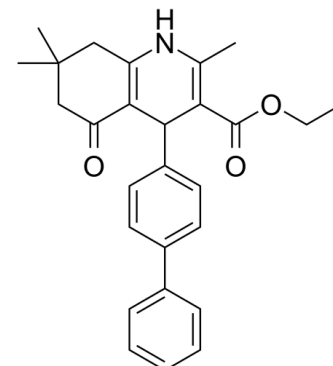


Data Sheet

Product Name:	ITD-1
Cat. No.:	CS-4939
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
Solubility:	DMSO : 28 mg/mL (67.39 mM; Need ultrasonic and warming); H ₂ O : < 0.1 mg/mL (insoluble)



BIOLOGICAL ACTIVITY:

ITD-1 is the first selective **TGFβ receptor** inhibitor with an **IC₅₀** of 460 nM. **IC₅₀ & 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 (IC₅₀= 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.

PROTOCOL (Extracted from published papers and Only for reference)

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.

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.

CAIndexNames:

3-Quinolinecarboxylic acid, 4-[1,1'-biphenyl]-4-yl-1,4,5,6,7,8-hexahydro-2,7,7-trimethyl-5-oxo-, ethyl ester

SMILES:

O=C(C1=C(C)NC2=C(C(C(C)(C)C2)=O)C1C3=CC=C(C4=CC=CC=C4)C=C3)OCC

Caution: Product has not been fully validated for medical applications. For research use only.

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