3CLp dimer binds α-Ketoamides

Acencio, ML., Jassal, B.
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: 77

This document contains 1 reaction (see Table of Contents)
3CLp dimer binds α-Ketoamides

**Stable identifier:** R-HSA-9694592

**Type:** omitted

**Compartments:** cytosol

**Diseases:** COVID-19

The rep proteases that are essential for viral polyprotein processing by the coronaviruses and enteroviruses exhibit a strong preference for substrates containing Gln at P1 position, and share an active-site conformation that engages the substrate's P1 residue. PF-00835231, compound 11r and compound 13b are peptidomimetic α-ketoamides that function as high-affinity non-cleavable substrate analogues and thus exhibit antiviral activity against dimeric 3C-like proteinases (3CLp dimer) of coronaviruses and enteroviruses (Chen et al. 2005, Zhang et al. 2020). PF-07321332 contains the amide as part of a heterocycle and is optimized for oral delivery (Vandyck & Deval, 2021).

The clinical safety and efficacy of α-ketoamides in Covid-19 are under investigation. The compound PF-00835231 is in a phase I trial NCT04535167 (as phosphate prodrug), and PF-07321332 is the subject of the phase I trial NCT04756531.

**Literature references**


**Editions**

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