BAY-069: A Chemical Probe for BCAT1/2

Version 1.0 (24th March 2021)

Web link for more details: https://www.sgc-ffm.uni-frankfurt.de/#!specificprobeoverview/BAY-069

Overview

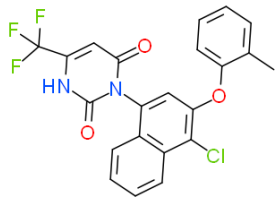
BCAT1 and BCAT2 catalyse the first reaction in the metabolism of the essential branched chain amino acids leucine, isoleucine, and valine. BCAT1 is a validated target for the treatment of various cancer types such as breast and prostate cancer.

Summary

Chemical Probe Name	BAY-069
Negative control compound	BAY-771
Target(s) (synonyms)	BCAT1/2 (branched chain amino acid transaminase 1/2)
Recommended cell assay concentration	Warning: BAY-069 shows a high plasma protein binding. Therefore, the probe is not recommended for use in cell assays with serum. Use with negative control for best interpretation of data
Suitability for *in* vivo use and recommended dose	BAY-069 may be suitable for in vivo studies at higher concentrations: Tested in mice with an oral dose of 100 mg/kg once daily.
Publications	None at time of writing.
Orthogonal chemical probes	
In vitro assay(s) used to characterise	Biochemical assay
Cellular assay(s) for target-engagement	Cellular mechanistic assay – BCAA measurement

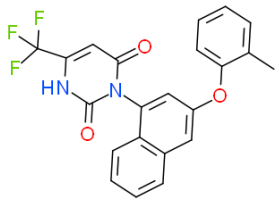
Chemical Probe & Negative Control Structures and Use

BAY-069 Chemical Probe



SMILES: Cc1ccccc1Oc1cc(c2ccccc2c1[Cl])N1C(C=C(C(F)(F)F)NC1=O)=O
InChiKey: UNSHMXUHOHBLIQ-UHFFFAOYSA-N
Molecular weight: 446.06
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

BAY-771 *Negative* Control



SMILES: Cc1ccccc1Oc1cc(c2ccccc2c1)N1C(C=C(C(F)(F)F)NC1=O)=O
InChiKey: LZLNIHXKWZZQLE-UHFFFAOYSA-N
Molecular weight: 412.10
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:

BAY-069 shows potent activity on BCAT1/2 in a biochemical assay: BCAT1 (IC_{50} = 27 nM), BCAT2 (IC_{50} = 130 nM). No activity was found on aspartate transaminase: GOT1/2 with IC_{50} > 50 µM and a panel of 30 kinases, 30 proteases and 77 other targets. BAY-771 is inactive on BCAT1 (IC_{50} = 6.5 µM) and BCAT2 (IC_{50} = 10.8 µM).

Potency in Cells and Cellular Target Engagement:

BAY-069 displays potent binding in a cellular mechanistic assay with the measurement of BCAA in U-87-MG (high BCAT1 expressing) cells (IC_{50} =358 nM) and MDA-MB-231 (high BCAT2 expressing) cells (IC_{50} = 874 nM). BAY-771 shows no activity in U-87-MG cells (IC_{50} = 6.2 µM).