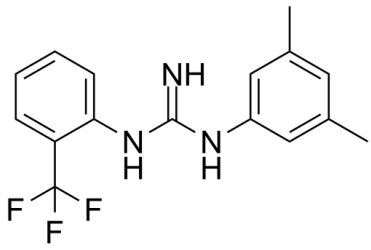
Data Sheet

Product Name:	1A-116
Cat. No.:	CS-8141
CAS No.:	1430208-73-3
Molecular Formula:	$C_{16}H_{16}F_3N_3$
Molecular Weight:	307.31
Target:	Apoptosis; Ras
Pathway:	Apoptosis; GPCR/G Protein
Solubility:	DMSO : 100 mg/mL (325.40 mM; Need ultrasonic)



BIOLOGICAL ACTIVITY:

1A-116, a potent **Rac1** inhibitor, is specific for W56 residues, can prevent **EGF**-induced **Rac1** activation and block **Rac1-P-Rex1** interaction. 1A-116 can induce **apoptosis** and inhibit cell proliferation, migration and cycle progression in a concentration-dependent manner. 1A-116 also demonstrates a high antimetastatic activity in vivo[1][2][3]. IC50 & Target: IC50: 4 μM (F3II); 21 μM (MDA-MB-231)[1].

Rac1[1]

Apoptosis[2] **In Vitro:** 1A-116 (48 h) inhibits F3II and MDA-MB-231 cells proliferation in a concentration-dependent manner with IC_{50}s of 4 μM and 21 μM, respectively[1].

1A-116 (1, 10 μM; 12 h) dramatically impaires Rac1 activation, and reduces Rac1-GTP intracellular levels in a concentration-dependent manner in F3II cells[1].

1A-116 (50, 100 μM; 12 h) blocks Rac1-P-Rex1 interaction[1].

1A-116 (20 μM; 5 h intervals over 25 h) inhibits LN229 cells proliferation in a circadian manner[2].

1A-116 (10 μM; 16 h) significantly reduces cell migration at 10 HPS which exhibits temporal dependence. (HPS: After the serum shock, the elapsed time (in hours) is recorded as the hours post-synchronization (HPS))[2].

1A-116 (20, 50 μM; 6 h) induces cells apoptosis and in a circadian-dependent manner[2].

1A-116 (100 nM) decreases the thickness of the epidermal layers of Vav2 and Rac1-mediated hyperplasia, but not the PAK1-mediated one, which exhibits the activity of inhibiting Rac1 at the GEF-Rac1 level[3]. **In Vivo:** 1A-116 (3 mg/kg; i.v.; once a day for 21 days) demonstrates a high antimetastatic activity with about 60% formation reduction of total metastatic lung colonies in vivo and shows no apparent toxicity[1].

1A-116 (20 mg/kg; i.p.; once a day, 73 days for ZT12, 68 days for ZT3) increases survival time when treated at ZT12 compare to ZT3 in tumor-bearing mice. (ZT: Zeitgeber time 12 (ZT12) defined as the time of lights off (local time 7 p.m.) and ZT0 defined as lights on (local time 7 a.m.))[2].

1A-116 shows good oral availability[3].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: 1A-116 is prepared as 1000× stock solutions in absolute ethanol and the corresponding dilutions of ethanol are used as control treatments.[1]5×10^3 MCF7::pcDNA.3 and MCF7::C1199 cells are plated in 96-wells plates and 24 hours later are treated for 72 hours with different concentrations of 17-β-Estradiol to evaluate hormone response. To evaluate the reversion of 4-hydroxytamoxifen (Tam) resistance by 1A-116, MCF7::C1199 cells are treated with Tam (0.01 μM, 0.1 μM and 1 μM), 1A-116 (4 μM) or combination of both for 72 hours. Cell growth is measured by colorimetric crystal violet assay. The analysis of hormone-dependent

growth and Tam resistance reversion is determined using PRISM 6, Version 6.01. Results shown correspond to the average of three independent experiments[1]. **Animal Administration:** [2]Specific pathogen-free female BALB/c inbred mice with an age of 8 to 10 weeks and an average weight of 20 g, are used. They are housed in plastic cages under standard conditions and have access to rodent chow and water ad libitum. On day 0, 2×10^5 viable F3II cells in 0.3 mL Dulbecco's modified Eagle medium (DMEM) are injected into the lateral tail vein. Mice are injected i.p at daily doses of 3 mg/kg body weight 1A-116 or vehicle. Treatment is carried out from day 0 to day 21. On day 21 mice are sacrificed and lungs are excised and immediately fixed in Bouin's solution. Superficial lung nodules are counted under dissection microscope[2].

References:

[1]. Cardama GA, et al. Preclinical development of novel Rac1-GEF signaling inhibitors using a rational design approach in highly aggressive breast cancer cell lines. Anticancer Agents Med Chem. 2014;14(6):840-51.

[2]. Trebucq LL, et al. Timing of Novel Drug 1A-116 to Circadian Rhythms Improves Therapeutic Effects against Glioblastoma. Pharmaceutics. 2021 Jul 16;13(7):1091.

[3]. González N, et al. Computational and in vitro Pharmacodynamics Characterization of 1A-116 Rac1 Inhibitor: Relevance of Trp56 in Its Biological Activity. Front Cell Dev Biol. 2020 Apr 15;8:240.

CAIndexNames:

Guanidine, N-(3,5-dimethylphenyl)-N'-[2-(trifluoromethyl)phenyl]-

SMILES:

N=C(NC1=CC=CC=C1C(F)(F)F)NC2=CC(C)=CC(C)=C2

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