

TP-061: A chemical probe for Brr2

Version 1.0 (4th July 2024)



Web link for more details: <https://www.thesgc.org/chemical-probes/TP-061>

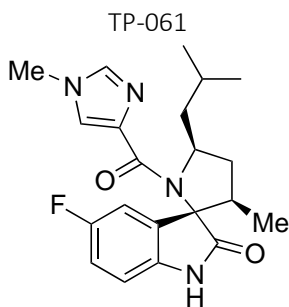
Overview

Takeda in collaboration with OICR and CMD has developed a chemical probe TP-061 for Brr2. TP-061 can be used to study the biological role of Brr2.

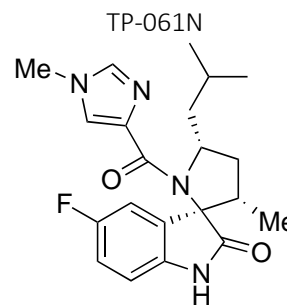
Summary

Chemical Probe Name	TP-061
Negative control compound	TP-061N
Target(s) (synonyms)	Brr2
Recommended <i>in vitro</i> assay concentration	5 μ M; use with negative control
Suitability for <i>in vivo</i> use and recommended dose	This chemical probe was not tested for <i>in vivo</i> use.
Publications	Bioorganic & Medicinal Chemistry 25 (2017) 4753–4767
Orthogonal chemical probes	
<i>In vitro</i> assay(s) used to characterise	ATPase, Unwindase, ASMS
Cellular assay(s) for target-engagement	NanoBRET
ChemicalProbes.org	

Chemical Probe & Negative Control Structures and Use



SMILES:
CC(C)C[C@H](N1C(C2=CN(C)C=N2)=O)C[C@@H](C)[C@]1(C3=CC(F)=CC=C3N4)C4=O
InChiKey: WAFNVKVWBPXGHK-CGSMKXTHSA-N
Molecular weight: 384.5
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 50 mM; use only 1 freeze/thaw cycle per aliquot



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Chemical Probe Profile

***In vitro* Potency & Selectivity:** In an ATPase assay, TP-061 inhibits Brr2 with $IC_{50} = 21$ nM and Unwindase FRET assay with $IC_{50} = 480$ nM. Inactive up to 100 μ M on eIF4A1, eIF4A3 and DHX29 (closest related enzymes).

Potency in Cells and Cellular Target Engagement: In an in-cell NanoBRET assay TP-061 inhibits target engagement of Brr2 with $IC_{50} = 680$ nM.