BAY-091: A Chemical Probe for PIP4K2A

Version 1.0 (20th October 2021)

Web link for more details: https://www.sgc-ffm.uni-frankfurt.de/#!specificprobeoverview/BAY-091

Overview

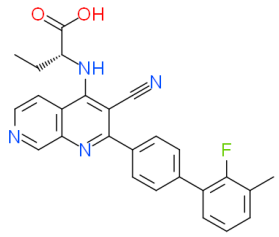
PIP4K2A catalyzes the phosphorylation of phosphatidylinositol-4-phosphate on the fifth hydroxyl of the myo-inositol ring to form phosphatidylinositol-4,5-bisphosphate (PI(4,5)P2). PI(4,5)P2 is thought to be involved in the regulation of secretion, cell proliferation, differentiation, and motility. The hypothesis that PIP4K2A inhibition induces cell death in p53 mutant tumours by hyperactivating AKT needs to be tested.

Summary

Chemical Probe Name	BAY-091
Negative control compound	BAY-0361
Target(s) (synonyms)	PIP4K2A (Phosphatidylinositol-5-phosphate 4-kinase type 2 alpha, PIP5KIIalpha, PIP5KIIA, PIP5K2A, PIPK, PIP5K2)
Recommended *in vitro* assay concentration	Use with control BAY-0361 for best interpretation of data
Suitability for *in* vivo use and recommended dose	Not for in vivo use.
Publications	PMID: 34699202
Orthogonal chemical probes	
In vitro assay(s) used to characterise	Quantification of produced ADP
Cellular assay(s) for target-engagement	CETSA lysate and intact cells

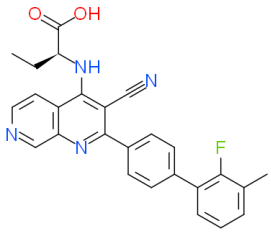
Chemical Probe & Negative Control Structures and Use

BAY-091 Chemical Probe



SMILES: CC[C@H](C(O)=O)Nc1c(C#N)c(c2ccc(cc2)c2cccc(C)c2F)nc2cnccc12
InChiKey: DVIVLYHDLNAXAT-OAQYLSRUSA-N
Molecular weight: 440.16 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-0361 Negative Control



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Chemical Probe Profile

In vitro Potency & Selectivity:

BAY-091 shows potent activity on PIP4K2A (IC_{50} = 1.3 nM with 10 µM ATP; Quantification of produced ADP and 2.6 nM with 250 µM ATP). It is also active in the HTRF assay used for the quantification of produced PI(4,5)P2 (IC_{50} = 8.5 nM with 10 µM ATP; 16.4 nM with 2 mM ATP). There is no off-target in the Eurofins Kinase Panel (373 at 1 µM) with all kinases having an inhibition > 60 %. Closest off-targets in the Eurofins safety panel (77 at 10 µM) are [% inhibition] TBXAS1 (98), HTR2B (98), MAOB (81), PDE3 (74) and PDE5A (62).

Potency in Cells and Cellular Target Engagement:

The cellular PIP4K2A target engagement was proven for BAY-091 (CETSA lysates, 60°C: EC_{50} (95% CI) = 1.8 µM; CETSA int. cells, 56°C: EC_{50} (95% CI) = 1.1 µM. No effect in cellular mechanistic (pAKT, ROS) or functional assays (p53 mutant proliferation) was found.