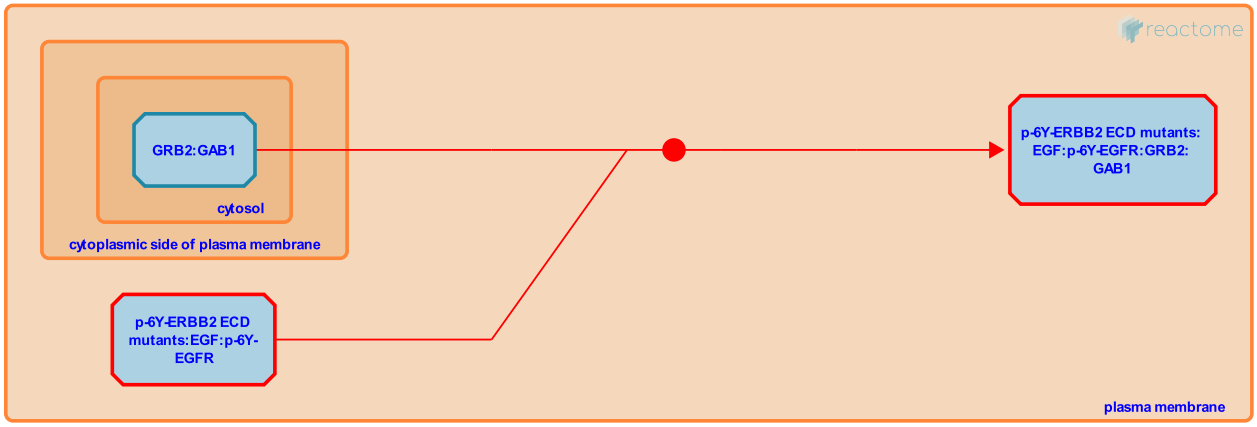
Location: Signaling by ERBB2 ECD mutants

Stable identifier: R-HSA-9665417

Type: binding

Compartments: plasma membrane, cytosol

Diseases: cancer



ERBB2 G309E and ERBB2 S310F activate PI3K/AKT signaling, demonstrated by activating phosphorylation of AKT1 (Greulich et al. 2012). Activation of PI3K/AKT signaling downstream of ERBB2 G309A has not been tested. It is assumed that phosphorylated heterodimers of ERBB2 ECD mutants and EGFR, like the wild type heterodimers of ERBB2 and EGFR, can bind to the GRB2:GAB1 complex.

Preceded by: Heterodimers of ERBB2 ECD mutants and EGFR trans-autophosphorylate

Followed by: Phosphorylated heterodimers of ERBB2 ECD mutants and EGFR, in complex with GRB2:GAB1, bind PI3K

Literature references

Walker, SR., Greulich, H., Pho, NH., Banerji, S., Berger, AH., Lawrence, MS. et al. (2012). Functional analysis of receptor tyrosine kinase mutations in lung cancer identifies oncogenic extracellular domain mutations of ERBB2. *Proc. Natl. Acad. Sci. U.S.A., 109*, 14476-81. ↗

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Phosphorylated heterodimers of ERBB2 ECD mutants and EGFR, in complex with GRB2:GAB1, bind PI3K ↗

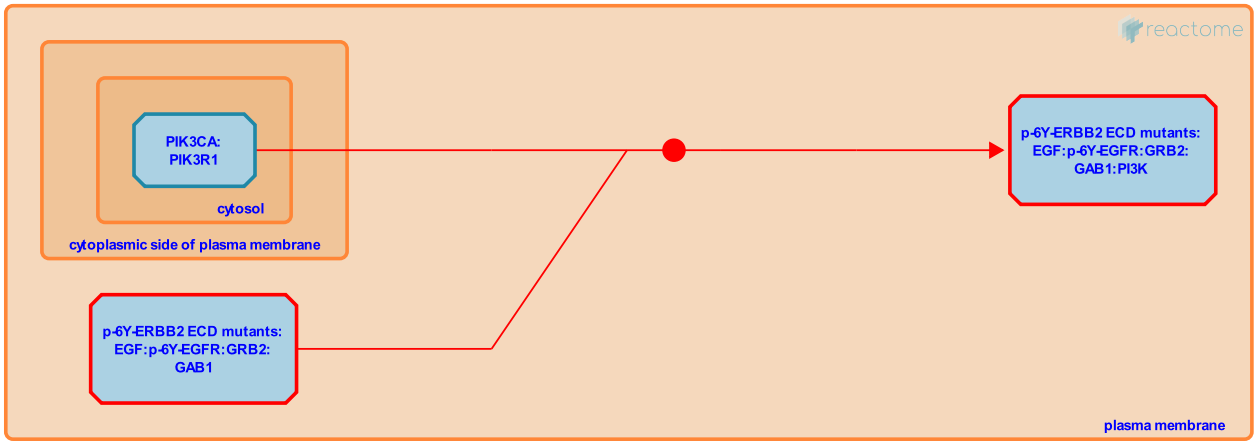
Location: Signaling by ERBB2 ECD mutants

Stable identifier: R-HSA-9665415

Type: binding

Compartments: plasma membrane, cytosol

Diseases: cancer



ERBB2 G309E and ERBB2 S310F activate PI3K/AKT signaling, demonstrated by activating phosphorylation of AKT1 (Greulich et al. 2012). It is assumed that phosphorylated heterodimers of ERBB2 ECD mutants and EGFR, like the wild type heterodimers of ERBB2 and EGFR, can bind to the GRB2:GAB1 complex, leading to the recruitment of the PI3K complex.

Preceded by: Phosphorylated heterodimers of ERBB2 ECD mutants and EGFR bind GRB2:GAB1

Followed by: PI3K bound to phosphorylated heterodimers of ERBB2 ECD mutants and EGFR converts PIP2 to PIP3

Literature references

Walker, SR., Greulich, H., Pho, NH., Banerji, S., Berger, AH., Lawrence, MS. et al. (2012). Functional analysis of receptor tyrosine kinase mutations in lung cancer identifies oncogenic extracellular domain mutations of ERBB2. *Proc. Natl. Acad. Sci. U.S.A., 109*, 14476-81. ↗

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PI3K bound to phosphorylated heterodimers of ERBB2 ECD mutants and EGFR converts PIP2 to PIP3 ↗

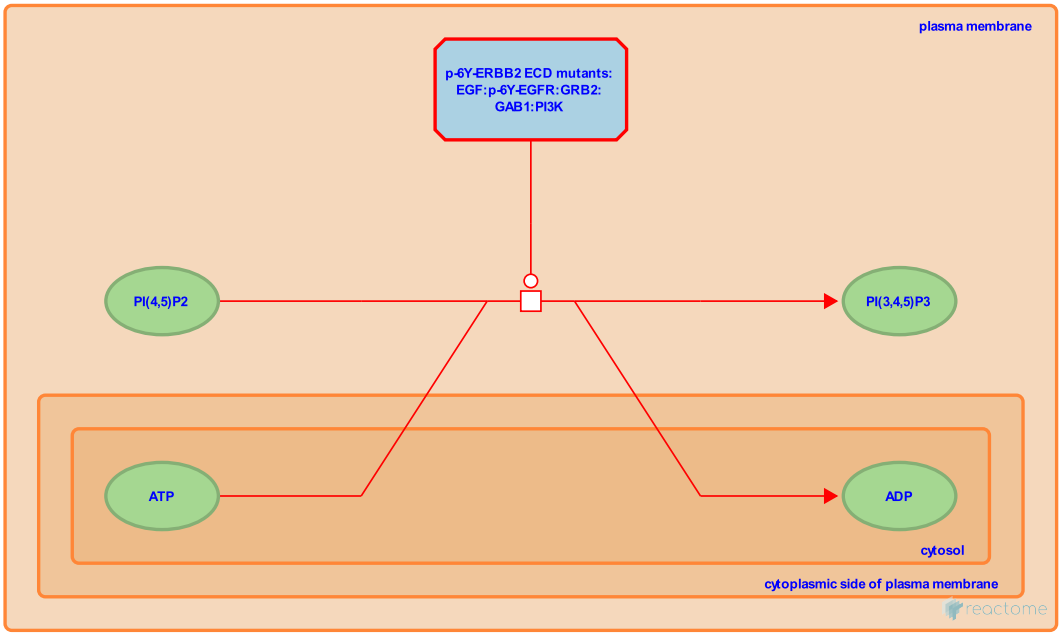
Location: Signaling by ERBB2 ECD mutants

Stable identifier: R-HSA-9665407

Type: transition

Compartments: plasma membrane, cytosol

Diseases: cancer



ERBB2 G309E and ERBB2 S310F activate PI3K/AKT signaling, demonstrated by activating phosphorylation of AKT1 (Greulich et al. 2012). It is assumed that phosphorylated heterodimers of ERBB2 ECD mutants and EGFR, like the wild type heterodimers of ERBB2 and EGFR, can bind to the GRB2:GAB1 complex, leading to recruitment of the PI3K complex, which results in conversion of PIP2 to PIP3 and activation of the AKT signaling.

Preceded by: Phosphorylated heterodimers of ERBB2 ECD mutants and EGFR, in complex with GRB2:GAB1, bind PI3K

Literature references

Walker, SR., Greulich, H., Pho, NH., Banerji, S., Berger, AH., Lawrence, MS. et al. (2012). Functional analysis of receptor tyrosine kinase mutations in lung cancer identifies oncogenic extracellular domain mutations of ERBB2. *Proc. Natl. Acad. Sci. U.S.A., 109*, 14476-81. ↗

Bose, R., Shen, W., Aronson, AB., Goel, N., Koboldt, DC., Li, S. et al. (2013). Activating HER2 mutations in HER2 gene amplification negative breast cancer. *Cancer Discov, 3*, 224-37. ↗

Editions

2019-10-25	Reviewed	Bose, R., Krishna, A.
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Phosphorylated heterodimers of ERBB2 ECD mutants and EGFR bind PLCG1 ↗

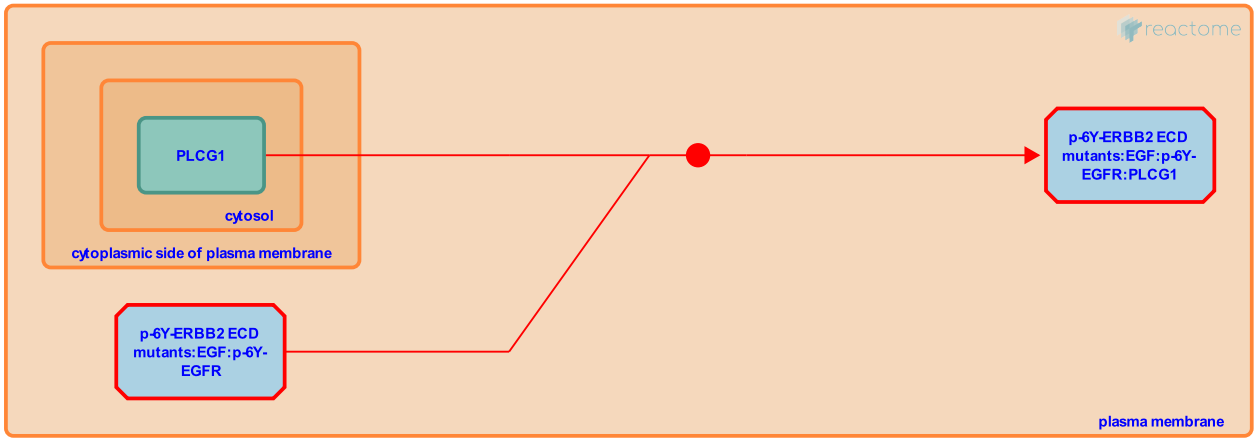
Location: Signaling by ERBB2 ECD mutants

Stable identifier: R-HSA-9665410

Type: binding

Compartments: plasma membrane, cytosol

Diseases: cancer



PLCgamma1 signaling is activated dowsntream of ERBB2 ECD mutants ERBB2 G309A (Bose et al. 2013), ERBB2 G309E (Greulich et al. 2012) and ERBB2 S310F (Greulich et al. 2012), as evidenced by activating phosphorylation of PLCG1. It is assumed that heterodimers of ERBB2 ECD mutants and EGFR, like the wild type heterodimers of ERBB2 and EGFR, bind to PLCG1.

Preceded by: Heterodimers of ERBB2 ECD mutants and EGFR trans-autophosphorylate

Followed by: Phosphorylated heterodimers of ERBB2 ECD mutants and EGFR phosphorylate PLCG1

Literature references

Walker, SR., Greulich, H., Pho, NH., Banerji, S., Berger, AH., Lawrence, MS. et al. (2012). Functional analysis of receptor tyrosine kinase mutations in lung cancer identifies oncogenic extracellular domain mutations of ERBB2. *Proc. Natl. Acad. Sci. U.S.A., 109*, 14476-81. ↗

Bose, R., Shen, W., Aronson, AB., Goel, N., Koboldt, DC., Li, S. et al. (2013). Activating HER2 mutations in HER2 gene amplification negative breast cancer. *Cancer Discov, 3*, 224-37. ↗

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Phosphorylated heterodimers of ERBB2 ECD mutants and EGFR phosphorylate PLCG1

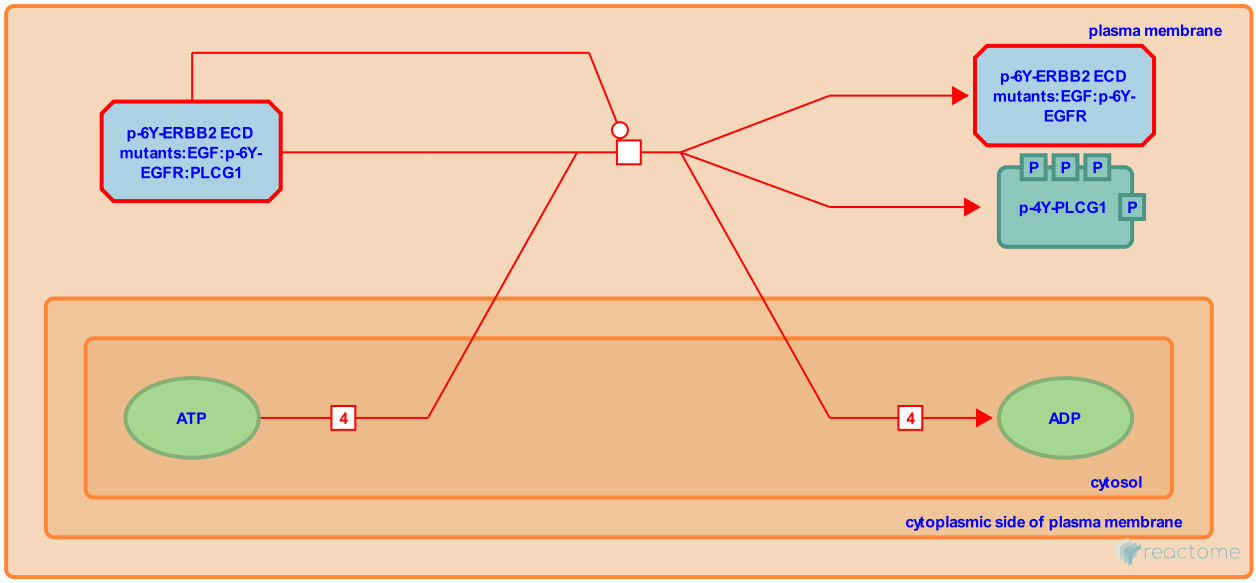
Location: Signaling by ERBB2 ECD mutants

Stable identifier: R-HSA-9665411

Type: transition

Compartments: plasma membrane, cytosol

Diseases: cancer



PLCgamma1 signaling is activated dowsntream of ERBB2 ECD mutants ERBB2 G309A (Bose et al. 2013), ERBB2 G309E (Greulich et al. 2012) and ERBB2 S310F (Greulich et al. 2012), as evidenced by activating phosphorylation of PLCG1. It is assumed that heterodimers of ERBB2 ECD mutants and EGFR, like the wild type heterodimers of ERBB2 and EGFR, bind to and phosphorylated PLCG1, leading to activation of PLCG1 signaling.

Preceded by: Phosphorylated heterodimers of ERBB2 ECD mutants and EGFR bind PLCG1

Literature references

Walker, SR., Greulich, H., Pho, NH., Banerji, S., Berger, AH., Lawrence, MS. et al. (2012). Functional analysis of receptor tyrosine kinase mutations in lung cancer identifies oncogenic extracellular domain mutations of ERBB2. *Proc. Natl. Acad. Sci. U.S.A., 109*, 14476-81.

Bose, R., Shen, W., Aronson, AB., Goel, N., Koboldt, DC., Li, S. et al. (2013). Activating HER2 mutations in HER2 gene amplification negative breast cancer. *Cancer Discov, 3*, 224-37.

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ERBB2 ECD mutants bind trastuzumab ↗

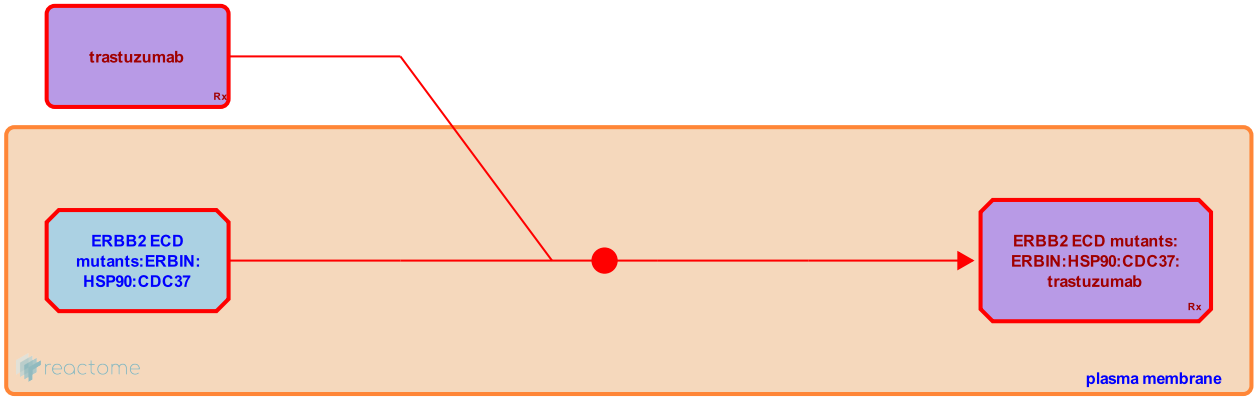
Location: Signaling by ERBB2 ECD mutants

Stable identifier: R-HSA-9665405

Type: binding

Compartments: plasma membrane

Diseases: cancer



Comapred with the wild type ERBB2, ERBB2 G309E, ERBB2 S310F and ERBB2 S310Y are more sensitive to the ERBB2-directed therapeutic antibody trastuzumab (herceptin) (Greulich et al. 2012). ERBB2 G309A was also responsive to trastuzumab (Bose et al. 2013).

Literature references

Walker, SR., Greulich, H., Pho, NH., Banerji, S., Berger, AH., Lawrence, MS. et al. (2012). Functional analysis of receptor tyrosine kinase mutations in lung cancer identifies oncogenic extracellular domain mutations of ERBB2. *Proc. Natl. Acad. Sci. U.S.A., 109*, 14476-81. ↗

Bose, R., Shen, W., Aronson, AB., Goel, N., Koboldt, DC., Li, S. et al. (2013). Activating HER2 mutations in HER2 gene amplification negative breast cancer. *Cancer Discov, 3*, 224-37. ↗

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ERBB2 ECD mutants bind TKIs ↗

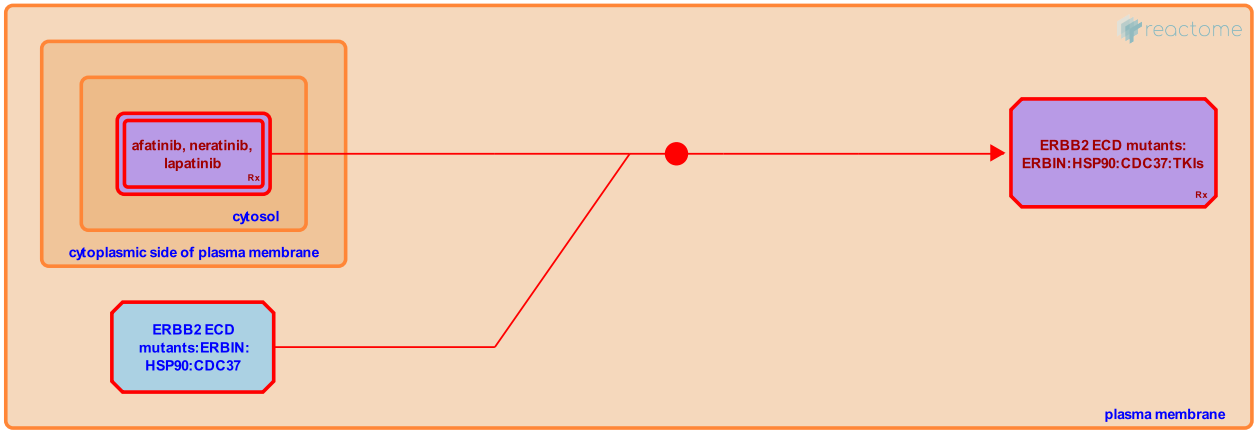
Location: Signaling by ERBB2 ECD mutants

Stable identifier: R-HSA-9665412

Type: binding

Compartments: plasma membrane, cytosol

Diseases: cancer



Comapred with the wild type ERBB2, ERBB2 G309E, ERBB2 S310F and ERBB2 S310Y are more sensitive to tyrosine kinase inhibitors lapatinib, neratinib and afatinib (Greulich et al. 2012). ERBB2 G309A was also responsive to lapatinib and neratinib (Bose et al. 2013).

Literature references

Walker, SR., Greulich, H., Pho, NH., Banerji, S., Berger, AH., Lawrence, MS. et al. (2012). Functional analysis of receptor tyrosine kinase mutations in lung cancer identifies oncogenic extracellular domain mutations of ERBB2. *Proc. Natl. Acad. Sci. U.S.A., 109*, 14476-81. ↗

Bose, R., Shen, W., Aronson, AB., Goel, N., Koboldt, DC., Li, S. et al. (2013). Activating HER2 mutations in HER2 gene amplification negative breast cancer. *Cancer Discov, 3*, 224-37. ↗

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