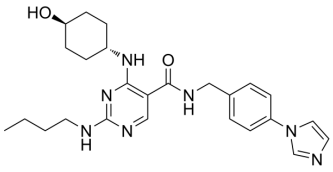
UNC2881

Cat. No.:	HY-15798
CAS No.:	1493764-08-1
Molecular Formula:	$C_{25}H_{33}N_7O_2$
Molecular Weight:	463.58
Target:	TAM Receptor; VSV
Pathway:	Protein Tyrosine Kinase/RTK; Anti-infection
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 : ≥ 44 mg/mL (94.91 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.1571 mL	10.7856 mL	21.5713 mL
5 mM	0.4314 mL	2.1571 mL	4.3142 mL
10 mM	0.2157 mL	1.0786 mL	2.1571 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: ≥ 2.5 mg/mL (5.39 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.39 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.39 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

UNC2881 is an orally active and specific Mer kinase inhibitor, inhibits steady-state Mer kinase phosphorylation with an IC_{50} value of 22 nM. UNC2881 shows additional inhibition against Axl and Tyro with IC_{50}s of 360 nM and 250 nM, respectively. UNC2881 potently inhibits collagen-induced platelet aggregation, can be used for pathologic thrombosis research[1].

IC_{50} & Target

IC50: 4.3 nM (Mer), 360 nM (Axl), 250 nM (Tyro)[1]

In Vitro

UNC2881 (compound 23) (0-1000 nM; 1 h) block ligand-stimulated activation of a chimeric EGFR-MerTK. UNC2881 also inhibits endogenous Mer tyrosine kinase activation in acute lymphoblastic leukemia cells[1].
UNC2881 (3 μM; 1 h) suppresses platelet aggregation by greater than 25% in human platelet-rich plasma in response to stimulation with fibrillar type I equine collagen[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Western Blot Analysis[1]

Cell Line:	32D cells
Concentration:	0, 10, 30, 100, 300, 1000 nM
Incubation Time:	1 hour; prior to stimulation with 100 ng/mL EGF ligand for 15 min
Result:	Reduced the phospho-tyrosine level in a dose-dependent manner.

In Vivo

UNC2881 (3 mg/kg; p.o.; single dose) has high systemic clearance (94.5 mL/min/kg) and 14% oral bioavailability, displays terminal half-life of 0.80 h[1].
UNC2881 (3 mg/kg; i.v.; injected with VSV on days -3, -2, -1, and 0) limits Mertk signaling, and promotes the antiviral immune response, reducing the viral replication of vesicular stomatitis virus (VSV) in infected mice[2].
Pharmacokinetics of UNC2881 in mice[1]

Route	Dose (mg/kg)	$T_{1/2}$ (h)	T_{max} (h)	C_{max} (ng/mL)	AUC_{last} (ng·h/mL)	CL_{obs} (mL/min)	V_{ss} (L/kg)	F (%)
IV	3	0.8		2609	527	94.5	1.65	
PO	3		0.30	90.0	71.7			14

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

Animal Model:	C57BL/6 mice (7-10 weeks old)[2]
Dosage:	3 mg/kg
Administration:	Intravenous injection; infected with 2×10^8 PFU vesicular stomatitis virus (VSV) (i.v.) on days -3, -2, -1, and 0
Result:	Reduced VSV replication in spleen, liver, kidney, lung.

REFERENCES

[1]. Tom Adomati, et al. Dead Cells Induce Innate Anergy Via Mertk after Acute Viral Infection. Cell Reports. 2020. 30(11):3671-3681.

[2]. Zhang W, et al. Discovery of Mer specific tyrosine kinase inhibitors for the treatment and prevention of thrombosis. J Med Chem. 2013 Dec 12;56(23):9693-700.

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