ADH-6 TFA

Cat. No.: HY-145785A

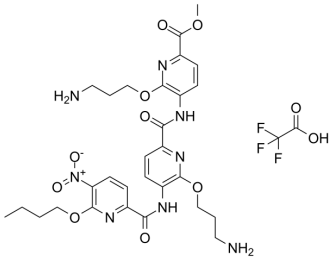
Molecular Formula: $C_{31}H_{37}F_3N_8O_{11}$

Molecular Weight: 754.67

Target: Apoptosis; MDM-2/p53

Pathway: Apoptosis

Storage: 4°C, sealed storage, away from moisture
* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (132.51 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.3251 mL	6.6254 mL	13.2508 mL
	5 mM	0.2650 mL	1.3251 mL	2.6502 mL
	10 mM	0.1325 mL	0.6625 mL	1.3251 mL

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

BIOLOGICAL ACTIVITY

Description

ADH-6 TFA is a tripyridylamide compound. ADH-6 abrogates self-assembly of the aggregation-nucleating subdomain of mutant p53 DBD. ADH-6 TFA targets and dissociates mutant p53 aggregates in human cancer cells, which restores p53's transcriptional activity, leading to cell cycle arrest and apoptosis. ADH-6 TFA has the potential for the research of cancer diseases[1].

In Vitro

ADH-6 (25 μM, 10 h) TFA inhibits aggregation of pR248W (indicated by dot blot assay)[1].
ADH-6 (5 μM, 6 h) TFA dissociates intracellular mutant p53 aggregates in MIA PaCa-2 cells[1].
ADH-6 (0-10 μM, 24 or 48 h) TFA causes selective cytotoxicity in cancer cells bearing mutant p53 (MIA PaCa-2)[1].
ADH-6 (5 μM, 24 h) TFA specifically targets and reactivates aggregation-prone mutant p53 in MIA PaCa-2 cells[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[1]

Cell Line:	MIA PaCa-2 (mutant R248W p53), SK-BR-3 (mutant R175H p53)
Concentration:	0, 2.5, 5, 7.5, 10 μM
Incubation Time:	24, 48 h

Result:	Caused death of cancer cells bearing mutant, but not WT, p53.

Western Blot Analysis[1]

Cell Line:	MIA PaCa-2 cells
Concentration:	5 μM
Incubation Time:	24 h
Result:	Increased expression of p53-inducible MDM2 and proapoptotic Bax.

In Vivo

ADH-6 (intraperitoneal injection, 15 mg/kg, every 2 days, for a total of 12 doses) TFA causes regression of mutant p53-bearing tumors [1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	MIA PaCa-2 xenografts[1]
Dosage:	716.4 μM in 0.02% DMSO
Administration:	Intraperitoneal injection, every 2 days, for a total of 12 doses
Result:	Reduced tumor growth relative to the saline-treated control group. Reduced mutant p53 levels and shrinked xenografts harboring aggregation-prone mutant p53.

Animal Model:	MIA PaCa-2 xenografts (pharmacokinetics assay)[1]
Dosage:	15 mg/kg
Administration:	Intraperitoneal injection, for a single dose
Result:	C_{max}: 21 μg/mL, $T_{1/2}$: 3.6 h

REFERENCES

[1]. Palanikumar L, et al. Protein mimetic amyloid inhibitor potently abrogates cancer-associated mutant p53 aggregation and restores tumor suppressor function. Nat Commun. 2021;12(1):3962.

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