PROTAC EGFR degrader 3

Cat. No.: HY-144605

CAS No.: 2768472-28-0

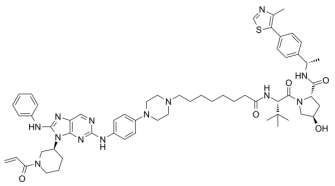
Molecular Formula: $C_{60}H_{77}N_{13}O_5S$

Molecular Weight: 1092.4

Target: EGFR; PROTACs

Pathway: JAK/STAT Signaling; Protein Tyrosine Kinase/RTK; PROTAC

Storage: 4°C, protect from light, stored under nitrogen
* In solvent : -80°C, 6 months; -20°C, 1 month (protect from light, stored under nitrogen)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (91.54 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	0.9154 mL	4.5771 mL	9.1542 mL
	5 mM	0.1831 mL	0.9154 mL	1.8308 mL
	10 mM	0.0915 mL	0.4577 mL	0.9154 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (2.29 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (2.29 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

PROTAC EGFR degrader 3 is a potent PROTAC EGFR degrader. PROTAC EGFR degrader 3 shows excellent cellular activity against the H1975 and HCC827 cells with high selectively. PROTAC EGFR degrader 3 shows that the lysosome is involved in the degradation process of EGFR mutant degradation[1].

In Vitro

PROTAC EGFR degrader 3 (compound CP17) shows anti-proliferative activity of PROTACs with IC_{50}s of 32 nM, 1.60 nM, >10000nM for H1975 ($EGFR^{L858/T790M}$), HCC827 ($EGFR^{del19}$), A431 ($EGFR^{WT}$) cells, respectively[1].

PROTAC EGFR degrader 3 (0, 10, 100, 1000, 10000 nM) exhibits poor cellular activity with IC_{50} of 481 nM, 669 nM for Ba/F3 ($EGFR^{del19/T790M/C797S}$) and Ba/F3 ($EGFR^{L858/T790M/C797S}$) cells, respectively[1].

PROTAC EGFR degrader 3 (0-10000 nM) suppresses the proliferation of the PC9 ($EGFR^{del19/T790M/C797S}$) and H1975 ($EGFR^{L858/T790M/C797S}$) cells, respectively[1].

PROTAC EGFR degrader 3 (30 nM; 0-72 h) decreases the expression level of $EGFR^{L858/T790M}$ after 8h, and degradation rate

maximizes after 48 h[1].
PROTAC EGFR degrader 3 (0.3, 1, 3, 10, 100, 300 nM; 24, 48 h) induces the degradation of $EGFR^{L858/T790M}$ and $EGFR^{del19}$ with DC_{50}s of 1.56 nM and 0.49 nM, respectively[1].
PROTAC EGFR degrader 3 (100, 1000 nM; 24 h) shows selective against mutant EGFR in the H1975 and HCC827 cells[1].
PROTAC EGFR degrader 3 (0.3, 1, 3, 10, 100, 300 nM; 24 h) effectively blocks EGFR singnal transduction, leading to cell proliferation inhibition[1].
PROTAC EGFR degrader 3 (30 nM) induces EGFR mutant degradation, and the lysosome is involved in the degradation process[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay[1]

Cell Line:	H1975 ($EGFR^{L858/T790M}$), HCC827 ($EGFR^{del19}$), A431 ($EGFR^{WT}$) cells
Concentration:	
Incubation Time:	72 h
Result:	Exhibited anti-proliferative activity of PROTACs with IC_{50}s of 32 nM, 1.60 nM, >10000nM for H1975 ($EGFR^{L858/T790M}$), HCC827 ($EGFR^{del19}$), A431 ($EGFR^{WT}$) cells, respectively.

Western Blot Analysis[1]

Cell Line:	H1975, HCC827 cells
Concentration:	0.3, 1, 3, 10, 30 nM
Incubation Time:	24 h
Result:	Remarkably decreased the phosphorylated EGFR, ERK, AKT in the H1975 and HCC827 cells.

REFERENCES

[1]. Zhao HY, et al. Discovery of Potent PROTACs Targeting EGFR Mutants through the Optimization of Covalent EGFR Ligands. J Med Chem. 2022; 65(6):4709-4726.

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