LH168: A chemical degrader probe for WDR5

Version 2.0 (18th August 2025)

Web link for more details: https://www.thesgc.org/chemical-probes/lh168

Overview

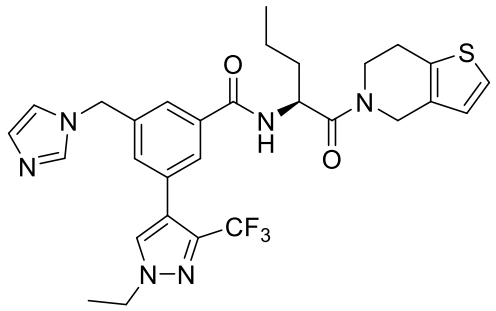
WDR5 is incorporated into Histone Lysine Methyltransferase complex MLL1 that is a crucial epigenetic writer to modify DNA accessibility. WDR5 was shown to be crucial to recruit the transcription factor MYC to chromatin. Both interaction partners are oncoproteins that are known to be strong drivers for lymphoid and leukaemia cancers (MLL1) and neuroblastoma (MYC). Their overexpression trigger substantial oncogenic programs or deregulate cell lineage differentiation mechanisms.

Summary

Chemical Probe Name	LH168
Negative control compounds	LH222
Target(s) (synonyms)	WDR5 (WD40-repeat containing protein 5)
Recommended *in vitro* assay concentration	Up to 1 µM
Suitability for *in* vivo use and recommended dose	This chemical probe was not tested for *in vivo* use
Publications	https://doi.org/10.1039/D5CB00109A
Orthogonal chemical probes	Homer, OICR9429
In vitro assay(s) used to characterise	ITC, SPR, DSF
Cellular assay(s) for target-engagement	NanoBRET, quantitative Proteomics
ChemicalProbes.org	

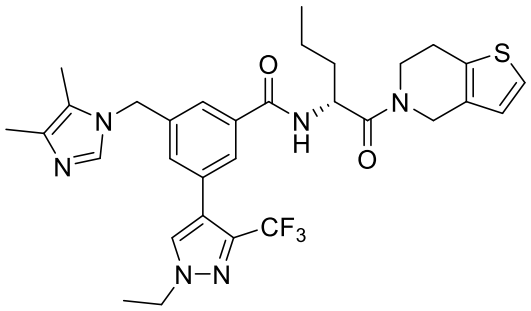
Chemical Probe & Negative Control Structures and Use

LH168



SMILES:
O=C([C@H](CCC)NC(C1=CC(CN2C=CN=C2)=CC(C3=CN(CC)N=C3C(F)(F)F)=C1)=O)N4CCC(SC=C5)=C5C4
InChiKey: UFKFTBGGMLIIME-DEOSSOPVSA-N
Molecular weight: 584.665
Storage: As a dry powder or as DMSO stock solutions (10 mM) at -20 °C.
Dissolution: Soluble at 10 mM in DMSO

LH222



SMILES:
O=C([C@@H](CCC)NC(C1=CC(CN2C(C)=C(C)N=C2)=CC(C3=CN(CC)N=C3C(F)(F)F)=C1)=O)N4CCC(SC=C5)=C5C4
InChiKey: RVPFWIYUOKYZMI-AREMUKBSSA-N
Molecular weight: 612.719
Storage: As a dry powder or as DMSO stock solutions (10 mM) at -20 °C.
Dissolution: Soluble at 10 mM in DMSO

Chemical Probe Profile

In vitro Potency & Selectivity:

LH168 binds to WDR5 with a KD of 13 nM as determined by SPR. ITC measuremet provided Kd of 38 nM. No off-targets have been identified in proteome-wide studies.

Potency in Cells and Cellular Target Engagement:

No cell toxicity has been observed in HEK293T cells up to 10 µM at 24h treatment with LH168 (CellTiter-Glo Assay). NanoBRET measurements showed an EC_{50} below 10 nM.