

BI-3231: A Chemical Probe for HSD17B13

Version 1.0 (31st August 2023)

Web link for more details: <https://www.sgc-ffm.uni-frankfurt.de/#!specificprobeoverview/BI-3231>

Overview

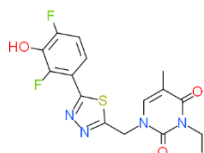
[HSD17B13](#) is a lipid droplet-associated member of the 17-beta hydroxysteroid dehydrogenases (HSD17B) family, primarily expressed in hepatocytes. It acts on a broad range of lipid substrates, including estradiol. NAD⁺ plays an important role as co-factor. Its biological function is unknown. Genome-wide association studies in patients revealed HSD17B13 as a potential new target for the treatment of nonalcoholic steatohepatitis (NASH) and other liver diseases.

Summary

Chemical Probe Name	BI-3231
Negative control compound	BI-0955
Target(s) (synonyms)	HSD17B13 (Hydroxysteroid 17-beta dehydrogenase 13, SCDR9)
Recommended <i>in vitro</i> assay concentration	Use at concentration of 1 μM for BI-3231 and BI-0955; use with control probe for best interpretation of data
Suitability for <i>in vivo</i> use and recommended dose	Tested in mouse (dose i.v.: 5 μM/kg, p.o.: 50 μM/kg, s.c.: 80 μM/kg); rapid <i>in vivo</i> clearance; Multiple daily dosing or extended-release formulation might be needed for subchronic PD/NASH model. The negative control has only a moderate metabolic stability and could potentially go through the metabolic pathway. Therefore the control is not suitable for animal use.
Publications	PMID: 6727857 (compound 45)
<i>In vitro</i> assay(s) used to characterise	Enzymatic assay
Cellular assay(s) for target-engagement	Cellular hHSD17B13 assay, HEK cells

Chemical Probe & Negative Control Structures and Use

BI-3231 Chemical Probe



SMILES: CCN1C(C(C)=CN(Cc2nnc(c3ccc(c(c3F)O)F)s2)C1=O)=O

InChIKey: XKDHFIPNTTUSIA-UHFFFAOYSA-N

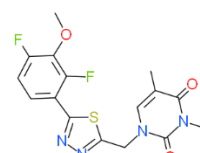
Molecular weight: 380.08 g/mol

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-0955 Negative Control



SMILES: CCN1C(C(C)=CN(Cc2nnc(c3ccc(c(c3F)OC)F)s2)C1=O)=O

InChIKey: TVCKWZATGBVYEN-UHFFFAOYSA-N

Molecular weight: 394.09 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-3231 shows potent activity on human HSD17B13 ($K_i = 0.7 \pm 0.2$ nM; DSF (temperature shift): 16.7 K in the presence of NAD⁺). For the closest family member HSD17B11 $IC_{50} > 10$ μM. The Eurofins Safety screen (44 targets) at 10 μM is clean except for PTGS2 (COX2) (49% ctrl).

Potency in Cells and Cellular Target Engagement:

In the cellular hHSD17B13 assay using HEK cells an $IC_{50} = 11 \pm 5$ nM was obtained.