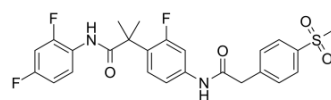


S18-000003

Cat. No.:	HY-119366		
CAS No.:	2068119-11-7		
Molecular Formula:	C ₂₆ H ₂₅ F ₃ N ₂ O ₄ S		
Molecular Weight:	518.55		
Target:	ROR		
Pathway:	Metabolic Enzyme/Protease		
Storage:	Powder	-20°C	3 years
	In solvent	-80°C	6 months
		-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro	DMSO : 100 mg/mL (192.85 mM; Need ultrasonic)					
	Preparing Stock Solutions	Solvent Concentration	Mass			
			1 mg	5 mg	10 mg	
			1 mM	1.9285 mL	9.6423 mL	19.2845 mL
			5 mM	0.3857 mL	1.9285 mL	3.8569 mL
10 mM	0.1928 mL	0.9642 mL	1.9285 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 (4.82 mM); Suspended solution; Need ultrasonic					
	2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline) Solubility: ≥ 2.5 mg/mL (4.82 mM); Clear solution					
	3. Add each solvent one by one: 10% DMSO >> 90% corn oil Solubility: ≥ 2.5 mg/mL (4.82 mM); Clear solution					

BIOLOGICAL ACTIVITY

Description	S18-000003 is a potent, selective and orally active inhibitor of retinoic acid receptor-related orphan receptor-gamma-t (RORγt), with an IC ₅₀ of <30 nM towards human RORγt in competitive binding assays. S18-000003 shows selectivity for RORγt over other ROR family members (IC ₅₀ >10 μM). S18-000003 can be used for the research of psoriasis with low risk of thymic aberrations ^{[1][2]} .
IC ₅₀ & Target	RORγt <30 nM (IC ₅₀)

<p>In Vitro</p>	<p>S18-000003 inhibits human and mouse RORγt-dependent transactivation, with IC₅₀s of 0.029 and 0.34 μM respectively in cell-based GAL4 promoter reporter assays^[1].</p> <p>S18-000003 (0.003-0.3 μM; 7 d) dose-dependently inhibits Th17 cell differentiation from human naive CD4⁺T cells, with an IC₅₀ of 0.024 μM^[2].</p> <p>S18-000003 (0.1-3 μM; 4 d) inhibits the differentiation of mouse Th17 cells from splenic naive CD4⁺T cells, with an IC₅₀ of 0.20 μM^[2].</p> <p>S18-000003 (0.03-1 μM; 3 d) reduces the IL-17 production in human PBMCs in a dose-dependent manner, and does not inhibit either the production of other cytokines (IL-2, IL-4, IL-10 and IFN-γ) or cell proliferation^[2].</p> <p>S18-000003 (0.1-3 μM; 3 d) reduces IL-17 and IL-22 production in PBMCs from psoriatic mice in a dose-dependent manner^[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>
<p>In Vivo</p>	<p>S18-000003 (30-100 mg/kg; p.o.) inhibits IL-17 production in the skin of IL-23-treated mice in a dose-dependent manner^[1].</p> <p>S18-000003 (0.1-8%; 100mL; topically administration once daily for 14 days) ameliorates psoriasis-like lesions in TPA-induced K14.Stat3C transgenic mice, and has little impact on the thymus^[2].</p> <p>S18-000003 (0.5 mg/kg; i.v.) exhibits the half-life (3.2 h), AUC (1930 ng•h/mL), CL_{tot} (4.33 mL/min/kg) and Vd_{ss} in rats^[1].</p> <p>S18-000003 (1 mg/kg; p.o.) exhibits the oral bioavailability (54.5%), C_{max} (185 ng/mL), AUC (2110 ng•h/mL) and T_{max} (4 h) in rats^[1].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>

REFERENCES

[1]. Sasaki Y, et, al. Discovery of a potent orally bioavailable retinoic acid receptor-related orphan receptor-gamma-t (ROR γ t) inhibitor, S18-000003. *Bioorg Med Chem Lett*. 2018 Dec 1;28(22):3549-3553.

[2]. Imura C, et, al. A novel ROR γ t inhibitor is a potential therapeutic agent for the topical treatment of psoriasis with low risk of thymic aberrations. *J Dermatol Sci*. 2019 Mar;93(3):176-185.

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

Tel: 609-228-6898

Fax: 609-228-5909

E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA