

# ERBB2 TMD/JMD heterodimers trans-auto- phosphorylate

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

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

The contents of this document may be freely copied and distributed in any media, provided the authors, plus the institutions, are credited, as stated under the terms of [Creative Commons Attribution 4.0 International \(CC BY 4.0\) License](https://creativecommons.org/licenses/by/4.0/). For more information see our [license](https://reactome.org/licenses/).

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. [↗](#)

Reactome database release: 88

This document contains 1 reaction ([see Table of Contents](#))

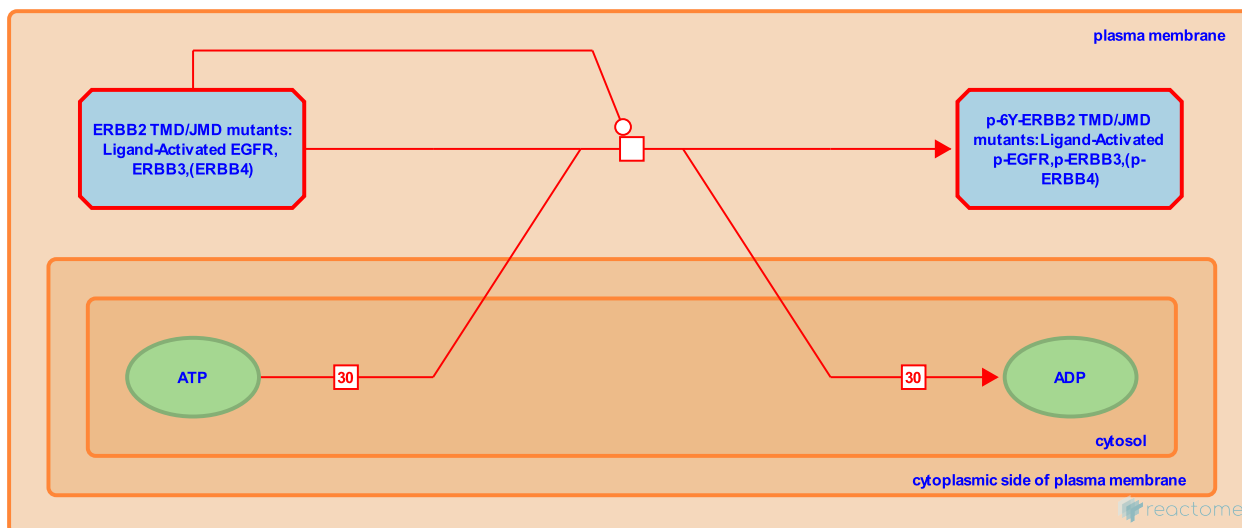
## ERBB2 TMD/JMD heterodimers trans-autophosphorylate [↗](#)

**Stable identifier:** R-HSA-9665709

**Type:** transition

**Compartments:** plasma membrane, cytosol

**Diseases:** cancer



Phosphorylation of tyrosine residues in the C-tail of ERBB2 was shown for the following ERBB2 TMD/JMD mutants:

ERBB2 V659E (Pahuja et al. 2018);

ERBB2 V659K (Pahuja et al. 2018);

ERBB2 G660D (Pahuja et al. 2018);

ERBB2 G660R (Pahuja et al. 2018);

ERBB2 S653C (de Martino et al. 2014 - phosphorylation at Y1248 demonstrated);

ERBB2 R677L (Pahuja et al. 2018);

ERBB2 R678Q (Bose et al. 2013; de Martino et al. 2014 - phosphorylation at Y1248 demonstrated; Pahuja et al. 2018); ERBB2 Q709L (Pahuja et al. 2018)

Phosphorylation of tyrosine residues in the C-tail of EGFR was demonstrated for ERBB2 S653C (de Martino et al. 2014 - phosphorylation at Y1068) and ERBB2 R678Q (Bose et al. 2013; de Martino et al. 2014 - phosphorylation at Y1068).

Phosphorylation of tyrosine residues in the C-tail of ERBB3 was demonstrated for ERBB2 S653C (de Martino et al. 2014 - phosphorylation at Y1197) and ERBB2 R678Q (Bose et al. 2013; de Martino et al. 2014 - phosphorylation at Y1197).

Signaling by ERBB2 V659K, ERBB2 G660D, ERBB2 G660R, ERBB2 R677L, ERBB2 E693K and ERBB2 Q709L has not been sufficiently studied and they are annotated as candidates.

### Literature references

Rieken, M., Xylinas, E., Klatte, T., Shariat, SF., Rouprêt, M., Elemento, O. et al. (2014). Impact of ERBB2 mutations on in vitro sensitivity of bladder cancer to lapatinib. *Cancer Biol. Ther.*, 15, 1239-47. [↗](#)

Antony, A., Khanna-Gupta, A., Singh, A., Pahuja, KB., Kljavin, NM., Bueno, R. et al. (2018). Actionable Activating Oncogenic ERBB2/HER2 Transmembrane and Juxtamembrane Domain Mutations. *Cancer Cell*, 34, 792-806.e5. [↗](#)

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.
2019-10-31	Authored	Orlic-Milacic, M.
2019-11-01	Edited	Orlic-Milacic, M.
2019-11-03	Reviewed	Kancha, RK.