BI-7190: A Chemical Probe for BPTF

Version 1.1 (24th Jan 2023)

Web link for more details: https://opnme.com/molecules/bptf-inhibitor-bi-7190

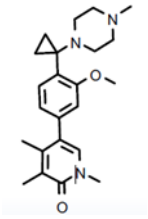
Bromodomain PHD Finger Transcription Factor (BPTF) is a histone-binding component of Nucleosome Remodeling Factor (NURF). BPTF recognises acetylated lysine on histone H4, through its bromodomain, as well as di- and tri-methylated lysine 4 on histone H3, through its PHD fingers. BPTF's role is in regulating transcription by direct binding to DNA or transcription factors.The entire NURF complex catalyses ATP-dependent nucleosome sliding and facilitates transcription of chromatin. BPTF is involved in brain development and mutations in the gene encoding this protein are associated with neurodevelopmental disorders. The potential pro-tumorigenic role of BPTF has been reported across several indications over the last few years.

Summary

Chemical Probe Name	BI-7190
Negative control compound	BI-4827
Target(s) (synonyms)	BPTF (Bromodomain PHD Finger Transcription Factor)
Recommended cell assay concentration	1 µM
Suitability for *in* vivo use and recommended dose	Yes. 30 mg/kg in mice
Publications	Martinelli P. et al, ChemMedChem 2023; https://doi.org/10.1002/cmdc.202200686
Orthogonal chemical probes	NVS-BPTF-1, TP-238
In vitro assay(s) used to characterise	DiscoveRx, ITC
Cellular assay(s) for target-engagement	NanoBRET

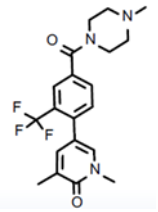
Chemical Probe & Negative Control Structures and Use

BI-7190 Chemical Probe



SMILES: COC1=C(C=CC(=C1)C1=CN(C)C(=O)C(C)=C1C)C1(CC1)N1CCN(C)CC1
InChiKey: ASRLBLHATMXGPC-UHFFFAOYSA-N
Molecular weight: 381.52
Storage: -20 °C
Dissolution: DMSO (10 mM), aqueous solubility @ pH 6.8 > 84 µg/ml

BI-4827 Negative Control



SMILES: CN1CCN(CC1)C(=O)C1=CC=C(C2=CN(C)C(=O)C(C)=C2)C(=C1)C(F)(F)F
InChiKey: YYHNDKBEGPYHKQ-UHFFFAOYSA-N
Molecular weight: 393.41
Storage: -20 °C
Dissolution: DMSO (10 mM), aqueous solubility @ pH 6.8 > 100 µg/ml

Chemical Probe Profile

In vitro Potency & Selectivity:

BI-7190 binds to the BPTF bromodomain with high affinity (DiscoveRx BROMOscan K_D = 3.5 nM, ITC K_D = 85 nM). No significant hits were observed in kinase and Cerep panels. BI-7190 shows high selectivity at 10 µM concentration versus a panel of 44 receptors (no inhibition observed) and a 38-member kinase panel (no hit at 10 µM).

The negative control BI-4827 shows high selectivity hitting 0/44 targets inhibition with more than 50% @10 µM.

Potency in Cells and Cellular Target Engagement:

Cellular target engagement was confirmed by NanoBRET (BPTF EC_{50} = 58 nM) and a more than 19-fold selectivity window towards the bromodomain family off-targets was observed (e.g., NanoBRET (BRD9) EC50 = 1100 nM).