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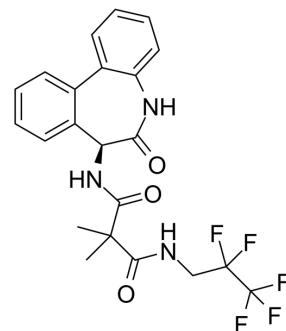
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RO4929097

Cat. No.:	HY-11102
CAS No.:	847925-91-1
Molecular Formula:	C ₂₂ H ₂₀ F ₅ N ₃ O ₃
Molecular Weight:	469.4
Target:	γ-secretase; Notch
Pathway:	Neuronal Signaling; Stem Cell/Wnt
Storage:	4°C, stored under nitrogen
	* In solvent : -80°C, 1 year; -20°C, 6 months (stored under nitrogen)



SOLVENT & SOLUBILITY

In Vitro	DMSO : ≥ 49 mg/mL (104.39 mM) * "≥" means soluble, but saturation unknown.				
	Preparing Stock Solutions	<div>Solvent Concentration</div> <div>Mass</div>	1 mg	5 mg	10 mg
		1 mM	2.1304 mL	10.6519 mL	21.3038 mL
		5 mM	0.4261 mL	2.1304 mL	4.2608 mL
		10 mM	0.2130 mL	1.0652 mL	2.1304 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 (5.33 mM); Clear solution				
	2. Add each solvent one by one: 10% DMSO >> 90% corn oil Solubility: ≥ 2.5 mg/mL (5.33 mM); Clear solution				

BIOLOGICAL ACTIVITY

Description	RO4929097 (RG-4733) is a γ secretase inhibitor with IC ₅₀ of 4 nM, inhibiting cellular processing of Aβ40 and Notch with EC ₅₀ of 14 nM and 5 nM, respectively ^[1] .
IC ₅₀ & Target	IC50: 4 nM (γ secretase) ^[1]
In Vitro	RO4929097 inhibits the production of ICN reducing the expression of the downstream Notch target, Hes1, producing a less transformed morphology in A549 cells. RO4929097 inhibits Notch processing in human tumor-derived cells ^[1] . RO4929097 (1 μM) inhibits the growth of breast cancer cells, and the inhibition is 20% for SUM149 and 10% for SUM190 cells. RO4929097 does not have a marked effect in invasiveness of SUM149 cells. RO4929097 significantly reduces colony formation by both cell lines with the effect being more notable in SUM149 than by SUM190 cells ^[2] . RO4929097 inhibits proliferation, anchorage

independent growth, and sphere formation of primary melanoma cells in vitro^[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

RO4929097 (3-60 mg/kg, p.o.) results in significant tumor growth inhibition in nude mice bearing A549 NSCLC xenografts, compared with vehicle-treated animals. When mice are treated with 60 mg/kg RO4929097 twice daily with the 7+/14-schedule, treatment initially causes regression of established A549 tumors^[1]. RO4929097 impairs the growth of primary melanoma cells in vivo. The percentage of secondary tumors formed by RO4929097-treated cells is lower; the secondary tumors formed by RO4929097-treated cells are smaller; a significant delay in tumor formation by the RO4929097-treated cells compared to the vehicle-treated ones is observed in mice injected with 10⁴ cells in vivo^[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay ^[2]

The IBC cell lines SUM149 and SUM190 are seeded at a density of 5 × 10⁴ cells. The next day, they are treated with vehicle or increasing doses of RO4929097, ranging from 0.1 nM to 10 μM. After 72 hrs, cells are trypsinized and viable cells counted with a hemocytometer.

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

Animal Administration ^[1]

Mice: RO4929097-treated mice are orally dosed with suspensions at 3 to 60 mg/kg RO4929097 according to the indicated regimens. In the Calu-6 xenograft model, RO4929097 is dosed at 60 mg/kg/d every other week for 4 weeks (7+/7- × 2 cycles). For all other xenograft models, RO4929097 is dosed once daily at 10 mg/kg for 21 days. Statistical analysis is determined by Mann-Whitney rank-sum test, one-way ANOVA, and post hoc Bonferroni t test. Differences between groups are considered significant when P ≤ 0.05. A549 tumors from vehicle-treated and selected RO4929097-treated groups are collected and fixed in 10% zinc-formalin overnight, processed, paraffin-embedded, sectioned at 5 μM, and stained with H&E for histopathology assessment. An Olympus BX51 microscope (×40 objective) mounted with a Nikon DS-Fi1 using the NIS-Elements F2.20 program collected the histology pictures. For Western blot analysis, three A549 tumors from each group, 7 (60 mg/kg) or 21 days (3 and 30 mg/kg), are flash-frozen. Collagen type V is detected using the H-200 antibody at a dilution of 1:1,000, and MFAP5 is detected using the antibody at a dilution of 1:1,000.

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

CUSTOMER VALIDATION

- Theranostics. 2019 Oct 12;9(25):7566-7582.
- J Exp Clin Cancer Res. 2019 Dec 30;38(1):505.
- Cell Syst. 2018 Apr 25;6(4):424-443.e7.
- Cell Chem Biol. 2022 Jun 9;S2451-9456(22)00204-5.
- Cell Commun Signal. 2021 Nov 15;19(1):112.

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REFERENCES

[1]. Luistro L, et al. Preclinical profile of a potent gamma-secretase inhibitor targeting notch signaling with in vivo efficacy and pharmacodynamic properties. Cancer Res. 2009, 69(19), 7672-7680.

[2]. Debeb BG, et al. Pre-clinical studies of Notch signaling inhibitor RO4929097 in inflammatory breast cancer cells. Breast Cancer Res Treat. 2012.

Caution: Product has not been fully validated for medical applications. For research use only.

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