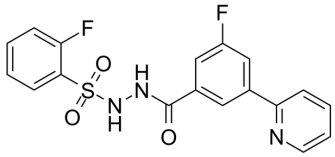
WM-1119

Cat. No.:	HY-102058
CAS No.:	2055397-28-7
Molecular Formula:	$C_{18}H_{13}F_2N_3O_3S$
Molecular Weight:	389.38
Target:	Histone Acetyltransferase
Pathway:	Epigenetics
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 : 125 mg/mL (321.02 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.5682 mL	12.8409 mL	25.6819 mL
	5 mM	0.5136 mL	2.5682 mL	5.1364 mL
	10 mM	0.2568 mL	1.2841 mL	2.5682 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.42 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (5.34 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (5.34 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

WM-1119 is a highly potent and selective KAT6A inhibitor, with an IC_{50} of 0.25 μM for KAT6A in lymphoma cells, the binding K_D values of WM-1119 with KAT6A, KAT5 and KAT7 are 2 nM, 2.2 μM, 0.5 μM , respectively[1].

IC_{50} & Target

IC50: 0.25 μM (KAT6A in lymphoma cells), KD: 2 nM (KAT6A), 2.2 μM (KAT5), 0.5 μM (KAT7)[1].

In Vitro

WM-1119 induces cell cycle exit and cellular senescence without causing DNA damage. WM-1119 is 1,100-fold and 250-fold more active against KAT6A than against KAT5 or KAT7, respectively, and so shows greater specificity for KAT6A than does

	WM-8014. Treatment of MEFs with WM-1119 results in cell cycle arrest in G1 and a senescence phenotype similar to that seen upon treatment with WM-8014. Notably, the activity of WM-1119 in this cell-based assay is an order of magnitude greater than WM-8014 and WM-1119 is able to induce cell cycle arrest at 1 μM. Treatment with WM-1119 inhibits the proliferation of the EMRK1184 lymphoma cells in vitro, WM-1119 (IC_{50}=0.25 μM) is ninefold more active than WM-8014 (IC_{50}=2.3 μM), as expected on the basis of reduced protein binding[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	By day 14, the cohorts that are treated four times per day with WM-1119 have arrested tumour growth, with the exception of one mouse that does not respond. Spleen weights in the WM-1119-treatment group (treated four times per day) are substantially lower than spleen weights in the vehicle-treated group. Treatment with WM-1119 three times per day leads to a significant reduction in tumour burden and spleen weight, but is not as effective as treatment four times per day. WM-1119 is well-tolerated; mice show no generalized ill effects and weight loss is not observed. The proportion and overall number of tumour cells is substantially reduced by WM-1119 treatment (four times per day)[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [1]	Mice[1] Male C57BL/6-albino (B6(Cg)-Tyr^{c-2J}/J) mice are injected intravenously with 100,000 EMRK1184 cells transfected with a luciferase-expression construct. Lymphoma growth is monitored. Three days after the lymphomacell transplant, all mice show luciferase activity, which indicate the expansion of lymphoma cells. Mice are then divided randomly into WM-1119-treatment with different conentrations (1, 2.5, 5, 10 μM) and vehicle-control groups. Because WM-1119 is rapidly cleared after intraperitoneal injection, with the plasma concentration decreasing to below 1 μM after 4-6 h cohorts of mice are injected every 8 h (three times per day, two cohorts of three mice per treatment group) or every 6 h (four times per day, two cohorts of three and six mice per treatment group)[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cancer Discov. 2022 May 2;candisc.0646.2021.
- Cancer Discov. 2022 Mar 1;12(3):792-811.
- Oncogene. 2021 Apr;40(15):2711-2724.
- University of Pennsylvania. 2022 Jan 1.

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REFERENCES

[1]. Baell JB et al. Inhibitors of histone acetyltransferases KAT6A/B induce senescence and arrest tumour growth. Nature. 2018 Aug;560(7717):253-257.

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