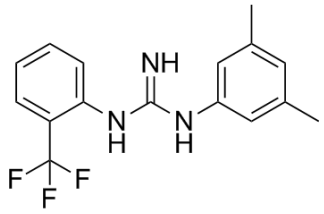
1A-116

Cat. No.:	HY-104064
CAS No.:	1430208-73-3
Molecular Formula:	$C_{16}H_{16}F_3N_3$
Molecular Weight:	307.31
Target:	Ras
Pathway:	GPCR/G Protein
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (325.40 mM; Need ultrasonic)

H_2O : < 0.1 mg/mL (insoluble)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	3.2540 mL	16.2702 mL	32.5404 mL
5 mM	0.6508 mL	3.2540 mL	6.5081 mL
10 mM	0.3254 mL	1.6270 mL	3.2540 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 (8.14 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (8.14 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (8.14 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

1A-116 is a Rac1 inhibitor, with antitumoral and antimetastatic effects in several types of cancer, such as breast cancer. 1A-116 prevents Rac1-regulated processes involved in the primary tumorigenesis and metastastic processes [1] [2].

IC_{50} & Target

Rac1[1]

In Vitro

1A-116 shows lesser effect on MCF7::pcDNA.3 cells than on MCF7::C1199 cells. 1A-116 treatment decreases phospho-PAK1

	levels in a time-dependent manner. The presence of 1A-116 reverts the PAK1 phosphorylation induced by 4-hydroxytamoxifen (Tam). The presence of 1A-116 also effectively reverts Rac1-PAK1-mediated estrogen receptor (ER) phosphorylation at Ser305[1]. 1A-116 shows a significant increase in antiproliferative activity on F3II cells, showing an IC_{50} value of 4 μM. A-116 also dramatically impairs Rac1 activation at low micromolar range (1 μM)[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Daily treatment of mice with compound 1A-116 at 3mg/kg body weight/day reduces about 60% the formation of total metastatic lung colonies. A significant antitumor activity is obtained for macronodules (more than 1 mm in diameter) by treatment with 1A-116 in this highly aggressive breast cancer model. The treatment with 1A-116 reduces the total lung weight compare to the control group, leading to a total weight similar to the average pulmonary weight of Balb/c mice[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

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

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]. Nazareno González, 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.

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