PFI-8: A pan chemical probe for the YEATS family.

Version 1.0 (28th January 2024)

Web link for more details: https://www.thesgc.org/chemical-probes/PFI-8

Overview

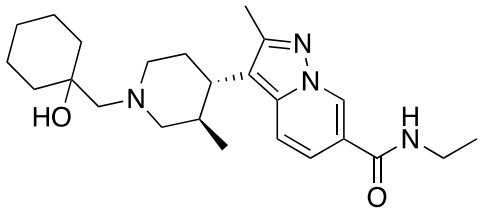
The SGC in collaboration with Pfizer has discovered a potent chemical probe for the YEATS family, PFI-8. The YEATS-domain containing proteins are responsible for epigenetic signaling via acylated lysines including acetylation and higher order acylations such as propionylation, butyrylation, and crotonylation.

Summary

Chemical Probe Name	PFI-8
Negative control compound	PFI-8N
Target(s) (synonyms)	YEATS family
Recommended concentration for cellular use	Use at 1 µM; recommend to perform a dose-response as different cell lines may require different concentrations. Use with negative control for best interpretation of data.
Suitability for *in* vivo use and recommended dose	This chemical probe was not tested for *in vivo* use.
Publications	https://doi.org/10.1021/acs.jmedchem.2c01421
Orthogonal chemical probes	
In vitro assay(s) used to characterise	FRET, SPR, ITC
Cellular assay(s) for target-engagement	NanoBRET, in cell western

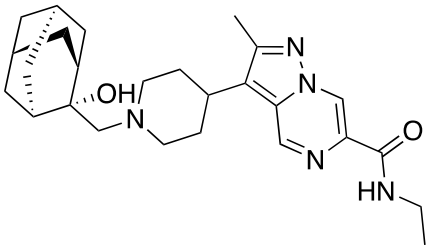
Chemical Probe & Negative Control Structures and Use

PFI-8



SMILES: O=C(NCC)C1=CN2C(C=C1)=C([C@H]3CCN(CC4(O)CCCCC4)C[C@@H]3C)C(C)=N2
InChiKey: MJLJMNMVTQVARE-PXNSSMCTSA-N
Molecular weight: 412.6
Storage: As a dry powder or as DMSO stock solutions (10 mM) at -20 °C. DMSO stocks beyond 3-6 months or 2 freeze/thaw cycles should be tested for activity before use
Dissolution: Soluble in DMSO up to 50 mM; use only 1 freeze/thaw cycle per aliquot

PFI-8N



SMILES: CCNC(C1=CN2N=C(C)C(C3CCN(CC4(O)[C@H]5C[C@H]6C[C@@H]4C[C@H](C6)C5)CC3)=C2C=N1)=O
InChiKey: GGHBKBALXANODH-GLJKLTJVSA-N
Molecular weight: 451.6
Storage: As a dry powder or as DMSO stock solutions (10 mM) at -20 °C. DMSO stocks beyond 3-6 months or 2 freeze/thaw cycles should be tested for activity before use
Dissolution: Soluble in DMSO up to 50 mM; use only 1 freeze/thaw cycle per aliquot

Chemical Probe Profile

In vitro (cell free) Potency & Selectivity: PFI-8 binds to YEATS4 with K_D = 52 nM (ITC). PFI-8 binds YEATS 1-4 with FRET Ki's of 495, 330, 462, and 33 nM respectively using a biotin-tagged crotonylated H3 peptide.

Potency in Cells and Cellular Target Engagement: NanoBRET measurements showed EC_{50} = 170 nM.