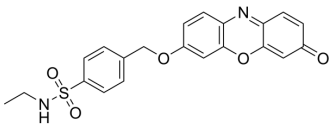
WRG-28

Cat. No.:	HY-114169
CAS No.:	1913291-02-7
Molecular Formula:	$C_{21}H_{18}N_2O_5S$
Molecular Weight:	410.44
Target:	Discoidin Domain Receptor
Pathway:	Protein Tyrosine Kinase/RTK
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 15.62 mg/mL (38.06 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.4364 mL	12.1820 mL	24.3641 mL
	5 mM	0.4873 mL	2.4364 mL	4.8728 mL
	10 mM	0.2436 mL	1.2182 mL	2.4364 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 1.56 mg/mL (3.80 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

WRG-28 is a selective, extracellularly acting DDR2 allosteric inhibitor, with an IC_{50} of 230 nM. WRG-28 inhibits tumor invasion, migration and tumor-supporting effects of cancer-associated fibroblasts (CAFs). WRG-28 inhibits metastatic breast tumor cell colonization in the lungs. WRG-28 also shows good activity of relieving rheumatoid arthritis in CAIA model of mice[1][2].

IC_{50} & Target

DDR2
230 nM (IC_{50})

In Vitro

WRG-28 (1, 2 μM; 4 h) blunts collagen I-mediated DDR2 tyrosine phosphorylation and (1 μM; 7 h) ERK activation as well as SNAIL1 protein stabilization in HEK293 cells (expressing DDR2) (IC_{50}=286 nM)[1].
WRG-28 (1 μM; 48 h) blunts tumor cell invasion and migration by inhibiting DDR2 in BT549 and 4T1 breast cancer cells[1].
WRG-28 (1 μM; 4 days) inhibits tumor-promoting effects of CAFs[1].
WRG-28 (0.5, 1 μM; 4 h) maintains inhibitory action toward acquired DDR2 mutations that are resistant to TKIs[1].

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

Cell Viability Assay[1]

Cell Line:	HEK293 cells (transfected with DDR2-Flag)
Concentration:	0.25, 0.5, 1, 2 μM
Incubation Time:	4 h
Result:	Significantly inhibited collagen I-mediated DDR2 tyrosine phosphorylation at 1 or 2μM, and with an IC>sub>50 of 286 nM.

Cell Viability Assay[1]

Cell Line:	HEK293 cells (transfected with DDR2-Flag)
Concentration:	1 μM
Incubation Time:	7 h
Result:	Inhibited collagen I-mediated ERK activation and SNAIL1 protein stabilization (IC_{50}=286 nM).

Cell Viability Assay[1]

Cell Line:	BT549 and 4T1 breast cancer cells (expressing endogenous DDR2)
Concentration:	1 μM
Incubation Time:	48 h
Result:	Inhibited DDR2 induced invasion and migration of tumor cells.

Cell Viability Assay[1]

Cell Line:	CAF cells (with tumor organoids)
Concentration:	1 μM
Incubation Time:	4 days
Result:	Inhibited the activity of DDR2 that supported invasion of primary tumor organoids in CAFs.

Cell Viability Assay[1]

Cell Line:	HEK293 cells (expressing $DDR2^{T654I}$)
Concentration:	0.5, 1 μM
Incubation Time:	4 h
Result:	Inhibited phosphorylation of the $DDR2^{T654I}$ mutant in response to collagen I.

In Vivo

WRG-28 (10 mg/kg; i.v.; single) attenuates biochemical signaling of DDR2 in breast tumors in vivo[1].
WRG-28 (10 mg/kg; i.v.; single daily for 7 days) reduces metastatic lung colonization of breast tumor cells[1].
WRG-28 (10 mg/kg; i.v.; single daily for 21 days) decreases both the inflammatory reaction and joint destruction in mice with collagen antibody-induced arthritis (CAIA)[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Female BALB/cJ mice (8-week-old; 4T1-Snail-CBG tumor-bearing mice model)[1].
Dosage:	10 mg/kg
Administration:	Intravenous injection, single.
Result:	Reduced 60% SNAIL1-clic beetle green (SNAIL1.CBG) level within the tumor in mice.

Animal Model:	Female BALB/cJ mice (8-week-old; injected with 4T1 GFP-luc expressing cells)[1].
Dosage:	10 mg/kg
Administration:	Intravenous injection, single daily for 7 days.
Result:	Reduced lung colonization to a level comparable to shDDR2-depleted cells.

Animal Model:	Male DBA/1 mice (8-week-old; CAIA model)[2].
Dosage:	10 mg/kg
Administration:	Intravenous injection, single daily for 21 days.
Result:	Significantly ameliorated arthritis in the mice (reduced production of IL-15 and Dkk-1), the hind- paw thickness of the mice was also reduced. Inhibited inflammatory cell infiltration and destruction of cartilage in mouse ankle and serum. Significantly alleviated bone destruction, reduced the extent of joint space enlargement and bone mineral density, as well as decreased the severity of bone loss.

REFERENCES

[1]. Mu N, et al. Blockade of Discoidin Domain Receptor 2 as a Strategy for Reducing Inflammation and Joint Destruction in Rheumatoid Arthritis Via Altered Interleukin-15 and Dkk-1 Signaling in Fibroblast-Like Synoviocytes. Arthritis Rheumatol. 2020 Jun;72(6):943-956.

[2]. Grither WR, et al. Inhibition of tumor-microenvironment interaction and tumor invasion by small-molecule allosteric inhibitor of DDR2 extracellular domain. Proc Natl Acad Sci U S A. 2018 Aug 14;115(33):E7786-E7794.

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