JYQ-173: A Chemical Probe for PRAK7

Version 1.0 (24th April 2025)

Web link for more details: https://www.sgc-ffm.uni-frankfurt.de/#!specificprobeoverview/JYQ-173

Overview

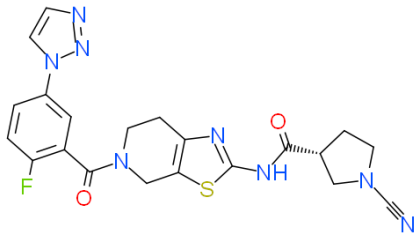
PARK7 belongs to the peptidase C56 family of proteins and has a glyoxalase activity. PARK7 plays a crucial role in cellular processes such as transcriptional regulation, mitochondrial function, and the stabilization of certain proteins. Some forms of Parkinson's disease are caused by a PARK7 gene defect.

Summary

Chemical Probe Name	JYQ-173
Negative control compound	MB078
Target(s) (synonyms)	PARK7
Recommended *in vitro* assay concentration	Use at concentration of up to 1 µM for JYQ-173 and MB078; use with control for best interpretation of data
Suitability for *in* vivo use and recommended dose	Not tested.
Publications	PMID: 38713163
In vitro assay(s) used to characterise	DiFMUAc assay
Cellular assay(s) for target-engagement	ABPP assay

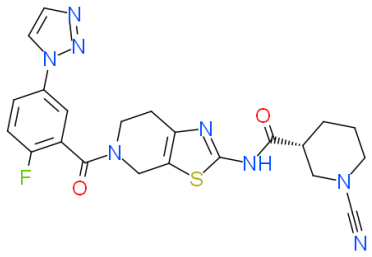
Chemical Probe & Negative Control Structures and Use

JYQ-173 Chemical Probe



SMILES:
C1CN(Cc2c1nc(NC([C@@H]1CCN(C1)C#N)=O)s2)C(c1cc(ccc1F)n1ccnn1)=O
InChiKey: VLGBFCNSBOLUFH-CYBMUJFWSA-N
Molecular weight: 466.13 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

MB078 Negative Control



SMILES:
C1C[C@H](CN(C1)C#N)C(Nc1nc2CCN(Cc2s1)C(c1cc(ccc1F)n1ccnn1)=O)=O
InChiKey: ZWLZOQJKXRNBFL-CQSZACIVSA-N
Molecular weight: 480.15 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:

JYQ-173 is a potent covalent inhibitor of PARK7 binding irreversibly to Cys106 with IC_{50} = 19 nM in the DiFMUAc assay (Activity assay that relies on the deacetylation of the fluorogenic substrate 6,8-difluoro-4-methylumbelliferyl; kinact/KI = 12093 M-1s-1, kinact = 0.052 s-1, KI(app) = 4.3 µM) and IC_{50} = 100 nM in the fluorescence polarization assay. No inhibition of DUBs within the carbonic anhydrases superfamily was observed (UCHL1: IC_{50} = 18.96 µM using Ub-RhoMorpholine as substrate). No off-targets were detected in a SLC-ABPP experiment (cysteine activity-based protein profiling). Only PARK7 Cys106 peptide was detected among >5000 Cys sites in A549 cells.

Potency in Cells and Cellular Target Engagement:

In an ABPP assay full inhibition was observed at a JYQ-173 concentration of < 1 µM (1h, 37°C).