

# 8RK64: A Chemical Probe for UCHL1

Version 1.0 (19<sup>th</sup> April 2021)

Web link for more details: *Pending*

## Overview

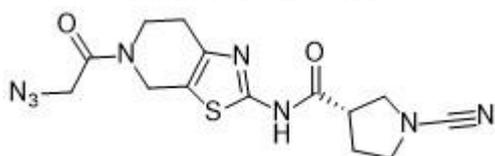
Ubiquitin carboxy-terminal hydrolase L1 (UCHL1), also known as neuron-specific protein PGP9.5 (PGP9.5) or Parkinson disease 5 (PARK5), is a DUB active in neurons that constitutes 1 to 2% of the total brain protein. UCHL1 variants have been linked with neurodegenerative disorders Parkinson's and Alzheimer's disease. In addition, high levels of UCHL1 also correlate often with cancer and especially metastasis. The function of UCHL1 activity, and its role in cancer and neurodegenerative disease is poorly understood and few UCHL1-specific, high quality, activity tools are available.

## Summary

Chemical Probe Name	8RK64 (Fluorescent probe: 8RK59)
Negative control compound	JYQ88
Target(s) (synonyms)	UCHL1
Recommended cell assay concentration	Use at concentrations up to 3 $\mu$ M.
Suitability for <i>in vivo</i> use and recommended dose	Use in zebrafish up to 50 $\mu$ M.
Publications	<a href="#">PMID: 32886496</a>
Orthogonal chemical probes	Flourescent probe: 8RK59
<i>In vitro</i> assay(s) used to characterise	ABPP, Ub-RhoMP Assay
Cellular assay(s) for target-engagement	ABPP, Cell Titer blue assay

## Chemical Probe & Negative Control Structures and Use

8RK64 Chemical Probe



**SMILES:**

O=C(CN=[N+]=[N-])N1CCC2=C(SC(NC([C@H]3CCN(C#N)C3)=O)=N2)C1

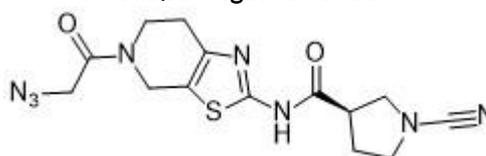
**InChiKey:** KIWKRCIIHSGWQS-VIFPVBQESA-N

**Molecular weight:** 360.4

**Storage:** Store as dry powder/DMSO stock solution (Conc mM) at Temp°C. DMSO stocks should be aliquoted in single-use volumes (and not re-frozen). DMSO stocks older than 3-6 months should be tested for activity before use

**Dissolution:** Soluble in DMSO up to 10 mM.

JYQ88 Negative Control



**SMILES:**

O=C(CN=[N+]=[N-])N1CCC2=C(SC(NC([C@@H]3CCN(C#N)C3)=O)=N2)C1

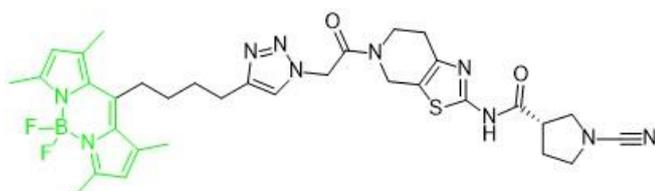
**InChiKey:** KIWKRCIIHSGWQS-SECBINFHSA-N

**Molecular weight:** 360.4

**Storage:** Store as dry powder/DMSO stock solution (Conc mM) at Temp°C. DMSO stocks should be aliquoted in single-use volumes (and not re-frozen). DMSO stocks older than 3-6 months should be tested for activity before use

**Dissolution:** Soluble in DMSO up to 10 mM.

8RK59 – Fluorescent Probe



**SMILES:**

O=C(CN1N=NC(CCCCC(C2=C(C)C=C(C)N2B3(F)F)=C4[N]3=C(C)C=C4C)=C1)N5

CCC6=C(SC(NC([C@H]7CCN(C#N)C7)=O)=N6)C5

**InChiKey:** DHXYPFJKDQWPKY-DEOSSOPVSA-N

**Molecular weight:** 688.61

**Storage:** Store as dry powder/DMSO stock solution (Conc mM) at Temp°C. DMSO stocks should be aliquoted in single-use volumes (and not re-frozen). DMSO stocks older than 3-6 months should be tested for activity before use

**Dissolution:** Soluble in DMSO up to 10 mM..

## Chemical Probe Profile

**In vitro Potency & Selectivity:** IC<sub>50</sub>= 300 nM, covalent and slowly reversible. Probe only targets the active enzyme. Selective within target family, no inhibition of other DUBs in ABPP experiments. Outside target family, one off target identified (deglycase PARK7/DJ1).

**Potency in Cells and Cellular Target Engagement:** Full inhibition at 3  $\mu$ M in ABPP assay.