Drug-mediated inhibition of ERBB2 signaling

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26/04/2021
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


Reactome database release: 76

This document contains 1 pathway and 3 reactions (see Table of Contents)
Drug-mediated inhibition of ERBB2 signaling

Stable identifier: R-HSA-9652282


Literature references


Editions

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ERBB2 can bind to and be inhibited by the following tyrosine kinase inhibitors (TKIs):

lapatinib (Xia et al. 2002, Wood et al. 2004)
neratinib (Rabindran et al. 2004)
afatinib (Li et al. 2008)
AZ5104 (Hanker et al. 2017)
tesevatinib (Gendreau et al. 2007)
canertinib (Nelson and Fry 2001)
sapitinib (Hickinson et al. 2010)
CP-724714 (Jani et al. 2007)

AEE788 (Traxler et al. 2014). Tyrosine kinase inhibitors do not prevent ERBB2 heterodimerization, but interfere with its kinase activity.

The following tyrosine kinase inhibitors were shown to be especially effective against overexpressed ERBB2 and to inhibit kinase activity of ERBB2 homodimers:

afatinib (Rabindran et al. 2004)
neratinib (Rabindran et al. 2004)
lapatinib (Rabindran et al. 2004).

**Literature references**


Editions

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ERBB2 binds trastuzumab

**Location:** Drug-mediated inhibition of ERBB2 signaling

**Stable identifier:** R-HSA-9652277

**Type:** binding

**Compartments:** extracellular region, plasma membrane

**Diseases:** cancer

ERBB2 signaling is inhibited by binding of ERBB2 to ERBB2-directed therapeutic recombinant antibody trastuzumab (herceptin), used as an anti-cancer therapeutic in tumors that overexpress ERBB2 (Hudziak et al. 1989, Carter et al. 1992). Trastuzumab does not prevent homodimerization of overexpressed ERBB2 and remains bound to ERBB2 (HER2) homodimers (Maadi et al. 2018). Autophosphorylation of ERBB2 homodimers and downstream signaling is inhibited by trastuzumab (Pickl and Ries 2009). It is unclear whether trastuzumab mainly acts through endocytosis-mediated downregulation of ERBB2 receptor on the cell surface or through interference with the kinase activity. The mechanism of trastuzumab action may also rely on antibody-dependent cellular cytotoxicity (ADCC) (Maadi et al. 2008).

**Literature references**


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Pertuzumab is an ERBB2-directed therapeutic antibody that binds to ERBB2 and sterically blocks receptor dimerization and signaling (Franklin et al. 2004).

**Literature references**


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