

产品名称: IWP-2

产品别名: IWP-2

生物活性:

Description	IWP-2 is an inhibitor of Wnt processing and secretion with an IC50 of 27 nM. IWP-2 targets the membrane-bound O-acyltransferase porcupine (Porcn) and thus preventing a crucial Wnt ligand palmitoylation. IWP-2 is also an ATP-competitive CK1δ inhibitor with an IC50 of 40 nM for the gatekeeper mutant <sup>M82F</sup> CK1δ[1][2].				
IC50 & Target	Wnt	CK1δ			
	27 nM (IC50)	40 nM (IC50)			
In Vitro	IWP-2 inhibits the proliferation of the investigated cell lines within the single digit μM range. IWP-2 inhibits cell proliferation in A818-6, MiaPaCa2, Panc-1,Panc-89, HT29, HEK293, SW620 and Capan cell with EC50s of 8.96 μM, 1.90 μM, 2.33 μM, 3.86 μM, 4.67 μM, 2.76 μM, 1.90 μM and 2.05 μM, respectively[2]. Panc-1 cells are either untreated or treated with 2.33 μM IWP-2 for 48 h. In IWP-2 treated cells, the CK1δ kinase peak activity is reduced to approximately 66% residual activity compared to the activity in untreated cells, respectively. IWP-2 reduces the activity of CK1δ in Panc1 cells[2].				
In Vivo	To evaluate the efficacy of IWP-2 in vivo, 200 μL each of IWP-2-liposome or free liposome i separately injected into C57BL/6 mice intraperitoneally about 2 h before injection of a similar volume of either blue-dye-filled latex beads or E. coli DH5α. IWP-2 causes significant reduction in the uptake of blue beads as well as E. coli as assessed by CFUs in peritoneal lavage cells within 2 h. In addition, the levels of TNF-α and IL-6 in the lavage fluid of the corresponding mice are reduced by 2-4-fold compared with control values. Interestingly, IWP-2 even induces a considerable increase in secretion of the anti-inflammatory cytokine IL-10[3].				
Solvent&Solubility	<b>In Vitro:</b> <b>DMSO : 2 mg/mL (4.29 mM; Need ultrasonic)</b> <b>H2O : &lt; 0.1 mg/mL (insoluble)</b>				
	Preparing Stock Solutions	Solvent Mass Concentration	1 mg	5 mg	10 mg
		1 mM	2.1432 mL	10.7158 mL	21.4316 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]. Chen B, et al. Small molecule-mediated disruption of Wnt-dependent signaling in tissue regeneration and cancer. Nat Chem Biol. 2009 Feb;5(2):100-7.  [2]. García-Reyes B, et al. Discovery of Inhibitor of Wnt Production 2 (IWP-2) and Related Compounds As Selective ATP-Competitive Inhibitors of Casein Kinase 1 (CK1) δ/ε. J Med Chem. 2018 May 10;61(9):4087-4102.  [3]. Maiti G, et al. The Wingless homolog Wnt5a stimulates phagocytosis but not bacterial killing. Proc Natl Acad Sci U S A. 2012 Oct 9;109(41):16600-5.				

**实验参考:**

<b>Cell Assay</b>	<p>The human RCC cell lines 786O and Caki-2 (<math>5 \times 10^3</math>) are seeded into 96-well plates. Cell viability is estimated by MST assay after Caki-2 cells are incubated with increasing concentrations of LEF together with 20 <math>\mu</math>M IWP-2 for 48 h. After treatment, 10 <math>\mu</math>L MTS is added into each well for 2 h incubation. The absorbance is measured using a model ELX800 Micro Plate Reader at 490 nm. For colony formation assay, Caki-2 cells are trypsinized to single cell suspensions and seeded into fresh 6-well plates at 1000 cells/well. Then cells are incubated with LEF at depicted concentrations for 7 days. Colonies are fixed with absolute methanol for 15 min and then stained with 0.1% crystal violet for 20 min. After washing with PBS three times, the colonies with a diameter over 2 mm are visualized by a digital camera[2].</p>
<b>Animal Administration</b>	<p><b>Mice[4]</b></p> <p>About 3-mo-old C57BL/6 mice are housed four to five in a cage at 23°C in a 12-h light/dark cycle. Mice are injected intraperitoneally (i.p.) first with either 200 <math>\mu</math>L of liposome-IWP2 (LI) or liposome (L) and then after 2 h with <math>1 \times 10^8</math> or <math>2 \times 10^8</math> CFU E. coli in 200 <math>\mu</math>L of sterile PBS. After 2 h or 24 h mice are killed, and the peritoneal cavity is washed with 5 mL of sterile ice-cold PBS. The peritoneal lavage fluid is centrifuged at <math>300 \times g</math> for 5 min, the cell pellet is resuspended in RPMI 1640 complete medium, and the supernatant is used for cytokine assay. For ex vivo experiments, peritoneal phagocytes are isolated as above from normal mice, and equal numbers of cells are plated in medium overnight at 37°C in 5% CO<sub>2</sub> before performing further experiments.</p> <p><b>Rats[5]</b></p> <p>Adult, male, and healthy Wistar rats weighing 220-280 g are used. Rats are randomly divided into 6 groups as follows (n=72, 12 per group): (1) Sham group (Group S), (2) I/R group (Group I/R), (3) I/R+DMSO group (Group DMSO), (4) I/R+IWP group (Group IWP), (5) SP group (Group SP), and (6) SP+Wnt inhibitor IWP-2 group (Group SP+IWP). The hearts are continuously perfused for 120 min in Group S. After 10 min of equilibration, the isolated hearts are continuously perfused for 20 min, then subjected to 30 min of ischemia followed by 60 min of reperfusion in Group I/R; Groups DMSO, IWP, SP and SP+IWP receive 15 min of perfusion with K-H solution containing 0.5 mL/L DMSO, 10 <math>\mu</math>M IWP (SIGMA-ALDRICH, USA), 2.4 vol% Sevoflurane, 2.4 vol% Sevoflurane+10 <math>\mu</math>M IWP, respectively, followed by 5 min washout before I/R.</p>
<b>References</b>	<p>[1]. <u>Chen B, et al. Small molecule-mediated disruption of Wnt-dependent signaling in tissue regeneration and cancer. Nat Chem Biol. 2009 Feb;5(2):100-7.</u></p> <p>[2]. <u>García-Reyes B, et al. Discovery of Inhibitor of Wnt Production 2 (IWP-2) and Related Compounds As Selective ATP-Competitive Inhibitors of Casein Kinase 1 (CK1) <math>\delta/\epsilon</math>. J Med Chem. 2018 May 10;61(9):4087-4102.</u></p> <p>[3]. <u>Maiti G, et al. The Wingless homolog Wnt5a stimulates phagocytosis but not bacterial killing. Proc Natl Acad Sci U S A. 2012 Oct 9;109(41):16600-5.</u></p>