Salirasib

Cat. No.: HY-14754

CAS No.: 162520-00-5

Molecular Formula: $C_{22}H_{30}O_2S$

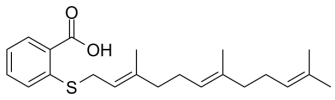
Molecular Weight: 358.54

Target: Ras; Autophagy

Pathway: GPCR/G Protein; Autophagy

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 : ≥ 50 mg/mL (139.45 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.7891 mL	13.9454 mL	27.8909 mL
	5 mM	0.5578 mL	2.7891 mL	5.5782 mL
	10 mM	0.2789 mL	1.3945 mL	2.7891 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 (6.97 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (6.97 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.97 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Salirasib is a Ras inhibitor that inhibits specifically both oncogenically activated Ras and growth factor receptor-mediated Ras activation, resulting in the inhibition of Ras-dependent tumor growth.

IC_{50} & Target

Ki: 2.6 μM (PPMTase)

In Vitro

Salirasib (12.5-100 μM) inhibits the proliferation of ELT3 cells in a dose-dependent manner with an average IC_{50} of

	58.57±4.59 μM. The effects of Salirasib on the TSC2-null cells are evidently mimicked by DN-Rheb but not by DN-Ras. Salirasib reduces Rheb in TSC2-null cells and TSC2 expression rescues the cells from the inhibitory effect of Salirasib. Salirasib reduces phosphorylation of S6K but not of ERK in the TSC2-null ELT3 cells[1]. Salirasib (50, 100, 150 μM) induces a dose- and time-dependent decrease of cell growth in HCC cells. Salirasib reduces cell proliferation through modulation of cell cycle effectors and inhibitors. Salirasib induces apoptosis in HepG2 and Hep3B cells. The growth inhibitory effect of salirasib in HCC cell lines is associated with mTOR inhibition independent of ERK or Akt activation[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Salirasib (40, 60 or 80 mg/kg, p.o.) significantly inhibits the tumor growth in a dose dependent manner in vivo[1]. Salirasib (5 mg/kg, i.p.) significantly decreases Ras expression in the dy^{2J}/dy^{2J}mice, and causes an increase in Ras expression which is by far much lower than the increase observed in the dy^{2J}/dy^{2J} mice. Salirasib treatment is associated with significantly inhibition of both MMP-2 and MMP-9 activities in the dy^{2J}/dy^{2J} mice[2]. Salirasib (10 mg/kg, i.p.) inhibits tumour growth in a subcutaneous xenograft mice model without weight loss[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [3]	For time dependent response studies, cells are harvested with 0.05% Trypsin-EDTA daily for 1 to 7 days and counted under the microscope using the Trypan blue exclusion method.For dose response studies, cells are incubated in medium supplemented with salirasib or DMSO for 3 days. Cell viability is determined using a colorimetric WST-1 assay according to the manufacturer's instructions. The IC_{50} value, at which 50% of the cell growth is inhibited compared with DMSO control, is calculated by nonlinear regression analysis using GraphPad Prism software. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [3]	Six week old female athymic NMRI nu/nu mice are housed in filter-topped cages andreceive food and water ad libitum. Tumors are generated by subcutaneous injection into the right lower flank with 5×10^6 HepG2 cells suspended in 100 μL PBS in 12 mice. Two weeks after cell inoculation, when palpable tumours are established, mice are separated into salirasib-treated (n=6) and control group (n=4). Two animals do not develop tumours at that time point and had to be excluded from the study. They receive daily i.p. injections of 10 mg/kg salirasib or a similar volume of vehicle solution (PBS containing 2.5% v/v ethanol, pH 8.0) for 12 days. Tumor dimensions are recorded three times per week with a digital calliper starting with the first day of treatment. Tumor volumes are estimated as follows: $V\ (mm^3)=(length\times width^2)/2$. Tumour weights are recorded at the time of sacrifice in order to evaluate treatment response. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Adv Sci (Weinh). 2021 Jan 29;8(6):2002831.
- Cell Death Dis. 2018 Dec 5;9(12):1170.
- Life Sci. 2021 Mar 9;274:119332.
- Int J Pharm. 2019 Dec 15;572:118823.
- Lab Invest. 2022 Aug 17.

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REFERENCES

[1]. Makovski V, et al. Farnesylthiosalicylic acid (salirasib) inhibits Rheb in TSC2-null ELT3 cells: a potential treatment for lymphangioleiomyomatosis. Int J Cancer. 2012 Mar

15;130(6):1420-9.

[2]. Nevo Y, et al. Chapman J. The Ras antagonist, farnesylthiosalicylic acid (FTS), decreases fibrosis and improves muscle strength in dy/dy mouse model of muscular dystrophy. PLoS One. 2011 Mar 22;6(3):e18049.

[3]. Charette N, et al. Salirasib inhibits the growth of hepatocarcinoma cell lines in vitro and tumor growth in vivo through ras and mTOR inhibition. Mol Cancer. 2010 Sep 22;9:256.

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