Product Data Sheet

Product Name: PFI-2
Cat. No.: GC17956

Chemical Properties

Cas. No.	1627676-59-8		
Chemical Name	8-fluoro-N-[(2R)-1-oxo-1-pyrrolidin-1-yl-3-[3-(trifluoromethyl)phenyl]propan-2-yl]-1,2,3,4-tetrahydroisoquinoline-6-sulfonamide		
SMILES	C1CCN(C1)C(=O)C(CC2=CC(=CC=C2)C(F)(F)F)NS(=O)(=O)C3=CC(=C4CNCCC4=C3)F		
Formula	$C_{23}H_{25}F_4N_3O_3S$	M.Wt	499.52
Solubility	≥ 50mg/mL in DMSO	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure	PFI-2		

Protocol

Kinase experiment [1]:

Methyltransferase activity	Recombinant human SETD7 (residues 1–366) and SET domain only (residues109–366) were expressed in Escherichia coli and purified to homogeneity. Methyltransferase activity of SETD7(1-366) was assayed using a scintillation proximity assay monitoring the incorporation of the tritium-labeled methyl group of 3H-SAM into a peptide substrate corresponding to histone H3 residues 1-25 at 2 μM SAM and 2 μM H3(1–25) and 2 nM enzyme.

Cell experiment [1]:

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com
Address: 10292 Central Ave. #205, Montclair, CA, USA

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Cell lines	MEFs and MCF7 cells
Preparation method	The solubility of this compound in DMSO is > 10 mM. General tips for obtaining a higher concentration: Please warm the tube at 37℃ for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20℃ for several months.
Reacting condition	0-10 μM, 2h
Applications	In Setd7+/+ murine embryonic fibroblasts (MEFs) in the presence of (R)-PFI-2 (10 μM), Setd7+/+ MEFs grown to confluence and displayed increased nuclear localization of YAP, as well as increased expression of YAP-dependent genes Ctgf, Gli2, and Cdc20. (R)-PFI-2 had no effect in Setd7-/- MEFs. In confluent MCF7 cells, (R)-PFI-2 (1 μM for 2h) dose-dependently increased nuclear YAP and increased expression of the YAP target genes AREG and CYR61.

References:

[1]. Barsyte-Lovejoy D, Li F, Oudhoff MJ, et al. (R)-PFI-2 is a potent and selective inhibitor of SETD7 methyltransferase activity in cells. Proc Natl Acad Sci U S A, 2014, 111(35): 12853-12858.

Background

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PFI-2 is a potent and selective inhibitor of SETD7 methyltransferase with IC50 value of 2.0 nM [1].

SET domain containing (lysine methyltransferase) 7 (SETD7) is a protein lysine methyltransferase that acts as monomethyltransferase of lysine 4 on histone H3 (H3K4) and regulates DNA methyltransferase 1 (DNMT1) [1].

PFI-2 is a potent and selective SETD7 methyltransferase inhibitor. (R)-PFI-2 inhibited human SETD7 methyltransferase activity with IC50 value of 2.0 nM. However, (S)-PFI-2 was 500-fold less active with IC50 value of only 1.0 μM. (R)-PFI-2 potently inhibited SETD7 with Morrison Kiapp value of 0.33 nM. (R)-PFI-2 occupied the peptide binding groove and effectively inhibited the binding of SETD7 substrates. In the presence of 20 μM SAM, (R)-PFI-2 bound to SETD7 with KD value of 4.2 nM in a SAM-dependent way. In HEK293 cells, (R)-PFI-2 (10 μM) bound to and stabilized SETD7. In Setd7+/+ murine embryonic fibroblasts (MEFs), (R)-PFI-2 increased nuclear localization of Yes-associated protein (YAP) and the expression of YAP target genes Ctgf, Gli2 and Cdc20 [1].

Reference:
[1]. Barsyte-Lovejoy D, Li F, Oudhoff MJ, et al. (R)-PFI-2 is a potent and selective inhibitor of SETD7 methyltransferase activity in cells. Proc Natl Acad Sci U S A, 2014, 111(35): 12853-12858.

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