



上海源叶生物科技有限公司
Shanghai yuanye Bio-Technology Co., Ltd
电话: 021-61312973 传真: 021-55068248
网址: www.shyuanye.com
邮箱: shyysw@sina.com

产品名称: **NMS-P715**
产品别名: **NMS-P715**

生物活性:					
Description	NMS-P715 is a selective, ATP-competitive inhibitor of MPS1, with an IC50 of 182 nM.				
IC50 & Target	Mps1	CK2	MELK	NEK6	
	182 nM (IC50)	5.7 μM (IC50)	6.01 μM (IC50)	6.02 μM (IC50)	
In Vitro	NMS-P715 is a selective inhibitor of MPS1, with an IC50 of 182 nM. NMS-P715 is highly specific for MPS1, with no other kinases inhibited below an IC50 value of 5 μM and only 3 kinases inhibited below 10 μM (CK2, MELK, and NEK6). NMS-P715 promotes massive spindle assembly checkpoint (SAC) override with an EC50 of 65 nM. NMS-P715 (1 μM) causes mitotic acceleration in U2OS cells overexpressing YFP-α-tubulin, induces aneuploidy and inhibits the proliferation of HCT116 cells. NMS-P715 (0.5, 1 μM) affects mitotic checkpoint complex (MCC) stability and cdc20 ubiquitylation[1]. NMS-P715 (1 μM) exhibits bypass of the spindle assembly checkpoint and apoptosis in pancreatic ductal adenocarcinoma (PDAC) cell lines. NMS-P715 (0-25 μM) also selectively inhibits growth of PDAC cells[2].				
In Vivo	NMS-P715 (10 mg/kg) exhibits an oral bioavailability of 37% and good pharmacokinetic properties in nude mice bearing subcutaneous implanted human tumor cell xenografts. NMS-P715 (90 mg/kg, p.o.) is well tolerated and cuases no signs of body weight loss or other overt toxicities in an A2780 ovary carcinoma xenograft model. NMS-P715 (100 mg/kg, p.o.) inhibits the tumor growth by appr 43% in the A375 melanoma xenograft model[1].				
Solvent&Solubility	In Vitro: DMSO : 2 mg/mL (2.96 mM; Need ultrasonic)				
	Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
		1 mM	1.4777 mL	7.3885 mL	14.7769 mL
		5 mM	---	---	---
		10 mM	---	---	---
*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。					
References	[1]. Colombo R, et al. Targeting the mitotic checkpoint for cancer therapy with NMS-P715, an inhibitor of MPS1 kinase. Cancer Res. 2010 Dec 15;70(24):10255-64. [2]. Slee RB, et al. Selective inhibition of pancreatic ductal adenocarcinoma cell growth by the mitotic MPS1 kinase inhibitor NMS-P715. Mol Cancer Ther. 2014 Feb;13(2):307-315.				
实验参考:					
Cell Assay	Cells lines are seeded in 384 well-plates in the appropriate complete medium and treated with compounds (NMS-P715, etc.) dissolved in 0.1% DMSO 24 hours after seeding. The cells are incubated at 37°C and 5% CO2 and after 72 hours the plates are processed using CellTiter-Glo assay. Inhibitory activity is evaluated comparing treated versus control data using Assay Explorer				



上海源叶生物科技有限公司
Shanghai yuanye Bio-Technology Co., Ltd
电话: 021-61312973 传真: 021-55068248
网址: www.shyuanye.com
邮箱: shyysw@sina.com

	software. IC ₅₀ of proliferation is calculated using sigmoidal interpolation curve fitting. Activity Ratio is calculated as the ratio of the single cell line IC ₅₀ and the IC ₅₀ average of all the cell lines tested ^[1] .
Animal Administration	<p>Mice^[1]</p> <p>Athymic nu-nu mice, 5-6 weeks of age (20-22 g) are used in the assay. A2780 ovary carcinoma and A375 melanoma cells are transplanted s.c. into female nu-nu mice. Mice bearing a palpable tumor (100-200 mm³) are selected and randomized into control and treated groups. Treatment starts one day after randomization. NMS-P715 is typically administered by oral administration at doses of 90-100 mg/kg daily for more than seven days. Each group includes 8 animals. Tumor dimension is measured regularly by calipers during the experiments and tumor mass is calculated^[1].</p>
Kinase Assay	<p>The potency of the compound towards MPS1 and 60 additional kinases belonging to kinase selectivity screening (KSS) panel is determined using either a strong anion exchanger based assay or P81 Multiscreen plate. MPS1 activity is measured using 5 nM of MPS1 recombinant protein in 50 mM HEPES pH 7.5, 2.5 mM MgCl₂, 1 mM MnCl₂, 1 mM DTT, 3 μM NaVO₃, 2 mM β-glycerophosphate, 0.2 mg/mL BSA, 200 μM P38-βtide substrate-peptide (KRQADEEMTGYYVATRWYRAE) and 8 μM ATP with 1.5 nM ³³P-γ-ATP. The assay is run in a robotized format, 10 serial 1:3 compounds dilutions (including NMS-P715, from 30 μM to 1.5 nM) are tested and IC₅₀ determined^[1].</p>
References	<p>[1]. Colombo R, et al. Targeting the mitotic checkpoint for cancer therapy with NMS-P715, an inhibitor of MPS1 kinase. Cancer Res. 2010 Dec 15;70(24):10255-64.</p> <p>[2]. Slee RB, et al. Selective inhibition of pancreatic ductal adenocarcinoma cell growth by the mitotic MPS1 kinase inhibitor NMS-P715. Mol Cancer Ther. 2014 Feb;13(2):307-315.</p>

源叶生物