

BI-3802: A Chemical Probe for BCL6

Version 1.0 (15th September 2023)

Web link for more details: <https://www.sgc-ffm.uni-frankfurt.de/#!specificprobeoverview/BI-3802>

Overview

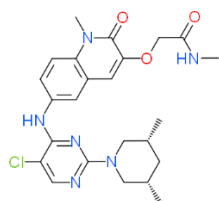
BCL6 is a zinc finger transcription factor. By binding to DNA and recruiting one of its co-repressors (NCoR, SMRT, or BCOR) to its dimeric BTB domain, BCL6 represses genes involved in cell cycle control, cell death, differentiation, and the DNA damage response. This results in B-cells in the germinal centre to proliferate rapidly, evade growth checkpoint controls, and tolerate high levels of DNA damage which is required for the process of somatic hypermutation of antibodies and may lead to lymphomagenesis.

Summary

Chemical Probe Name	BI-3802 (degrader)
Negative control compound	BI-5273
Target(s) (synonyms)	BCL6 (BCL6 transcription repressor, Zinc Finger Protein 51)
Recommended <i>in vitro</i> assay concentration	Use at concentration up to 1 μ M for BI-3802 and BI-5273; use with control and orthogonal probes for best interpretation of data
Suitability for <i>in vivo</i> use and recommended dose	Not for <i>in vivo</i> use.
Publications	PMID: 28930682 , PMID: 33208943
Orthogonal chemical probes	TP-021 , CCT369260 , BI-3812
<i>In vitro</i> assay(s) used to characterise	BCL6:BCOR ULight TR-FRET
Cellular assay(s) for target-engagement	BCL6::NCOR LUMIER in cells, BCL6 protein degradation in SU-DHL-4 cells

Chemical Probe & Negative Control Structures and Use

BI-3802 Chemical Probe



SMILES:

C[C@H]1C[C@@H](C)CN(C1)c1ncc(c(Nc2ccc3c(C=C(C(N3C)=O)OCC(NC)=O)c2)n1)[Cl]

InChIKey: GXTJETQFYHZHNB-GASCZTMLSA-N

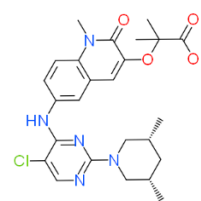
Molecular weight: 484.2 g/mol

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

BI-5273 Negative Control



SMILES:

C[C@H]1C[C@@H](C)CN(C1)c1ncc(c(Nc2ccc3c(C=C(C(N3C)=O)OC(C)(C)C(=O)O)c2)n1)[Cl]

InChIKey: KWMGIHUWUICDA-GASCZTMLSA-N

Molecular weight: 499.2 g/mol

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:

BI-3802 shows potent activity on human BCL6 with $IC_{50} \leq 3$ nM in the BCL6:BCOR ULight TR-FRET assay. There are no other BTB/POZ domain containing close family members. The Eurofins Safety screen (44 targets) at 10 μ M is clean except for [HTR2B \(agonist\)](#) (12% ctrl). The Invitrogen kinase panel (54 kinases) at 1 μ M is clean.

Potency in Cells and Cellular Target Engagement:

The cellular BCL6::NCOR LUMIER assay yields an $IC_{50} = 43$ nM. $DC_{50} = 20$ nM for the BCL6 protein degradation in SU-DHL-4 cells.