

Homer: A chemical degrader probe for WDR5

Version 1.0 (4th December 2024)

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

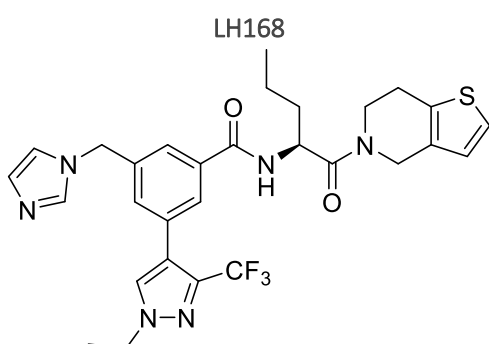
Overview

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 triggers 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 <i>in vitro</i> assay concentration	Up to 1 μ M
Suitability for <i>in vivo</i> use and recommended dose	This chemical probe was not tested for <i>in vivo</i> use
Publications	
Orthogonal chemical probes	Homer, OICR9429
<i>In vitro</i> 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



SMILES:

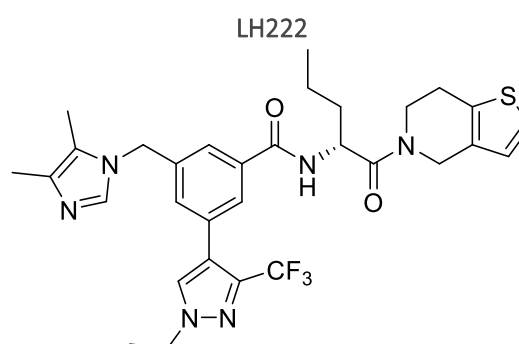
O=C([C@H](CCC)NC(C1=CC(CN2C=CN=C2)=CC(C3=CN(CC)N=C3C(F)(F)F)=C1)=O)N4CCC(SC=C5)=C5C4

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



SMILES:

O=C([C@@H](CCC)NC(C1=CC(CN2C=CN=C2)=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 measurement 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 μ M at 24h treatment with LH168 (CellTiter-Glo Assay). NanoBRET measurements showed an EC₅₀ below 10 nM.