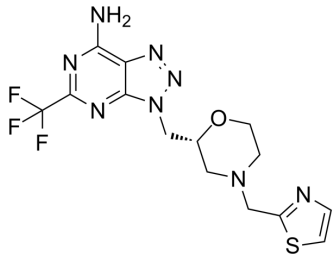
PF-04957325

Cat. No.:	HY-15426
CAS No.:	1305115-80-3
Molecular Formula:	$C_{14}H_{15}F_3N_8OS$
Molecular Weight:	400
Target:	Phosphodiesterase (PDE)
Pathway:	Metabolic Enzyme/Protease
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 : ≥ 100 mg/mL (250.00 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.5000 mL	12.5000 mL	25.0000 mL
	5 mM	0.5000 mL	2.5000 mL	5.0000 mL
	10 mM	0.2500 mL	1.2500 mL	2.5000 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 (6.25 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.25 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.25 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

PF-04957325 is a highly potent and selective PDE8 inhibitor, with IC_{50}s of 0.7 nM and 0.3 nM for PDE8A and PDE8B, respectively.

IC_{50} & Target

IC50: 0.7 nM (PDE8A), less than 0.3 nM (PDE8B)[1]

In Vitro

PF-04957325 is over two orders of magnitude less efficient than PICL in suppressing polyclonal Teff cell proliferation, and

shows no effect on cytokine gene expression in these cells, despite its robust effect on T cell adhesion[1]. PF-04957325 is a selective PDE8 inhibitor and inhibits breast cancer cell migration[2]. PF-04957325 greatly potentiates steroidogenesis in WT adrenal cells. PF-04957325 shows a reported IC_{50} of 0.7 nM against PDE8A, 0.2 nM against PDE8B, and > 1.5 μM against all other PDE isoforms[3]. PF-04957325 treatment of WT Leydig cells or MA10 cells increases steroid production but has no effect in PDE8A (-/-)/B(-/-) double-knockout cells, confirming the selectivity of the drug. Moreover, under basal conditions, cotreatment with PF-04957325 plus rolipram, a PDE4-selective inhibitor, synergistically potentiates steroid production[4].

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

PROTOCOL

Cell Assay [2]

Breast cancer cells are in a total volume of 0.1 mL of fresh medium containing the test reagents or vehicle (PF-04957325). Following incubation at 37°C for 72 h, 20 μL of a combined solution of MTS (2 mg/mL)/PMS (0.92 mg/mL) (20:1, mixed immediately before use) is added to each well, and the plates incubated for an additional 2 h at 37°C, protected from light, following which the absorbency of the formazan product formed is determined at 492 nm using a microtiter plate reader. All reagents tested are dissolved in DMSO and diluted into the cell culture medium[2].

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

CUSTOMER VALIDATION

- Cell Chem Biol. 2019 Oct 17;26(10):1393-1406.e7.
- EMBO Rep. 2021 Dec 23;e53135.
- Sci Signal. 2020 Nov 24;13(659):eaax0273.
- Endocrinology. 2018 May 1;159(5):2142-2152.
- Sci Rep. 2024 Jan 3;14(1):436.

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REFERENCES

[1]. Vang AG, et al. Differential Expression and Function of PDE8 and PDE4 in Effector T cells: Implications for PDE8 as a Drug Target in Inflammation. Front Pharmacol. 2016 Aug 23;7:259.

[2]. Dong H, et al. Inhibition of breast cancer cell migration by activation of cAMP signaling. Breast Cancer Res Treat. 2015 Jul;152(1):17-28.

[3]. Tsai LC, et al. Regulation of adrenal steroidogenesis by the high-affinity phosphodiesterase 8 family. Horm Metab Res. 2012 Sep;44(10):790-4.

[4]. Shimizu-Albergine M, et al. cAMP-specific phosphodiesterases 8A and 8B, essential regulators of Leydig cell steroidogenesis. Mol Pharmacol. 2012 Apr;81(4):556-66.

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