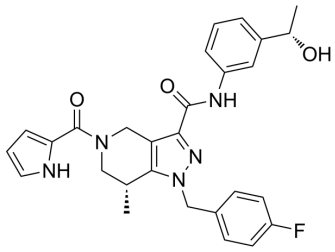
GSK321

Cat. No.:	HY-18948
CAS No.:	1816331-63-1
Molecular Formula:	$C_{28}H_{28}FN_5O_3$
Molecular Weight:	501.55
Target:	Isocitrate Dehydrogenase (IDH)
Pathway:	Metabolic Enzyme/Protease
Storage:	4°C, protect from light * In solvent : -80°C, 6 months; -20°C, 1 month (protect from light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 250 mg/mL (498.45 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9938 mL	9.9691 mL	19.9382 mL
	5 mM	0.3988 mL	1.9938 mL	3.9876 mL
	10 mM	0.1994 mL	0.9969 mL	1.9938 mL

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

BIOLOGICAL ACTIVITY

Description

GSK321 is a potent inhibitor of mutant isocitrate dehydrogenase 1 (IDH1) enzymes. GSK321 has high inhibitory and selectivity for mutant IDH1 enzymes. GSK321 can be used for the research of acute myeloid leukemia[1][2].

IC_{50} & Target

IC50 for mutant IDH1 enzymes: 4.6 nM (R132H), 3.8 nM (R132C), 2.9 nM (R132G)[1].

In Vitro

GSK321 has high inhibitory for mutant IDH1 enzymes, with IC_{50} values of 4.6 nM against R132H, 3.8 nM against R132C and 2.9 nM against R132G, respectively[1].

GSK321 (0, 0.5, 5 μM; 48 h) induces markedly decreased H3K9me2 levels[1].

GSK321 decreases intracellular 2-HG and affects proliferation of primary IDH1 mutant AML cells[1].

GSK321 has inhibition activity for mutant IDH1 that overcomes the pathognomonic differentiation block of AML cells, and induces myeloid differentiation of IDH1 mutant cells at the level of leukemic blasts and more stem-like cells[1].

GSK321 leads to genome-wide DNA cytosine hypomethylation in IDH1-mutant AML cells[1].

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

Western Blot Analysis[1]

Cell Line:	HT-1080 cells

Concentration:	0, 0.5, 5 μM
Incubation Time:	48 h
Result:	Lead to the reduction of histone H3K9 dimethylation (H3K9me2).

Cell Proliferation Assay[1]

Cell Line:	IDH1 mutant AML cells
Concentration:	3 μM
Incubation Time:	15 days
Result:	Showed a significant, initial increase in cell numbers (2-fold to 15-fold) in IDH1 mutant AML cells.

Cell Cycle Analysis[1]

Cell Line:	IDH1 mutant AML cells
Concentration:	
Incubation Time:	7 days
Result:	Observed a reproducible and significant decrease in quiescent (G0)-phase cells in R132G IDH1 and R132C IDH1 AML cells.

REFERENCES

[1]. Ujunwa C Okoye-Okafor, et al. New IDH1 mutant inhibitors for treatment of acute myeloid leukemia. Nat Chem Biol. 2015 Nov;11(11):878-86.

[2]. Stuart Jones, et al. Discovery and Optimization of Allosteric Inhibitors of Mutant Isocitrate Dehydrogenase 1 (R132H IDH1) Displaying Activity in Human Acute Myeloid Leukemia Cells. J Med Chem. 2016 Dec 22;59(24):11120-11137.

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