SGC-UBD1031: A dual activity chemical probe for the ubiquitin binding domain of USP16 and HDAC6

Version 1.0 (1st May 2024)

Web link for more details: https://www.thesgc.org/chemical-probes/SGC-UBD1031

Overview

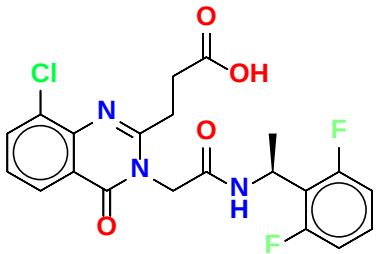
SGC in collaboration with the Mark Lautens' lab at University of Toronto has developed a dual activity chemical probe SGC-UBD1031 for USP16 UBD and HDAC6 UBD. When used in parallel with selective chemical probe for HDAC6 UBD (SGC-UBD253), SGC-UBD1031 can be used to study the biological role of USP16 UBD.

Summary

Chemical Probe Name	SGC-UBD1031
Negative control compound	SGC-UBD1031N
Target(s) (synonyms)	USP16/HDAC6
Recommended *in vitro* assay concentration	< 10 µM; use with negative control, and orthogonal controls for HDAC6 for best interpretation of data
Suitability for *in* vivo use and recommended dose	This chemical probe was not tested for *in vivo* use.
Publications	
Orthogonal chemical probes	SGC-UBD253
In vitro assay(s) used to characterise	SPR, ITC
Cellular assay(s) for target-engagement	NanoBRET
ChemicalProbes.org	

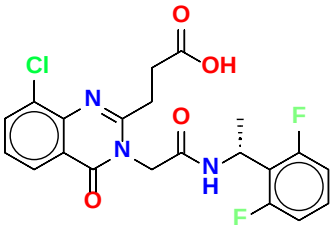
Chemical Probe & Negative Control Structures and Use

SGC-UBD1031



SMILES: OC(CCC1=Nc2c(C(N1CC(N[C@@H](C)c3c(F)cccc3F)=O)=O)cccc2Cl)=O
InChiKey: DBOPLVMSXSBHQW-NSHDSACASA-N
Molecular weight: 449.8
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

SGC-UBD1031N



SMILES: OC(CCC1=Nc2c(C(N1CC(N[C@H](C)c3c(F)cccc3F)=O)=O)cccc2Cl)=O
InChiKey: DBOPLVMSXSBHQW-LLVKDONJSA-N
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Chemical Probe Profile

In vitro Potency & Selectivity: In a SPR assay, SGC-UBD1031 binds USP16 UBD with K_d = 48 nM and HDAC6 UBD with K_d = 16 nM.

Potency in Cells and Cellular Target Engagement: In an intact cellular nanoBRET assay, SGC-UBD1031 inhibited interaction of USP16 and HDAC6 with ubiquitin-like ISG15 with IC_{50} = 1.7µM, and 1.5µM respectively