

# TP-030-1: A Chemical Probe for RIPK1

Version 1.0 (25<sup>th</sup> March 2021)

Web link for more details: <https://www.sgc-ffm.uni-frankfurt.de/#!specificprobeoverview/TP-030-1>

## Overview

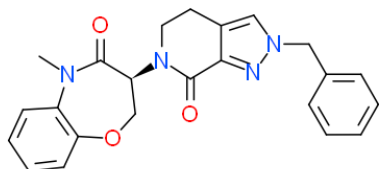
The serine/threonine protein kinase [RIPK1](#) functions in various cellular pathways and is a crucial upstream regulator of necroptosis. It forms a complex with various proteins, e.g. RIPK3 and is associated with a variety of pathologies such as ischemic injury, inflammatory diseases, neurodegenerative diseases.

## Summary

Chemical Probe Name	TP-030-1
Negative control compound	TP-030n
Target(s) (synonyms)	RIPK1 (receptor interacting serine/threonine kinase 1, RIP)
Recommended cell assay concentration	Use at concentration of 100 nM for TP-030-1 and TP-030n; use with control and orthogonal probe for best interpretation of data
Suitability for <i>in vivo</i> use and recommended dose	Suitable for <i>in vivo</i> use, preliminary tests were done in mice.
Publications	<a href="#">PMID: 29485864</a>
Orthogonal chemical probes	<a href="#">TP-030-2</a>
<i>In vitro</i> assay(s) used to characterise	TR-FRET
Cellular assay(s) for target-engagement	HT29 necroptosis assay

## Chemical Probe & Negative Control Structures and Use

TP-030-1 Chemical Probe



SMILES: CN1C([C@H](COc2ccccc12)N1CCc2cn(Cc3ccccc3)nc2C1=O)=O

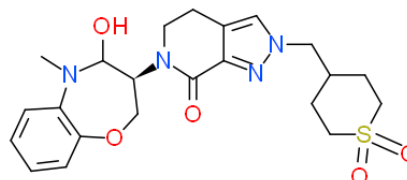
InChIKey: MAHFVAHQSLJIF-IBGZPJMESA-N

Molecular weight: 402.17

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

TP-030n Negative Control



SMILES: CN1C([C@H](COc2ccccc12)N1CCc2cn(CC3CCS(CC3)(=O)=O)nc2C1=O)=O

InChIKey: IVVSBEQDCAZLFY-SFHVURJKSA-N

Molecular weight: 458.2

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:

TP-030-1 shows potent activity on human RIPK1 (K<sub>i</sub> = 3.9 nM, TR-FRET), but less on mouse (IC<sub>50</sub> = 4.2 μM). No significant binding was observed at 1 μM for 303 kinases tested (Takeda Global Kinase Panel). The Eurofins-Panlabs screen of 68 targets was clean for TP-030-1 and TP-030n. TP-030n is not active in the TR\_FRET assay: hRIPK1 (K<sub>i</sub> = 6.9 μM), mRIPK1 (K<sub>i</sub> > 10 μM).

### Potency in Cells and Cellular Target Engagement:

TP-030-1 displays a high potency in the HT29 necroptosis assay with IC<sub>50</sub> = 18 nM.