产品名称：STF 083010
产品别名：STF-083010

生物活性：

Description	STF-083010 is a specific IRE1α inhibitor. STF-083010 inhibits Ire1 endonuclease activity, without affecting its kinase activity, after endoplasmic reticulum stress.
IC_{50} & Target	Ire1[1]
In Vitro	STF-083010 shows cytostatic and cytotoxic activity in a dose- and time-dependent manner. Treatment with STF-083010 shows significant antimyeloma activity in model human multiple myeloma (MM) xenografts. RPMI 8226 human MM cells grown as tumor xenografts are treated in NSG mice. Intraperitoneal injection of STF-083010 alone (day 1, day 8) significantly inhibits the growth of these tumors[1]. STF-083010 is an IRE1α-specific inhibitor. Four pancreatic cancer cell lines (Panc0403, Panc1005, BxPc3, MiaPaCa2) are treated with different combination of Bortezomib (10 or 50 nM) and STF (10 or 50 μM). The normalized isobologram analysis demonstrates synergistic activity between 10 μM STF and either 10 or 50 nM bortezomib in all four cell lines. Moreover, a higher concentration of STF (50 μM) attains synergy after addition of bortezomib either at a concentration of 10 nM when tested against BxPc3 cells, at a concentration of 50 nM against Panc1005 cells, and at either 10 or 50 nM against Panc0403 cells[2]. STF-083010 (50 μM) suppresses the growth of p53-deficient human cancer cells[3].
In Vivo	Treatment with STF-083010 reduces the viability of HCT116 *p53*$^{-/-}$ cells by approximately 20% compared with that of HCT116 *p53*$^{-/-}$cells. Administration of STF-083010 to tumors induced by HCT116 *p53*$^{-/-}$ cells significantly reduces tumor volume and weight by 75% and 73% at the endpoint, respectively[3].

Solvent&Solubility

In Vitro:

DMSO : 100 mg/mL (**315.08 mM;** Need ultrasonic)

H_2O : < 0.1 mg/mL (insoluble)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	3.1508 mL	15.7540 mL	31.5080 mL
	5 mM	0.6302 mL	3.1508 mL	6.3016 mL
	10 mM	0.3151 mL	1.5754 mL	3.1508 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: ≥ 3.25 mg/mL (10.24 mM); Clear solution

此方案可获得 ≥ 3.25 mg/mL (10.24 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 32.5 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。

References	[1]. Papandreou I, et al. Identification of an Ire1alpha endonuclease specific inhibitor with cytotoxic activity against human multiple myeloma. Blood. 2011 Jan 27;117(4):1311-4. [2]. Chien W, et al. Selective inhibition of unfolded protein response induces apoptosis in pancreatic cancer cells. Oncotarget. 2014 Jul 15;5(13):4881-94. [3]. Namba T, et al. Loss of p53 enhances the function of the endoplasmic reticulum through activation of the IRE1α/XBP1 pathway. Oncotarget. 2015 Aug 21;6(24):19990-20001.

实验参考：

Cell Assay	Cell viability is determined using the MTT method. After treatment with Tunicamycin (Tm), STF-083010 (50 μM), or both, cells are incubated with MTT solution (1 mg/mL) for 2 h. Isopropanol and HCl are added to the final concentrations of 50% and 20 mM, respectively. The optical density at 570 nm is determined using a spectrophotometer using a reference wavelength of 630 nm[3].
Animal Administration	Mice[3] Each BALB/c nude mouse (male, 5 weeks of age) is subcutaneously inoculated in the right and left hind footpads with 5×10^6 HCT116 *p53*$^{+/+}$ or HCT116 *p53*$^{-/-}$ cells. Four days later, DMSO or STF-083010 (40 mg/kg) is intraperitoneally administrated every 3 days. Tumors are measured every 5 days, and their volumes are calculated using the equation $mm^3=(length\ (mm))\times(width\ (mm))^2/2$.
Kinase Assay	The hIre1α protein, containing both Ire1 cytoplasmic kinase and RNase domains, is expressed and purified from baculovirus. Autophosphorylation activity is determined by the addition of ^{32}P-γATP. Endonuclease activity is determined by the addition of radiolabeled *HAC1* 508-nt RNA substrate synthesized in vitro using α ^{32}P-UTP. STF083010 is incubated with recombinant hIRE1α protein, radiolabeled *HAC1* 508 nt RNA, and appropriate buffers. Kinase activity and RNAse cleavage products are quantitated by polyacrylamide gel electrophoresis and ^{32}P-γATP or ^{32}P-UTP autoradiography, respectively[1].
References	[1]. Papandreou I, et al. Identification of an Ire1alpha endonuclease specific inhibitor with cytotoxic activity against human multiple myeloma. Blood. 2011 Jan 27;117(4):1311-4. [2]. Chien W, et al. Selective inhibition of unfolded protein response induces apoptosis in pancreatic cancer cells. Oncotarget. 2014 Jul 15;5(13):4881-94. [3]. Namba T, et al. Loss of p53 enhances the function of the endoplasmic reticulum through activation of the IRE1α/XBP1 pathway. Oncotarget. 2015 Aug 21;6(24):19990-20001.