

WM-1119: A Chemical Probe for KAT6A and KAT6B

Version 1.0 (25th March 2021)

Web link for more details: <https://www.sgc-ffm.uni-frankfurt.de/#!specificprobeoverview/WM-1119>

Overview

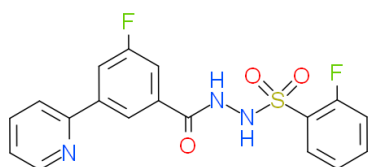
[KAT6A](#) and [KAT6B](#) are histone acetyltransferase that acetylates lysine residues in histone H3 and H4 in vitro. KAT6A is a component of the MOZ/MORF complex that shows histone H3 acetyltransferase activity and may act as a transcriptional coactivator for RUNX1 and RUNX2. In addition, it acetylates p53/TP53 at 'Lys-120' and 'Lys-382' and controls its transcriptional activity via association with PML. It is implicated in the suppression of senescence.

Summary

Chemical Probe Name	WM-1119
Negative control compound	WM-2474
Target(s) (synonyms)	KAT6A (lysine acetyltransferase 6A, MYST3), KAT6B (lysine acetyltransferase 6B, MYST4)
Recommended cell assay concentration	Use at concentration of 1 μ M (and < 10 μ M) for WM-1119 and WM-2474; use with control for best interpretation of data.
Suitability for <i>in vivo</i> use and recommended dose	Arrests the progression of lymphoma in mice (Dosing: 50 mg/kg 4 times a day (IV))
Publications	PMID: 30069049 , PMID: 32118427
Orthogonal chemical probes	
<i>In vitro</i> assay(s) used to characterise	SPR, HAT activity assay (AlphaScreen)
Cellular assay(s) for target-engagement	Cell cycle arrest in Fucci MEFs ; EMRK1184 cell growth inhibition
ChemicalProbes.org	Link to chemicalprobes.org

Chemical Probe & Negative Control Structures and Use

WM-1119 Chemical Probe



SMILES: c1ccc(c(c1)F)S(NNC(c1cc(cc(c1)F)c1cccn1)=O)(=O)=O

InChIKey: QLXULUNLCRKWRD-UHFFFAOYSA-N

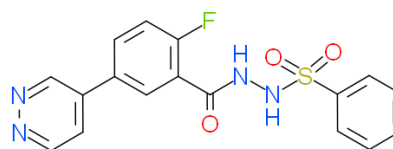
Molecular weight: 389.1

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 10 mM; use only 1 freeze/thaw cycle per aliquot

WM-2474 Negative Control



SMILES: c1ccc(cc1)S(NNC(c1cc(ccc1)F)c1ccnnc1)=O)(=O)=O

InChIKey: WYMCVPPNOFFNGE-UHFFFAOYSA-N

Molecular weight: 372.1

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 10 mM; use only 1 freeze/thaw cycle per aliquot

Chemical Probe Profile

In vitro Potency & Selectivity:

WM-1119 shows potent activity on KAT6A (SPR: K_d = 2 nM; HAT activity assay (AlphaScreen: IC_{50} = 37 nM). It is > 200-fold selective on all other HATs tested. No significant activity was found on 166 targets (Kinases, GPCRs, HDACs, phosphatases etc.) at 10 μ M. WM-2474 displays no activity on KAT6A in the HAT assay (IC_{50} > 50 μ M).

Potency in Cells and Cellular Target Engagement:

WM-1119 administration at 1 μ M results in cell cycle arrest in Fucci MEFs (Mouse Embryonic Fibroblast). EMRK1184 cell growth is inhibited with IC_{50} = 0.25 μ M. WM-2474 shows no effect at 10 μ M on Fucci MEFs.