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产品名称: **Tenovin 6 (Hydrochloride)**

产品别名: **Tenovin-6 Hydrochloride**

生物活性:					
Description	Tenovin-6 Hydrochloride is an inhibitor of SIRT1 and SIRT2, slightly inhibits HDAC8, and is also a potent activator of p53, with IC50s of 21 μ M, 10 μ M, and 67 μ M for SirT1, SirT2, and SirT3, respectively.				
IC ₅₀ & Target	SIRT2	SIRT1	SIRT3	HDAC8	MDM-2/p53
	10 μ M (IC ₅₀)	21 μ M (IC ₅₀)	67 μ M (IC ₅₀)		
In Vitro	Tenovin-6 inhibits the growth of <i>S. cerevisiae</i> 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].				
Solvent&Solubility	In Vitro: DMSO : $\geq$ 49 mg/mL (99.78 mM) * " $\geq$ " means soluble, but saturation unknown.				
	Preparing Stock Solutions	Solvent	Mass	1 mg	5 mg
		Concentration			
		1 mM	2.0363 mL	10.1814 mL	20.3629 mL
		5 mM	0.4073 mL	2.0363 mL	4.0726 mL
		10 mM	0.2036 mL	1.0181 mL	2.0363 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。					
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				



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	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 IC₅₀ 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 mm³. 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 $V = \pi d^3 / 6$. 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 DMSO 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.