产品名称：Tenovin 6
产品别名：Tenovin-6

生物活性：

Description	Tenovin-6 is an inhibitor of SIRT1 and SIRT2, slightly inhibits HDAC8, and is also a potent activator of p53, with IC_{50}s of 21 μM, 10 μM, and 67 μM for SirT1, SirT2, and SirT3, respectively.

IC_{50} & Target	SIRT2	SIRT1	SIRT3	HDAC8	MDM-2/p53
	10 μM (IC_{50})	21 μM (IC_{50}	67 μM (IC_{50})		

In Vitro

Tenovin-6 inhibits the growth of S. cerevisiae cultures with an IC50 of 30 μM and is more toxic to yeast than the less water-soluble tenovin-1. Tenovin-6 rapidly increases the levels of endogenous K382-Ac p53 in MCF-7 cells[1]. Tenovin-6 (0 to 15 μM) dose dependently increases the level of LC3-II in diverse cell types, and the increase is ATG5/7 dependent. Tenovin-6 treatment also increases the number and intensity of autophagic vesicles with or without the presence of Torin 1, and prevents Torin 1-induced SQSTM1/p62 degradation. Tenovin-6 affects the acidification of autolysosomes and impairs the hydrolytic activity of lysosomes but does not affect the fusion between autophagosomes and lysosomes. That tenovin-6 inhibits autophagy does not correlate with p53 activation and SIRT1/2 inhibition by knockdown or knockout cannot mimic the effect of tenovin-6 on LC3B accumulation[2]. Tenovin-6 (0, 1, 2.5, 5 or 10 μM) potently inhibits cell proliferation in a dose- and time-dependent manner in all OCI-Ly1, DHL-10, U2932, RIVA, HBL1 and OCI-Ly10 cell lines. Tenovin-6 consistently increases LC3B-II level in DLBCL cell lines by inhibiting the classical autophagy pathway, without activating p53, and the increase is independent of SIRT1/2/3 and p53. Tenovin-6 induces apoptosis through the extrinsic cell-death pathway[3]. Tenovin-6 suppresses the growth of UM cells with IC50 of 12.8 μM, 11.0 μM, 14.58 μM and 9.62 μM for 92.1, Mel 270, Omm 1 and Omm 2.3 cells, respectively[4].

In Vivo

Tenovin-6 (50 mg/kg, i.p.) inhibits the growth of tumor in mice[1].

Solvent&Solubility

In Vitro:

DMSO : ≥ 31 mg/mL (68.19 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.1996 mL	10.9980 mL	21.9959 mL
	5 mM	0.4399 mL	2.1996 mL	4.3992 mL
	10 mM	0.2200 mL	1.0998 mL	2.1996 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 (5.50 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.50 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 (5.50 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.50 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 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。
References	[1]. Lain S, et al. Discovery, in vivo activity, and mechanism of action of a small-molecule p53 activator. Cancer Cell. 2008 May;13(5):454-63. [2]. Dai W, et al. Class III-specific HDAC inhibitor Tenovin-6 induces apoptosis, suppresses migration and eliminates cancer stem cells in uveal melanoma. Sci Rep. 2016 Mar 4;6:22622. [3]. Yuan H, et al. Tenovin-6 impairs autophagy by inhibiting autophagic flux. Cell Death Dis. 2017 Feb 9;8(2):e2608. [4]. Yuan H, et al. Tenovin-6 inhibits proliferation and survival of diffuse large B-cell lymphoma cells by blocking autophagy. Oncotarget. 2017 Feb 28;8(9):14912-14924.

实验参考：

Cell Assay	The MTS assay is used to evaluate cell viability. UM cells are seeded into each well of 96-well plates (5,000 cells/well) and treated the next day with control or Tenovin-6 in an increasing concentrations from 0 to 20 μM for 68 h, and then MTS is added at 20 μL/well to be read at a wave length of 490 nm, the IC_{50} is determined by curve fitting of the sigmoidal dose-response curve. [4]
Animal Administration	Female SCID mice are injected subcutaneously with 1×10^6 ARN8 cells suspended in matrigel. Tumors are allowed to reach a size of approximately 10 mm^3. Tenovin-6 is administered daily at 50 mg/kg by intraperitoneal injection. Control animals are treated with vehicle solution containing cyclodextrin 20% (w/v) and DMSO 10% (v/v). Tumor diameters are measured using calipers, and volumes are calculated using the equation $V=\pi4/3[(d1 + d2)/4]^3$. Median values of tumor size are calculated for each time point as well as the corresponding 95% confidence intervals. Comparison of control and drug-treated tumor size distributions are made by Mann-Whitney U-test. An alpha-level of 0.05 is considered appropriate for determination of statistical significance. [1]
Kinase Assay	Assays are carried out using purified components in the Fluor de Lys Fluorescent Assay Systems. Relevant FdL substrates are used at 7 μM and NAD^+ at 1 mM. Tenovins are solubilized in DMSO with the final DSMO concentration in the reaction being less than 0.25%. For SirT1 and HDAC8, one unit of enzyme is used per reaction, and for SirT2 and SirT3, five units is used per reaction. Reactions are carried out at 37°C for 1 hr. [1]

References	[1]. Lain S, et al. Discovery, in vivo activity, and mechanism of action of a small-molecule p53 activator. Cancer Cell. 2008 May;13(5):454-63. [2]. Dai W, et al. Class III-specific HDAC inhibitor Tenovin-6 induces apoptosis, suppresses migration and eliminates cancer stem cells in uveal melanoma. Sci Rep. 2016 Mar 4;6:22622. [3]. Yuan H, et al. Tenovin-6 impairs autophagy by inhibiting autophagic flux. Cell Death Dis. 2017 Feb 9;8(2):e2608. [4]. Yuan H, et al. Tenovin-6 inhibits proliferation and survival of diffuse large B-cell lymphoma cells by blocking autophagy. Oncotarget. 2017 Feb 28;8(9):14912-14924.