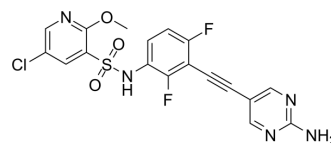


GCN2iB

Cat. No.:	HY-112654		
CAS No.:	2183470-12-2		
Molecular Formula:	C ₁₈ H ₁₂ ClF ₂ N ₅ O ₃ S		
Molecular Weight:	451.83		
Target:	Eukaryotic Initiation Factor (eIF); Autophagy		
Pathway:	Cell Cycle/DNA Damage; Autophagy		
Storage:	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	6 months
		-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro	DMSO : 16.67 mg/mL (36.89 mM; Need ultrasonic)				
		Solvent Concentration	Mass 1 mg	5 mg	10 mg
	Preparing Stock Solutions	1 mM	2.2132 mL	11.0661 mL	22.1322 mL
		5 mM	0.4426 mL	2.2132 mL	4.4264 mL
10 mM		0.2213 mL	1.1066 mL	2.2132 mL	
Please refer to the solubility information to select the appropriate solvent.					
In Vivo	<ol style="list-style-type: none"> Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline Solubility: ≥ 1.67 mg/mL (3.70 mM); Clear solution Add each solvent one by one: 10% DMSO >> 90% corn oil Solubility: ≥ 1.67 mg/mL (3.70 mM); Clear solution 				

BIOLOGICAL ACTIVITY

Description	GCN2iB is an ATP-competitive inhibitor of a serine/threonine-protein kinase general control nonderepressible 2 (GCN2), with an IC ₅₀ of 2.4 nM.
IC₅₀ & Target	IC ₅₀ : 2.4 nM (GCN2) ^[1] .
In Vitro	GCN2iB shows an IC ₅₀ value of 2.4 nM for GCN2 and potent cellular activity. In a panel of 468 kinases, only GCN2 shows >99.5% inhibition, and three kinases (MAP2K5, STK10, and ZAK) show >95% inhibition at 1 μM GCN2iB, demonstrating high kinase selectivity ^[1] . MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

In the antitumor activity study of the CCRF-CEM xenografts, ASNase or GCN2iB alone does not significantly affect tumor growth. Notably, a combination of ASNase and GCN2iB elicit potent antitumor activity ($P=0.0002$) with synergistic effects. In MV-4-11 and SU.86.86 xenografts, robust antitumor activity of the combination of GCN2iB and ASNase is observed with synergistic effect, respectively. ASNase/GCN2iB-treated tumors do not show significant growth even after drug cessation. The combination of ASNase and GCN2iB yield survival advantage compared with the vehicle treated control with synergistic effect^[1].

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

PROTOCOL

Animal Administration ^[1]

Mice^[1]

A suspension of CCRF-CEM, HPB-ALL, MV-4-11, or SU.86.86 cells (1×10^7 cells/site) is subcutaneously injected into the right flanks of 6-week-old female SCID mice. Tumor volume is calculated as $\text{volume} = L \times l^2 \times 1/2$, where L represents the longest diameter across the tumor and l represents the corresponding perpendicular distance. Body weight is also measured. To assess the anti-tumor activity, mice with tumor mass $\sim 200 \text{ mm}^3$ are sorted into treatment groups ($N=5/\text{group}$). The tumors are monitored and mice are euthanized when an endpoint is reached, or at the end of the study, whichever comes first. From the next day of randomization, GCN2 inhibitors (e.g., GCN2iB, 10 mpk, twice a day) or ASNase is orally or intraperitoneally administered to mice bearing the xenografts for 7 to 10 days, respectively. T/C (%), an index of anti-tumor activity, is calculated by comparing the mean change in tumor volume during the treatment period in the control and treated groups^[1].

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

CUSTOMER VALIDATION

- Nat Chem Biol. 2021 Jun;17(6):665-674.
- EMBO Rep. 2022 Jan 7;e53373.
- Sci Total Environ. 2021, 146730.
- Cell Discov. 2021 Oct 26;7(1):98.
- J Biol Chem. 2021 Sep 28;101257.

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REFERENCES

[1]. Nakamura A, et al. Inhibition of GCN2 sensitizes ASNS-low cancer cells by disrupting the amino acid response. Proc Natl Acad Sci U S A. 2018 Aug 14;115(33):E7776-E7785.

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

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