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产品名称: OTSSP167 (hydrochloride)

产品别名: OTSSP167 hydrochloride

生物活性:				
Description	OTSSP167 (hydrochloride) is a highly potent MELK inhibitor with IC ₅₀ value of 0.41 nM.			
IC ₅₀ & Target	IC ₅₀ : 0.41 nM (MELK)			
In Vitro	OTSSP167 inhibits the growth of A549 (lung), T47D (breast), DU4475 (breast), 22Rv1 (prostate) and HT1197 (bladder) cancer cells with IC ₅₀ values of 6.7, 4.3, 2.3, 6.0 and 97 nM, respectively ^[1] . OTSSP167 can abrogate the mitotic checkpoint, disrupt MCC and MCC-APC/C interaction in MCF7 cells. OTSSP167 causes GFP-MELK localization to cell cortex in prometaphase cells ^[2] . OTSSP167 is a MELK selective inhibitor, exhibits a strong in vitro activity, conferring an IC ₅₀ of 0.41 nM ^[3] .			
In Vivo	OTSSP167 (20 mg/kg, i.v.) results in tumor growth inhibition (TGI) of 73% in xenograft mouse model; OTSSP167 (1, 5, and 10 mg/kg, p.o.) reveals TGI of 51, 91, and 108%, respectively. OTSSP167 (20 mg/kg, p.o.) shows no tumor growth suppressive effect on PC-14 xenografts ^[1] .			
Solvent&Solubility	In Vitro: DMSO : ≥ 5.6 mg/mL (10.69 mM) H₂O : 2 mg/mL (3.82 mM; Need ultrasonic and warming) * "≥" means soluble, but saturation unknown.			
	Preparing Stock Solutions	<div>Solvent / Mass / Concentration</div>	1 mg	5 mg
		1 mM	1.9088 mL	9.5442 mL
		5 mM	0.3818 mL	1.9088 mL
		10 mM	0.1909 mL	0.9544 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: ≥ 3 mg/mL (5.73 mM); Clear solution 此方案可获得 ≥ 3 mg/mL (5.73 mM, 饱和度未知) 的澄清溶液。 以 1 mL 工作液为例, 取 100 μL 30.0 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: ≥ 3 mg/mL (5.73 mM); Clear solution			



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	<p>此方案可获得 ≥ 3 mg/mL (5.73 mM, 饱和度未知) 的澄清溶液。</p> <p>以 1 mL 工作液为例, 取 100 μL 30.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水溶液中, 混合均匀。</p> <p>3.请依序添加每种溶剂: 10% DMSO \rightarrow 90% corn oil</p> <p>Solubility: 3 mg/mL (5.73 mM); Suspended solution; Need ultrasonic</p> <p>此方案可获得 3 mg/mL (5.73 mM)的均匀悬浊液, 悬浊液可用于口服和腹腔注射。</p> <p>以 1 mL 工作液为例, 取 100 μL 30.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中, 混合均匀。</p>
References	<p>[1]. Chung S, Suzuki H, Miyamoto T, et al. Development of an orally-administrative MELK-targeting inhibitor that suppresses the growth of various types of human cancer. <i>Oncotarget</i>. 2012 Dec 21.</p> <p>[2]. Ji W, et al. OTSSP167 Abrogates Mitotic Checkpoint through Inhibiting Multiple Mitotic Kinases. <i>PLoS One</i>. 2016 Apr 15;11(4):e0153518.</p> <p>[3]. Cho YS, et al. The crystal structure of MPK38 in complex with OTSSP167, an orally administrative MELK selective inhibitor. <i>Biochem Biophys Res Commun</i>. 2014 Apr 25;447(1):7-11.</p> <p>[4]. Jurmeister S, et al. Identification of potential therapeutic targets in prostate cancer through a cross-species approach. <i>EMBO Mol Med</i>. 2018 Feb 5. pii: e8274.</p> <p>[5]. Meel MH, et al. MELK inhibition in Diffuse Intrinsic Pontine Glioma. <i>Clin Cancer Res</i>. 2018 Jul 30. pii: clincanres.0924.2018.</p>
实验参考:	
Cell Assay	<p>In vitro cell viability is measured by the colorimetric assay using Cell Counting Kit-8. Cells are plated in 100 μL in 96-well plates at a density that generates continual linear growth (A549, 1×10^3 cells; T47D, 3×10^3 cells; DU4475, 4×10^3 cells; 22Rv1, 6×10^3 cells; and HT1197, 2×10^3 cells, in 100 μL per well). The cells are allowed to adhere overnight before exposure to OTSSP167 for 72 hours at 37°C. Plates are read using a spectrophotometer at a wavelength of 450 nm. All assays are carried out in triplicate. [1]</p>
Animal Administration	<p>MDA-MB-231 cells are injected into the mammary fat pads of NOD.CB17-<i>Prkdc</i>^{scid}/J mice. A549, MIA PaCa-2 and PC-14 cells (1×10^6 cells) are injected subcutaneously in the left flank of female BALB/cSLC-nu/nu mice. DU145 cells are injected subcutaneously in the left flank of male BALB/cSLC-nu/nu mice. When MDA-MB-231, A549, DU145, MIA PaCa-2, and PC-14 xenografts has reached an average volume of 100, 210, 110, 250, and 250 mm³, respectively, animals are randomized into groups of 6 mice (except for PC-14, for which groups of 3 mice are used). For oral administration, OTSSP167 and other compounds are prepared in a vehicle of 0.5% methylcellulose and given by oral gavage at the indicated dose and schedule. For intravenous administration, compounds are formulated in 5% glucose and injected into the tail vein. An administration volume of 10 mL per kg of body weight is used for both administration routes. Tumor volumes are determined every other day using a caliper. [1]</p>
Kinase Assay	<p>For in vitro kinase assay, MELK recombinant protein (0.4 μg) is mixed with 5 μg of each substrate in 20 μL of kinase buffer containing 30 mM Tris-HCl (pH), 10 mM DTT, 40 mM NaF, 10 mM MgCl₂, 0.1 mM EGTA with 50 μM cold-ATP and 10 Ci of [γ-³²P]ATP for 30 min at 30°C. The reaction is terminated by addition of SDS sample buffer and boiled for 5 min prior to SDS-PAGE. The gel is</p>



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	dried and autoradiographed with intensifying screens at room temperature. OTSSP167 (final concentration of 10 nM) is dissolved in DMSO and added to kinase buffer before the incubation. [1]
References	<p>[1]. Chung S, Suzuki H, Miyamoto T, et al. Development of an orally-administrative MELK-targeting inhibitor that suppresses the growth of various types of human cancer. <i>Oncotarget</i>. 2012 Dec 21.</p> <p>[2]. Ji W, et al. OTSSP167 Abrogates Mitotic Checkpoint through Inhibiting Multiple Mitotic Kinases. <i>PLoS One</i>. 2016 Apr 15;11(4):e0153518.</p> <p>[3]. Cho YS, et al. The crystal structure of MPK38 in complex with OTSSP167, an orally administrative MELK selective inhibitor. <i>Biochem Biophys Res Commun</i>. 2014 Apr 25;447(1):7-11.</p> <p>[4]. Jurmeister S, et al. Identification of potential therapeutic targets in prostate cancer through a cross-species approach. <i>EMBO Mol Med</i>. 2018 Feb 5. pii: e8274.</p> <p>[5]. Meel MH, et al. MELK inhibition in Diffuse Intrinsic Pontine Glioma. <i>Clin Cancer Res</i>. 2018 Jul 30. pii: clincanres.0924.2018.</p>

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