Spontaneous dimerization of ligand-responsive EGFR mutants

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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. ↗

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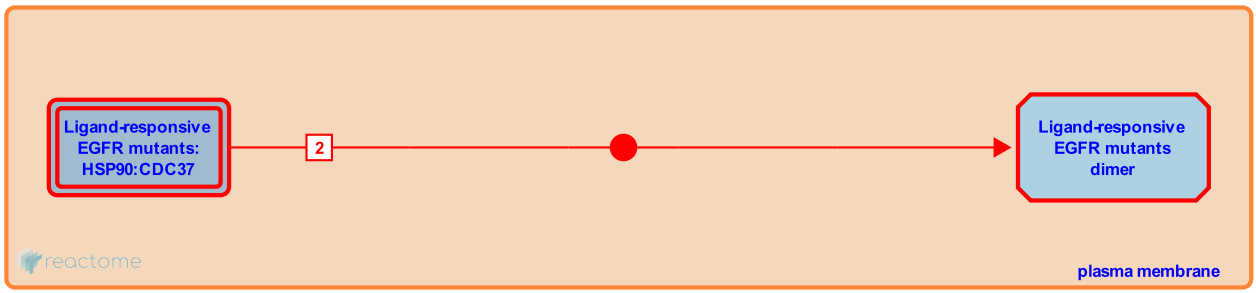
Stable identifier: R-HSA-1220614

Type: binding

Compartments: cytosol, plasma membrane

Diseases: cancer



EGFR ligand-responsive mutants dimerize spontaneously, without ligand binding, although ligand binding ability is preserved. This was experimentally demonstrated for EFGR L858R mutant and is presumed to happen in other constitutively active EGFR kinase domain mutants and EGFR extracellular domain point mutants.

Literature references

Feng, WL., Hahn, WC., Chen, TH., Meyerson, M., Frank, DA., Sellers, WR. et al. (2005). Oncogenic transformation by inhibitor-sensitive and -resistant EGFR mutants. *PLoS Med, 2*, e313.

Li, Y., Meyerson, M., Woo, MS., Boggon, TJ., Greulich, H., Eck, MJ. et al. (2007). Structures of lung cancer-derived EGFR mutants and inhibitor complexes: mechanism of activation and insights into differential inhibitor sensitivity. *Cancer Cell, 11*, 217-27.

Alvarado, D., Red Brewer, M., Pozzi, A., Choi, SH., Lemmon, MA., Moravcevic, K. et al. (2009). The juxtamembrane region of the EGF receptor functions as an activation domain. *Mol Cell, 34*, 641-51.

Zhang, X., Kuriyan, J., Shen, K., Cole, PA., Gureasko, J. (2006). An allosteric mechanism for activation of the kinase domain of epidermal growth factor receptor. *Cell, 125*, 1137-49.

Editions

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