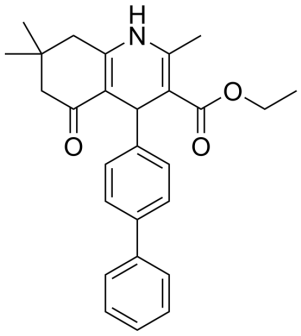
ITD-1



Cat. No.:	HY-12704
CAS No.:	1099644-42-4
Molecular Formula:	$C_{27}H_{29}NO_3$
Molecular Weight:	415.52
Target:	TGF-β Receptor
Pathway:	TGF-beta/Smad
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 : 28 mg/mL (67.39 mM; Need ultrasonic and warming)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.4066 mL	12.0331 mL	24.0662 mL
	5 mM	0.4813 mL	2.4066 mL	4.8132 mL
	10 mM	0.2407 mL	1.2033 mL	2.4066 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 (6.02 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.02 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

ITD-1 is the first selective TGFβ receptor inhibitor with an IC_{50} of 460 nM.

IC_{50} & Target

IC50: 460 nM (TGFβ receptor)

In Vitro

ITD-1 potently blocks phosphorylation of the effector SMAD2/3 proteins induced by TGFβ2, and only minimally in response to Activin A. HEK293T cells are transfected with a Smad4 response element driving luciferase (SBE4-Luc) to test whether ITD-1 blocks Activin A/Nodal and/or TGFβ signaling, which utilize the same intracellular signaling cascade through Smad4. ITD-1 strongly inhibits TGFβ2 signaling with similar efficacy (92% vs. 99% respectively), but with lower potency compared to SB-431542, an ACVR1B/TGFBR1 kinase inhibitor (IC_{50}= 850nM vs. 70nM respectively), and is a weak and partial inhibitor of Activin A signals. ITD-1 selectively enhances the differentiation of uncommitted mesoderm to cardiomyocytes, but not to

vascular smooth muscle and endothelial cells. ITD-1 reveals an unexpected role for TGFβ signaling in controlling cardiomyocyte differentiation from multipotent cardiovascular precursors[1].

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

PROTOCOL

Cell Assay

For the Smad4-Response element (SBE4) assay, 293T cells are grown in Phenol Free DMEM-high glucose supplemented with 1% FBS. About 30000 cells/cm2 are reverse transfected onto white 384-well cell-culture plates with 10ng of SBE4-Lux and CMV-Renilla-Lux using Lipofectamine 2000. Cells are allowed to adhere for at least 12 hours and induced with either TGFβ2 (15 ng/mL), Activin A (15 ng/mL). Simultaneously, ITD-1 (0.001, 0.01, 0.1, 1, and 10 μM) is added to cells. SB-431542 is used as a positive control for Activin A/TGFβ-signaling inhibition. To determine luminescence levels, Dual-Glo kit is used and measured on an Envision plate reader. Firefly luminescence is normalized against renilla luciferase.

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

CUSTOMER VALIDATION

- Cell Rep. 2022 Jun 21;39(12):110986.
- Cancer Manag Res. 2022 Jan 26;14:327-337.
- ACS Comb Sci. 2019 Dec 9;21(12):805-816.
- Oncotarget. 2017 Dec 14;9(3):3188-3197.

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REFERENCES

[1]. Willems E, et al. Small molecule-mediated TGF-β type II receptor degradation promotes cardiomyogenesis in embryonic stem cells. Cell Stem Cell. 2012 Aug 3;11(2):242-52.

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