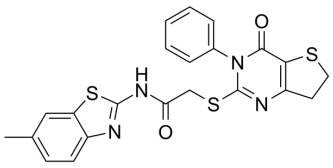
IWP-2

Cat. No.:	HY-13912
CAS No.:	686770-61-6
Molecular Formula:	$C_{22}H_{18}N_4O_2S_3$
Molecular Weight:	466.6
Target:	Wnt; Porcupine; Casein Kinase
Pathway:	Stem Cell/Wnt; Cell Cycle/DNA Damage
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMF : 12.5 mg/mL (26.79 mM; ultrasonic and warming and heat to 60°C)
DMSO : 2 mg/mL (4.29 mM; Need ultrasonic)

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	0.4286 mL	2.1432 mL	4.2863 mL
10 mM	0.2143 mL	1.0716 mL	2.1432 mL

Please refer to the solubility information to select the appropriate solvent.

BIOLOGICAL ACTIVITY

Description

IWP-2 is an inhibitor of Wnt processing and secretion with an IC_{50} 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 IC_{50} of 40 nM for the gatekeeper mutant ^{M82F}CK1δ[1][2].

IC_{50} & Target

Wnt	CK1δ
27 nM (IC_{50})	40 nM (IC_{50})

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 EC_{50}s 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].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [2]	The human RCC cell lines 786O and Caki-2 (5×10^3) are seeded into 96-well plates. Cell viability is estimated by MST assay after Caki-2 acells are incubated with ncreasing concentrations of LEF together with 20 μM IWP-2 for 48 h.After treatment, 10 μL 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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Adv Mater. 2021 Oct 10;e2104829.
- Dev Cell. 2020 Dec 21;55(6):679-694.e11.
- Stem Cells Transl Med. 2021 May;10(5):743-755.
- J Cell Physiol. 2020 Jul;235(7-8):5811-5822.
- Biochem Pharmacol. 2019 Nov;169:113608.

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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]. 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.

[3]. 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.

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