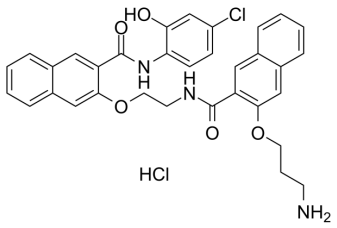
666-15

Cat. No.:	HY-101120
CAS No.:	1433286-70-4
Molecular Formula:	$C_{33}H_{31}Cl_2N_3O_5$
Molecular Weight:	620.52
Target:	Epigenetic Reader Domain
Pathway:	Epigenetics
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 : 125 mg/mL (201.44 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.6116 mL	8.0578 mL	16.1155 mL
	5 mM	0.3223 mL	1.6116 mL	3.2231 mL
	10 mM	0.1612 mL	0.8058 mL	1.6116 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: ≥ 2.08 mg/mL (3.35 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.08 mg/mL (3.35 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (3.35 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

666-15 is a potent and selective CREB inhibitor with an IC_{50} of 81 nM. 666-15 suppresses tumor growth in a breast cancer xenograft model[1][2].

IC_{50} & Target

IC50: 81 nM (CREB)[1]

In Vitro

666-15 (73 nM; for 12 hours) significantly blocks the effects caused by MSN overexpression, including cell proliferation, invasion, soft agar colony formation ability, and the expression of CREB downstream genes. 666-15 inhibits MSN overexpression-induced CREB phosphorylation[2].
666-15 (1μM; pretreated 2 hour) effectively inhibits PE-induced CREB phosphorylation. 666-15 significantly decreases the

protein expression of ANP and β-MHC and inhibits the activation of ER stress, including the expression of GRP78, CHOP, ATF6, and the phosphorylation of IRE1 in PE + siRNA + 666-15 group and PE + si-CTRP3 + 666-15 group[3].
666-15 potently inhibits cancer cell growth. In MDA-MB-231 and MDA-MB-468 cells, the GI_{50} for 666-15 is 73 and 46 nM, respectively. In A549 and MCF-7 cells, it exhibits robust activity as well with GI_{50} of 0.47 and 0.31 μM. 666-15 is also found to be a rather weak inhibitor of CREB-CBP interaction with IC_{50} of 18.27 μM. 666-15 inhibits CREB's transcription activity in living cells independent of direct CREB or CBP binding interaction. 666-15 is very potent in inhibiting CREB's transcription activity. 666-15 also inhibits endogenous CREB target gene expression, the transcript level of nuclear receptor related 1 protein (Nurr1/NR4A2)[1].

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

Cell Proliferation Assay[2]

Cell Line:	CTRL or MSN-overexpressing MDA-MB-231 cells
Concentration:	73 nM
Incubation Time:	For 12hours
Result:	Significantly blocked the cell proliferation caused by MSN overexpression.

Western Blot Analysis[3]

Cell Line:	NRCMs
Concentration:	1 μM
Incubation Time:	2 hour (pretreated)
Result:	Effectively inhibited PE-induced CREB phosphorylation.

In Vivo

666-15 (10 mg/kg; IP; once a week; for 11 weeks) alone can play a good role in inhibiting the growth of breast cancer, and the combination with RP-56976 (DOC) shows a better effect[2].

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

Animal Model:	1-month-old female nude mice with MDA-MB-231 or T47D cells[2]
Dosage:	10 mg/kg
Administration:	IP; once a week; for 11 weeks
Result:	Played a good role in inhibiting the growth of breast cancer.

CUSTOMER VALIDATION

- Sci Adv. 2020 Feb 19;6(8):eaaw9960.
- Nat Commun. 2022 Apr 26;13(1):2256.
- J Immunother Cancer. 2022 May;10(5):e003793.
- J Am Soc Nephrol. 2021 Jun 23;ASN.2021010101.
- Br J Pharmacol. 2020 Jan;177(2):432-448.

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REFERENCES

[1]. Xie F, et al. Identification of a Potent Inhibitor of CREB-Mediated Gene Transcription with Efficacious in Vivo Anticancer Activity. J Med Chem. 2015 Jun 25;58(12):5075-87.

[2]. Zhang B, et al. C1q-TNF-related protein-3 attenuates pressure overload-induced cardiac hypertrophy by suppressing the p38/CREB pathway and p38-induced ER stress. Cell Death Dis. 2019 Jul 8;10(7):520.

[3]. Qin Y, et al. Interfering MSN-NONO complex-activated CREB signaling serves as a therapeutic strategy for triple-negative breast cancer. Sci Adv. 2020 Feb 19;6(8):eaaw9960.

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