

Product Data Sheet

Product Name: GRL0617

Cat. No.: GC39172

Chemical Properties

Cas. No. 1093070-16-6

SMILES O=C(N[C@@H](C1=CC=CC=CC2=CC=CC=C1)C)C3=CC(N)=CC=C3C

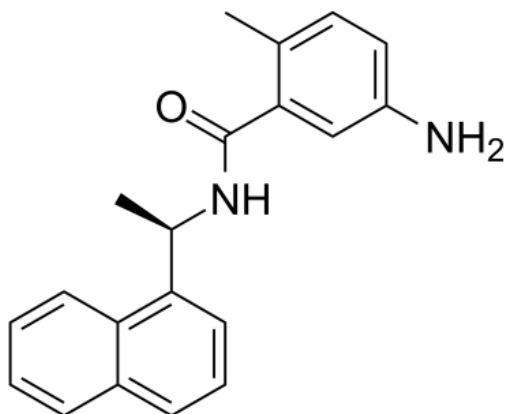
Formula C20H20N2O M.Wt 304.39

Solubility DMSO: 125 mg/mL (410.66 mM) Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution: ship with blue ice. All other available sizes: ship with RT, or blue ice upon request.

Structure



Protocol

Caution: Product has not been fully validated for medical applications. For research use only.

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

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Cell experiment [1]:

Cell lines	Vero E6 cells (African green monkey kidney epithelial cell line) and HEK293T cells (human embryonic kidney cell line)
Preparation Method	Vero E6 cells were cultured in DMEM supplemented with 10% FBS at 37°C, 5% CO ₂ . For antiviral assays, Vero E6 cells were infected with SARS-CoV-2 at MOI=0.01, and treated with GRL0617 (1.56-100µM). HEK293T cells were transfected with plasmids encoding GFP-PLpro, ISG15, E1/E2/E3 enzymes, and treated with GRL0617 (40-160µM) for ISGylation assays.
Reaction Conditions	1.56-100µM; 48h for antiviral assays; 40-160µM for ISGylation inhibition studies.
Applications	GRL0617 exhibited potent antiviral activity against SARS-CoV-2 with EC ₅₀ =21±2µM in Vero E6 cells. GRL0617 significantly inhibited PLpro-mediated deISGylation in HEK293T cells, showing dose-dependent recovery of ISG15-conjugated cellular substrates at concentrations ≥40µM.

References:

[1] Fu Z, Huang B, Tang J et al. The complex structure of GRL0617 and SARS-CoV-2 PLpro reveals a hot spot for antiviral drug discovery. Nat Commun. 2021 Jan 20;12(1):488.

Background

GRL0617 is a selective, competitive non-covalent inhibitor of severe acute respiratory syndrome coronavirus papain-like protease (SARS-CoV PLpro), with an IC₅₀ value of 0.6µM and a K_i value of 0.49µM^[1]. By inhibiting the proteolytic activity of PLpro, GRL0617 blocks the hydrolytic processing of viral polyproteins, thereby significantly reducing the replication efficiency of SARS-CoV-2. Its half-maximal effective concentration (EC₅₀) in Vero E6 cells ranges from 13.1 to 14.5µM^[2]. GRL0617

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effectively inhibits the deISGylating activity of PLpro, restoring the host innate immune pathway mediated by interferon-stimulated gene 15 (ISG15), thereby enhancing the cell's intrinsic immune response against viral infection^[3-4].

In vitro, pretreatment of SARS-CoV-2-infected Vero E6 cells with GRL0617 (1.56–100 μ M) for 24–48 hours significantly reduced viral replication efficiency by inhibiting the proteolytic activity of PLpro^[5]. Treatment of KYSE30 and KYSE510 esophageal squamous cell carcinoma cells with GRL0617 (5–10 μ M) for 24 hours reduced SLC7A11 protein expression levels by inhibiting deubiquitinase activity, significantly suppressing cell proliferation and colony formation ability, while increasing intracellular reactive oxygen species (ROS) levels^[6].

References:

- [1] Ratia K, Pegan S, Takayama J, et al. A noncovalent class of papain-like protease/deubiquitinase inhibitors blocks SARS virus replication. *Proc Natl Acad Sci U S A*. 2008 Oct 21;105(42):16119-24.
- [2] Calleja DJ, Lessene G, Komander D. Inhibitors of SARS-CoV-2 PLpro. *Front Chem*. 2022 Apr 26;10:876212.
- [3] Cho CC, Li SG, Lalonde TJ, et al. Drug Repurposing for the SARS-CoV-2 Papain-Like Protease. *ChemMedChem*. 2022 Jan 5;17(1):e202100455. doi: 10.1002/cmdc.202100455. Epub 2021 Oct 12. Erratum in: *ChemMedChem*. 2022 Mar 4;17(5):e202200053.
- [4] Shen Z, Ratia K, Cooper L, et al. Potent, Novel SARS-CoV-2 PLpro Inhibitors Block Viral Replication in Monkey and Human Cell Cultures. *bioRxiv* [Preprint]. 2021 Feb 15:2021.02.13.431008.
- [5] Fu Z, Huang B, Tang J et al. The complex structure of GRL0617 and SARS-CoV-2 PLpro reveals a hot spot for antiviral drug discovery. *Nat Commun*. 2021 Jan 20;12(1):488.
- [6] Li WT, Jin X, Song SJ, et al. Blocking SLC7A11 attenuates the proliferation of esophageal squamous cell carcinoma cells. *Anim Cells Syst (Seoul)*. 2024 May 11;28(1):237-250.

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