

产品名称: VER 155008

产品别名: VER-155008

生物活性:

Description	VER-155008 is an inhibitor of Hsp70, with IC50s of 0.5 μM, 2.6 μM, and 2.6 μM for Hsp70, Hsc70 and Grp7, respectively, and with a Kd of 0.3 μM for Hsp70.				
IC50 & Target	HSP70	HSC70	Grp78		
	0.5 μM (IC50)	2.6 μM (IC50)	2.6 μM (IC50)		
In Vitro	VER-155008 is an inhibitor of Hsc70 and Hsp70, with IC50s of 0.5 μM, 2.6 μM, and 2.6 μM for Hsp70, Hsc70 and Grp7, respectively, a with a Ka of 0.3 μM for Hsp70, but shows no activities against Hsp90, with an IC50 of >200 μM. VER-155008 inhibits the proliferation of a variety of human colon and breast tumor cell lines, such as BT474, MB-468, HCT116 and HT29 cells, with GI50s of 10.4 μM, 14.4 μM, 5.3 μM, and 12.8 μM, respectively. VER-155008 (5-40 μM) induces client protein degradation in HCT116 and BT474 carcinoma cells. VER-155008 also induces apoptosis in human tumor cell lines[1]. VER-155008 (0.05-5 μM) reverses Aβ-induced axonal degeneration in cultured neurons[2]. VER-155008 (10 μM or 25 μM) inhibits Hsp70 and suppresses the proliferation of LNCaP95 cells. VER-155008 also reduces full-length androgen receptor (AR-FL) and androgen receptor splice variant 7 (AR-V7) protein expression[3].				
In Vivo	VER-155008 (25 mg/kg, i.v.) exhibits plasma clearance in naive female BALB/c mice. VER-155008 (40 mg/kg, i.v.) also shows rapid plasma clearance, and reduces the tumor levels in the HCT116 tumor bearing nude BALB/c mice[1]. VER-155008 (10 μmol/kg/day, i.p.) rescues memory deficits, and reduces axonal swelling associated with amyloid plaques in 5XFAD mice. VER-155008 (89.9 μmol/kg/day, i.p.) penetrates into the brain after administration in 5XFAD mice. VER-155008 also decreases amyloid plaques and PHF-tau associated with amyloid plaques in 5XFAD mice[2].				
Solvent&Solubility	<b>In Vitro:</b> <b>DMSO : ≥ 37 mg/mL (66.50 mM)</b>  * "≥" means soluble, but saturation unknown.				
		<div>SolventMassConcentration</div>	1 mg	5 mg	10 mg
	Preparing	1 mM	1.7973 mL	8.9863 mL	17.9727 mL
	Stock Solutions	5 mM	0.3595 mL	1.7973 mL	3.5945 mL
		10 mM	0.1797 mL	0.8986 mL	1.7973 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℃, 6 months; -20℃, 1 month。 -80℃ 储存时，请在 6 个月内使用， -20℃ 储存时，请在 1 个月内使用。				
	<b>In Vivo:</b>				
	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 <b>In Vitro</b> 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 (4.49 mM); Clear solution					

	<p>此方案可获得 <math>\geq 2.5</math> mg/mL (4.49 mM, 饱和度未知) 的澄清溶液。</p> <p>以 1 mL 工作液为例, 取 100 <math>\mu</math>L 25.0 mg/mL 的澄清 DMSO 储备液加到 400 <math>\mu</math>L PEG300 中, 混合均匀向上述体系中加入 50 <math>\mu</math>L Tween-80, 混合均匀; 然后继续加入 450 <math>\mu</math>L 生理盐水定容至 1 mL。</p> <p>2. 请依序添加每种溶剂: 10% DMSO <math>\rightarrow</math> 90% (20% SBE-<math>\beta</math>-CD in saline) Solubility: <math>\geq 2.5</math> mg/mL (4.49 mM); Clear solution</p> <p>此方案可获得 <math>\geq 2.5</math> mg/mL (4.49 mM, 饱和度未知) 的澄清溶液。</p> <p>以 1 mL 工作液为例, 取 100 <math>\mu</math>L 25.0 mg/mL 的澄清 DMSO 储备液加到 900 <math>\mu</math>L 20% 的 SBE-<math>\beta</math>-CD 生理盐水平溶液中, 混合均匀。</p> <p>3. 请依序添加每种溶剂: 10% DMSO <math>\rightarrow</math> 90% corn oil Solubility: <math>\geq 2.5</math> mg/mL (4.49 mM); Clear solution</p> <p>此方案可获得 <math>\geq 2.5</math> mg/mL (4.49 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。</p> <p>以 1 mL 工作液为例, 取 100 <math>\mu</math>L 25.0 mg/mL 的澄清 DMSO 储备液加到 900 <math>\mu</math>L 玉米油中, 混合均匀。</p>
References	<p>[1]. Massey AJ, et al. A novel, small molecule inhibitor of Hsc70/Hsp70 potentiates Hsp90 inhibitor induced apoptosis in HCT116 colon carcinoma cells. <i>Cancer Chemother Pharmacol.</i> 2010 Aug;66(3):535-45.</p> <p>[2]. Yang X, et al. Heat Shock Cognate 70 Inhibitor, VER-155008, Reduces Memory Deficits and Axonal Degeneration in a Mouse Model of Alzheimer's Disease. <i>Front Pharmacol.</i> 2018 Jan 30;9:48.</p> <p>[3]. Kita K, et al. Heat shock protein 70 inhibitors suppress androgen receptor expression in LNCaP95 prostate cancer cells. <i>Cancer Sci.</i> 2017 Sep;108(9):1820-1827.</p>
实验参考:	
Cell Assay	<p>Embryos are removed from a pregnant ddY mouse at 14 days of gestation. Cells are treated with or without 10 <math>\mu</math>M A<math>\beta</math>25-35 for 3 days, followed by the addition of 0.05, 0.5, or 5 <math>\mu</math>M VER-155008 or vehicle solution (0.1% DMSO) for 4 days. The A<math>\beta</math>25-35 is incubated at 37°C for 4 days prior to treatment to facilitate aggregation. The cells are fixed with 4% paraformaldehyde and immunostained at 4°C for 24 h with antibodies against the axonal marker, mouse phosphorylated neurofilament heavy subunit, and against the neuronal marker, rabbit microtubule-associated protein 2. Alexa Fluor 488-conjugated goat anti-mouse IgG (1:400) and Alexa Fluor 568-conjugated goat anti-rabbit IgG (1:400) are used as secondary antibodies. Fluorescence images (864.98 <math>\mu</math>m <math>\times</math> 645.62 <math>\mu</math>m) are captured using a fluorescence microscopy system. The lengths of the pNF-H-positive axons are measured using MetaMorph version 7.8[2].</p>
Animal Administration	<p>Female BALB/c mice are dosed intravenously with 25 mg/kg VER-155008 into the lateral tail vein as a solution in 10% DMSO/5% Tween 80/85% saline (v/v/v). Animals are sacrificed at 5, 15 and 30 min, 1, 2, 4 and 6 h post dose[1].</p>
References	<p>[1]. Massey AJ, et al. A novel, small molecule inhibitor of Hsc70/Hsp70 potentiates Hsp90 inhibitor induced apoptosis in HCT116 colon carcinoma cells. <i>Cancer Chemother Pharmacol.</i> 2010 Aug;66(3):535-45.</p> <p>[2]. Yang X, et al. Heat Shock Cognate 70 Inhibitor, VER-155008, Reduces Memory Deficits and Axonal Degeneration in a Mouse Model of Alzheimer's Disease. <i>Front Pharmacol.</i> 2018 Jan 30;9:48.</p> <p>[3]. Kita K, et al. Heat shock protein 70 inhibitors suppress androgen receptor expression in</p>



源叶生物