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产品名称：PU-H71
产品别名：PU-H71

生物活性：

Description	PU-H71 is a potent Hsp90 inhibitor, with an IC50 of 51 nM in MDA-MB-468 cells.
IC_{50} & Target	HSP90
	51 nM (IC_{50}, MDA-MB-468 cells)
In Vitro	PU-H71 is a potent Hsp90 inhibitor, with an IC50 of 51 nM in MDA-MB-468 cells. PU-H71 inhibits the growth of several tumor cells, such as MDA-MB-468, MDA-MB-231 and HCC-1806 cells, with IC50s of 65 ± 8 nM, 140 ± 5 nM and 87 ± 3 nM, respectively, and such inhibition is associated with a G2-M block arrest. PU-H71 (10-1000 nM) induces significant apoptosis in triple-negative breast cancers (TNBCs). PU-H71 (0.5, 1 μM) also downregulates oncoproteins involved in the invasive potential of TNBCs[1]. PU-H71 (0.5 μM) decreases and depletes the BCR signaling kinases. PU-H71 (0.25-10 μM) is cytotoxic to CLL cells but shows minimal effects on PBMC or resting B cells. In addition, PU-H71 (0-1 μM) reduces CLL viability via the induction of mitochondrial apoptosis, and antagonizes the survival signals from CLL microenvironment at 0.5 μM[2]. PU-H71 (0.05 μM) induces apoptosis of MDA-MB-231, BT-474, and MCF7 cells, and such induction is enhanced by TNF-α. PU-H71 (0.05 μM) degradates IKKβ, and down-regulates the NF-κB transcriptional activity induced by TNF-α treatment[3].
In Vivo	PU-H71 (75 mg/kg, i.p.) causes intratumor accumulation, extends down-regulation of anti-tumor driving molecules, completes and retains responses at nontoxic doses in MDA-MB-468 tumor-bearing mice. PU-H71 (75 mg/kg 3×week, i.p.) suppresses the gowth of tumors, and such an effect is associated with down-regulation of several Hsp90-regulated malignancy driving proteins[1].
Solvent&Solubility	***In Vitro:*** **DMSO : ≥ 100 mg/mL (195.17 mM)** * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.9517 mL	9.7586 mL	19.5171 mL
5 mM	0.3903 mL	1.9517 mL	3.9034 mL
10 mM	0.1952 mL	0.9759 mL	1.9517 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 (4.88 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (4.88 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 (4.88 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (4.88 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。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (4.88 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (4.88 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。 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 玉米油中，混合均匀。
References	[1]. Caldas-Lopes E, et al. Hsp90 inhibitor PU-H71, a multimodal inhibitor of malignancy, induces complete responses in triple-negative breast cancer models. Proc Natl Acad Sci U S A. 2009 May 19;106(20):8368-73. [2]. Guo A, et al. HSP90 stabilizes B-cell receptor kinases in a multi-client interactome: PU-H71 induces CLL apoptosis in a cytoprotective microenvironment. Oncogene. 2017 Jun 15;36(24):3441-3449. [3]. Qu Z, et al. PU-H71 effectively induces degradation of IκB kinase β in the presence of TNF-α. Mol Cell Biochem. 2014 Jan;386(1-2):135-42.

实验参考：

Cell Assay	The antiproliferative effects of select Hsp90 inhibitors is evaluated using the CellTiter-Glo Luminescent Cell Viability Assay kit. Briefly, exponentially growing MDA-MB-468, MDA-MB-231, and HCC-1806 cells are seeded into black 96-well microtiter plates and incubated in medium containing either vehicle control (DMSO) or PU-H71 for the indicated time at 37°C. Plates containing 3 replicate wells per assay condition are seeded at a density of 8×10^3 cells for each cell line in 100 μL medium. After exposure of cells to the Hsp90 inhibitors, plates are equilibrated to room temperature (20-25°C) for approximately 30 min, and 100 μL CellTiter-Glo reagent are added to each well. Plates are mixed for 2 min on an orbital shaker and then incubated for 15 min to 2 h at room temperature. The luminescence signal in each well is measured in an Analyst GT microplate reader. The percentage cell growth inhibition is calculated by comparing luminescence readings obtained from treated versus control cells, accounting for initial cell population (time 0). The IC_{50} is calculated as the drug concentration that inhibits cell growth by 50%[1].
	Mice[1] Mice bearing MDA-MB-468 tumors reaching a volume of 100-150 mm^3 are treated i.p. using different doses and schedules: Group 01 (n = 8) PBS; group 02 (n = 8) PU-H71 at 50 mg/kg on alternate days; group 03 (n = 8) PU-H71 at 50 mg/kg 5xqd; group 04 (n = 8) PU-H71 at 75 mg/kg 3

Animal Administration	week; group 05 (n = 8) PU-H71 at 75 mg/kg on alternate days. Mice bearing HCC-1806 or MDA-MB-231 xenografted tumors receive PU-H71 at 75 mg/kg on alternate days. Tumor volume is determined by measurement with Vernier calipers, and tumor volume is calculated as the product of its length × width^2 × 0.4. Tumor volume is expressed on indicated days as the median tumor volume ± SD indicated for groups of mice[1].
Kinase Assay	Measurements are performed in black 96-well microtiter plates. In short, cell lysates are prepared by rupturing cellular membranes by freezing at -70°C and dissolving the cellular extract in HFB [20 mM Hepes (K), pH 7.3, 50 mM KCl, 5 mM $MgCl_2$, 20 mM Na_2MoO_4, 0.01% Nonidet P-40] with added protease and phosphatase inhibitors (PU-H71, etc.). Saturation curves are recorded in which fluorescently labeled geldanamycin (Cy3B-GM) (3 nM) is treated with increasing amounts of cellular lysates. The amount of lysate that results in polarization (mP) readings corresponding to 90%-99% bound ligand is chosen for the competition study. Here, each 96-well plate contains 3 nM Cy3B-GM, cellular lysate and tested Hsp90 inhibitor in a final volume of 100 µL. The plate is left for 24 h on a shaker at 4°C, and the fluorescence polarization (FP) values in mP are recorded. EC_{50} values are determined as the competitor concentrations at which 50% of the Cy3B-GM is displaced. FP measurements are performed on an Analyst GT microplate reader[1].
References	[1]. Caldas-Lopes E, et al. Hsp90 inhibitor PU-H71, a multimodal inhibitor of malignancy, induces complete responses in triple-negative breast cancer models. Proc Natl Acad Sci U S A. 2009 May 19;106(20):8368-73. [2]. Guo A, et al. HSP90 stabilizes B-cell receptor kinases in a multi-client interactome: PU-H71 induces CLL apoptosis in a cytoprotective microenvironment. Oncogene. 2017 Jun 15;36(24):3441-3449. [3]. Qu Z, et al. PU-H71 effectively induces degradation of IκB kinase β in the presence of TNF-α. Mol Cell Biochem. 2014 Jan;386(1-2):135-42.

源叶生物