UNC8732: A chemical probe (degrader) for NSD2.

Version 1.0 (28st January 2024)

Web link for more details: https://www.thesgc.org/chemical-probes/UNC8732

Overview

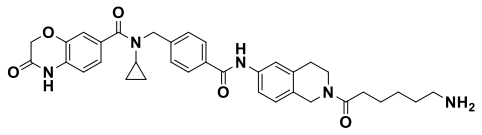
SGC in collaboration with Professor Lindsey Ingermann James at the University of North Carolina has developed a degrader-based chemical probe for NSD2.

Summary

Chemical Probe Name	UNC8732
Negative control compound	UNC8884
Target(s) (synonyms)	NSD2
Recommended concentration for cellular use	≤ 10 µM; recommend researchers 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	Prerequisite to the probe: https://doi.org/10.1021/jacs.3c01421
Orthogonal chemical probes	
In vitro assay(s) used to characterise	SPR, BLI, DSF, HDX
Cellular assay(s) for target-engagement	NanoBRET, in cell western, BioID, global proteomics
ChemicalProbes.org	

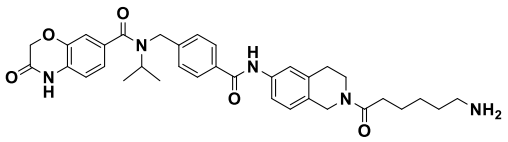
Chemical Probe & Negative Control Structures and Use

UNC8732



SMILES:
O=C(NC1=CC=C(C(CC2)=C1)CN2C(CCCCCN)=O)C3=CC=C(C=C3)CN(C(C4=CC(OC5)=C(C=C4)NC5=O)=O)C6CC6
InChiKey: CSTHTJLTORVUST-UHFFFAOYSA-N
Molecular weight: 609.7
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

UNC8884



SMILES:
O=C(NC1=CC=C(C(CC2)=C1)CN2C(CCCCCN)=O)C3=CC=C(C=C3)CN(C(C4=CC(OC5)=C(C=C4)NC5=O)=O)C(C)C
InChiKey: RNMKSPMOWMAMPV-UHFFFAOYSA-N
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Chemical Probe Profile

In vitro (cell-free) Potency & Selectivity: the potency is inferred from degradation; selectivity is inferred from chemoproteomics dataset for UNC8153 https://doi.org/10.1021/jacs.3c014211 .

Potency in Cells and Cellular Target Engagement: UNC8732 degrades NSD2 with DC_{50} of 60 nM (Dmax = 97%)