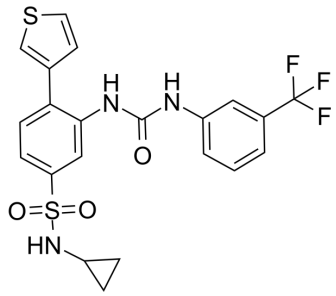
AGI-6780

Cat. No.:	HY-15734
CAS No.:	1432660-47-3
Molecular Formula:	$C_{21}H_{18}F_3N_3O_3S_2$
Molecular Weight:	481.51
Target:	Isocitrate Dehydrogenase (IDH)
Pathway:	Metabolic Enzyme/Protease
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 29 mg/mL (60.23 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.0768 mL	10.3840 mL	20.7680 mL
5 mM	0.4154 mL	2.0768 mL	4.1536 mL
10 mM	0.2077 mL	1.0384 mL	2.0768 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (5.19 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.19 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

AGI-6780 that potently and selectively inhibits the tumor-associated mutant $IDH2^{R140Q}$ with IC_{50} of 23±1.7 nM. AGI-6780 is less potent against $IDH2^{WT}$ with IC_{50} of 190±8.1 nM.

IC_{50} & Target

IC50: 23±1.7 nM ($IDH2^{R140Q}$), 190±8.1 nM ($IDH2^{WT}$)[1]

In Vitro

AGI-6780 is tested in both human glioblastoma U87 and TF-1 cells expressing $IDH2^{R140Q}$, as well as against $IDH1^{R132H}$ for 48 h incubation, with IC50 of 11±2.6 nM, 18±0.51 nM, and >1 mM, respectivly.Treatment of TF-1^{R140Q} cells with AGI-6780, at concentrations that lower 2HG to near-normal physiologic levels, restore expression of both HBG and KLF1 genes and the color change associated with differentiation. AGI-6780 can reverse the $IDH2^{R140Q}$-induced differentiation block in TF-1 cells.

Pretreatment with AGI-6780 (0.2 μM and 1 μM) markedly decreased the intracellular concentration of (R)-2-hydroxyglutarate in the $TF1^{R140Q}$ cells and restored their ability to undergo EPO-induced differentiation[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]

AGI-6780 is prepared as 10 mM stock in DMSO and diluted to 50X final concentration in DMSO, for a 50 μL reaction mixture. IDH enzyme activity converting alpha-ketoglutarate to 2-hydroxyglutarate is measured using a NADPH depletion assay. In the assay the remaining cofactor is measured at the end of the reaction with the addition of a catalytic excess of diaphorase and resazurin, to generate a fluorescent signal in proportion to the amount of NADPH remaining. IDH enzyme activity in the direction of isocitrate to alpha-ketoglutarate conversion is measured by direct coupling of the NADPH production to conversion of resazurin to resorufin by diaphorase. In both cases, resorufin is measured fluorometrically at Ex544 Em590[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Assay [1]

Cells are sorted from fresh or frozen bone marrow aspirates and blood samples after labelling with PE-CD34, APC-CD38, PE-CD14, FITC-CD3 (clone HIT3a) and PECy7-CD19 (clone SJ25C1) antibodies using a MoFlow cell sorter. Unfractionated nucleated blood or bone marrow cells are plated in Methocult H4434 methylcellulose medium at 10^4 cells/dish, in duplicate dishes per condition. AGI-6780 (5 mM) is directly added to the medium. Dishes are incubated in a humidified incubator at 37°C and colonies containing at least 30 cells are counted after 13 days[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell Metab. 2020 Dec 8;S1550-4131(20)30655-0.
- Clin Cancer Res. 2018 Apr 1;24(7):1705-1715.
- Cell Commun Signal. 2020 Apr 3;18(1):55.
- J Med Chem. 2023 Mar 23.
- Oncol Rep. 2018 Aug;40(2):635-646.

See more customer validations on www.MedChemExpress.com

REFERENCES

[1]. Wang F, et al. Targeted inhibition of mutant IDH2 in leukemia cells induces cellular differentiation. Science. 2013 May 3;340(6132):622-6.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA