

Spontaneous dimerization of ligand-responsive EGFR mutants

D'Eustachio, P., Greulich, H., Matthews, L., Orlic-Milacic, M., Savas, S., Wu, G.

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 <u>Creative Commons Attribution 4.0 International (CC BY 4.0)</u> <u>License</u>. For more information see our <u>license</u>.

18/05/2024

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. 7
- Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics*, 33, 3461-3467. A
- 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. *オ*

This document contains 1 reaction (see Table of Contents)

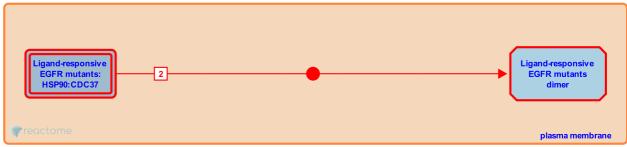
Spontaneous dimerization of ligand-responsive EGFR mutants 🛪

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. 7
- 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

2011-11-04	Authored	Orlic-Milacic, M.
2011-11-07	Edited	Wu, G., D'Eustachio, P., Matthews, L.
2011-11-15	Reviewed	Greulich, H., Savas, S.