

Product Data Sheet

Product Name: MLS8091

Cat. No.: GC78870

Chemical Properties

Cas. No. 848217-46-9

Formula $C_{21}H_{16}N_4O_2S_2$ M.Wt 420.51

Solubility DMSO: 50 mg/mL (118.90 mM; Need ultrasonic) 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 size: ship with RT, or blue ice upon request.

Structure



Background

MLS8091 is a highly selective inhibitor of the human cytomegalovirus (HCMV) helicase-primase complex with antiviral activity. MLS8091 inhibits HCMV replication during the early and late stages of

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the virus, and suppresses viral DNA replication as well as all HCMV viral proteins. MLS8091 inhibits guinea pig cytomegalovirus replication, and exerts an additive effect when combined with Letemovir. MLS8091 can be used in studies related to human cytomegalovirus infection [1] [2].

In Vitro, MLS8091 (8-10 days) potently inhibits HCMV Towne strain, GCV-resistant HCMV Towne strain, and HCMV TB40 strain in human foreskin fibroblasts (HFFs), with EC₅₀ values ranging from 0.26 to 0.39 μ M, and shows no cytotoxicity at concentrations up to 250 μ M^[1]. MLS8091 exhibits specific anti-HCMV activity and does not inhibit the replication of HSV1, HSV2, MCMV or lytic EBV in relevant cell systems^[1]. MLS8091 inhibits the replication of HCMV Towne in HFF from the early to late stages of the viral life cycle; in add-on assays, its timing of action overlaps with that of GCV, but it exhibits an earlier action effect in washout assays^[1]. MLS8091 (0-10 μ M; 72 h) reduces the expression of IE1, IE2, UL84, UL44 and pp65 proteins of HCMV Towne strain in human foreskin fibroblasts (HFFs)^[1]. MLS8091 (1.5 μ M; 0-120 hpi) significantly inhibits DNA replication of HCMV Towne strain in human foreskin fibroblasts (HFFs)^[1]. MLS8091 (dose based on 2 $\times$ EC₅₀ value; 72 h, 8-10 days) exhibits additive to mild synergistic anti-human cytomegalovirus activity when combined with GCV or Letemovir in human foreskin fibroblasts (HFFs), with a Bliss coefficient of 1.3 for both combinations^[1]. MLS8091 potently inhibits the replication of HCMV Towne strain in human foreskin fibroblasts, with an EC₅₀ of 0.4 μ M; it moderately inhibits the replication of GPCMV in guinea pig lung fibroblasts, with EC₅₀ values of 3.6 μ M and 3.1 μ M in plaque and PCR assays, respectively^[2]. MLS8091 (72 h) induces MLS8091-resistant HCMV Towne mutants (SS-8091-R1, SS-8091-R2, SS-8091-R3) in human foreskin fibroblasts; compared with the EC₅₀ value of 0.4 μ M for wild-type HCMV, the EC₅₀ values of these mutants range from 52.4 to 63.6 μ M (with a resistance fold of 131 to 158.9). This resistance is mediated by the D487Y mutation in the UL70 gene (accompanied by the P165S mutation in the UL102 gene in SS-8091-R1)^[2]. MLS8091 (Varying concentrations; 72 h) induces MLS8091-resistant HCMV Towne mutants (MS-8091-R1, MS-8091-R2, MS-8091-R3) in human foreskin fibroblasts; compared with the EC₅₀ value of 0.4 μ M for wild-type HCMV, these mutants have EC₅₀ values ranging from 58.4 to 88.6 μ M (with a resistance fold change of 145.9 to 221.6), and this resistance is mediated by UL102F275L or UL70D486H mutations^[2]. MLS8091 (0.1-10 μ M; 10 days) demonstrates that UL70D487Y and UL70D486H mutations both confer full resistance to MLS8091 in HCMV Towne strain. In human foreskin fibroblasts, neither mutant virus strain receives inhibitory effects under treatment with up to 10 μ M MLS8091, while wild-type HCMV

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displays dose-dependent viral suppression^[2]. MLS8091 (0.1-10 μ M; 10 days) exhibits drastically weakened antiviral activity against tagged UL70D487Y mutant HCMVAD169 in human foreskin fibroblasts: the EC₅₀ value reaches 40.84 μ M with a 97.3-fold resistance shift, whereas wild-type HCMVAD169 has an EC₅₀ of 0.42 μ M^[2]. MLS8091 (0.1–10 μ M; 96 h) fails to suppress the expression of HCMVAD169 viral proteins (IE1/2, UL44, UL84, pp65) in human foreskin fibroblasts if the virus harbors the UL70D487Y mutation^[2]. MLS8091 (0.1-10 μ M; 4 days) loses strong inhibitory activity against HCMV AD169 viral load in human foreskin fibroblast supernatants when virus carries the UL70D487Y mutation^[2]. MLS8091 (0.1-10 μ M; 48 h) reveals that the UL70D487Y mutation abolishes the inhibitory activity of MLS8091 against HCMV AD169 viral DNA replication in human foreskin fibroblasts^[2].

References:

- [1]. Kapoor A, et al. Validation and Characterization of Five Distinct Novel Inhibitors of Human Cytomegalovirus. *Journal of medicinal chemistry*. 2020 Apr 23;63(8):3896-3907.
- [2]. Kapoor A, et al. A novel inhibitor of human cytomegalovirus acts through a specific antiviral mechanism that involves the helicase-primase complex. *Antimicrobial agents and chemotherapy*. 2026 Jul 13.

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