Nilotinib-resistant KIT 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


Reactome database release: 78

This document contains 1 pathway and 1 reaction (see Table of Contents)
Nilotinib-resistant KIT mutants

Stable identifier: R-HSA-9669926

Diseases: cancer

Nilotinib is a type II tyrosine kinase inhibitor currently in clinical trials for treatment of KIT-mutant cancers, and shows variable effectiveness against mutations in exon 11, 13, 17 and 18. Nilotinib is ineffective against the gatekeeper mutation T670I (Kissova et al, 2016; Guo et al, 2007; Roberts et al, 2007; Serrano et al, 2019).

Literature references


Editions

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Nilotinib-resistant KIT mutants do not bind nilotinib

Location: Nilotinib-resistant KIT mutants

Stable identifier: R-HSA-9669868

Type: transition

Compartments: plasma membrane

Diseases: cancer

A number of secondary mutations that arise in mutated KIT receptors confer resistance to nilotinib. This is particularly true for the 'gate-keeper' mutation T760I that increases the affinity of the receptor for ATP, rendering it less susceptible to ATP-competitive inhibitors (Kissova et al, 2016; Serrano et al, 2019; Guo et al, 2007; Roberts et al, 2007; reviewed in Klug et al, 2018; Roskoski, 2018).

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