BAY-439: A Chemical Probe for PLA2G5

Version 1.0 (23rd June 2025)

Web link for more details: https://www.sgc-ffm.uni-frankfurt.de/#!specificprobeoverview/BAY-439

Overview

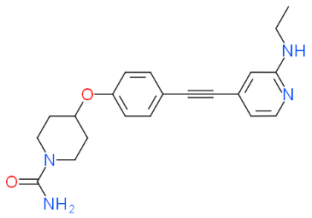
PLA2G5 belongs to the group of secretory, Ca^{2+}-dependent Phospholipases A2 (PLA2), that hydrolyse membrane phospholipids to generate lysophospholipids and free fatty acids (FFAs). The FFA arachidonic acid (AA) can be further metabolized to generate eicosanoids, including pro-inflammatory prostaglandins and leukotrienes. PLA2G5 is involved in e.g. LTC4, AA and PAF release and thus, in inflammatory processes.

Summary

Chemical Probe Name	BAY-439
Negative control compound	BAY-163
Target(s) (synonyms)	PLA2G5
Recommended *in vitro* assay concentration	Use at concentration up to 300 nM for BAY-439 and BAY-163; use with negative control for best interpretation of data
Suitability for *in* vivo use and recommended dose	For in vivo studies in rat, use a maximum dose of 6 mg/kg. Oral administration of BAY-439 (2-days QD treatment) reduced inflammatory pain in the complete Freund's adjuvant -induced arthritic rat model rat.
Publications	None at time of writing
In vitro assay(s) used to characterise	Biochemical assay using recombinant PLA2G5 and Red/Green BODIPY® PC-A2 as substrate
Cellular assay(s) for target-engagement	Cellular PLA2G5 assay using THP-1 cells and Bis-BODIPY® FL C11-PC

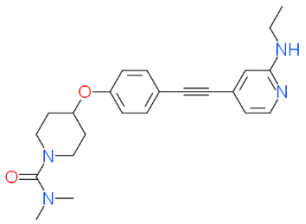
Chemical Probe & Negative Control Structures and Use

BAY-439 Chemical Probe



SMILES: CCNc1cc(C#Cc2ccc(cc2)OC2CCN(CC2)C(N)=O)ccn1
InChiKey: HRGRJDHSOFOGNO-UHFFFAOYSA-N
Molecular weight: 364.19 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

BAY-163 Negative Control



SMILES: CCNc1cc(C#Cc2ccc(cc2)OC2CCN(CC2)C(N(C)C)=O)ccn1
InChiKey: WURMOCOMRIDARO-UHFFFAOYSA-N
Molecular weight: 392.22 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:

BAY-439 is a potent inhibitor of PLA2G5 in a biochemical assay using recombinant PLA2G5 and Red/Green BODIPY® PC-A2 as substrate with IC_{50}= 7 nM and KD = 214 nM in the SPR binding assay. Closest off-targets in a biochemical assay within the family are (IC_{50} [µM]) hPLA2G2A (0.788), hPLA2G10 (2.85) and hPLA2G4A, hPLA2G7 both (>40). The Nuvisan Phospholipase C panel is clean (h PLCB3/PLCD1/PLCG1/PLCZ1: all IC_{50} >20 µM). Closest off-targets in the Eurofins Bayer Safety Screen (77 targets) at 10 µM are (IC_{50} [µM]) hPGR (1.19), hADRA2C (3.07), hSLC6A3 (3.55), hSLC6A2 (4.71). The kinase panel (378 kinases) at 10 µM is clean.

Potency in Cells and Cellular Target Engagement:

In a cellular PLA2G5 assay using THP-1 cells and Bis-BODIPY® FL C11-PC as substrate IC_{50} = 61 nM.