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产品名称：Salirasib

产品别名： S-Farnesylthiosalicylic acid; Farnesyl Thiosalicylic Acid; FTS；法尼基硫代水杨酸

生物活性：

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].
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].
Solvent&Solubility	***In Vitro:*** **DMSO : ≥ 50 mg/mL (139.45 mM)** **H_2O : < 0.1 mg/mL** (insoluble) * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / 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

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

In Vivo:

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 In Vitro 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

	1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline Solubility: ≥ 2.5 mg/mL (6.97 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.97 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。 2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline) Solubility: 2.5 mg/mL (6.97 mM); Suspended solution; Need ultrasonic 此方案可获得 2.5 mg/mL (6.97 mM)的均匀悬浊液，悬浊液可用于口服和腹腔注射。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (6.97 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.97 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
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.

实验参考：

Cell Assay	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. [3]
Animal Administration	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×$width^2$)/2. Tumour weights are recorded at the time of sacrifice in order to

	evaluate treatment response. [3]
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.