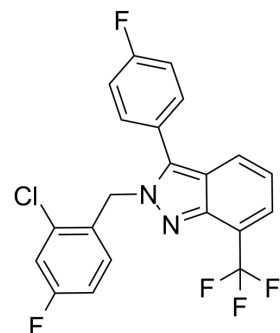


LXR-623

Cat. No.:	HY-10629		
CAS No.:	875787-07-8		
Molecular Formula:	C ₂₁ H ₁₂ ClF ₅ N ₂		
Molecular Weight:	422.78		
Target:	LXR		
Pathway:	Metabolic Enzyme/Protease		
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 : ≥ 47 mg/mL (111.17 mM)
 * "≥" means soluble, but saturation unknown.

Concentration	Solvent	Mass		
		1 mg	5 mg	10 mg
Preparing Stock Solutions	1 mM	2.3653 mL	11.8265 mL	23.6530 mL
	5 mM	0.4731 mL	2.3653 mL	4.7306 mL
	10 mM	0.2365 mL	1.1826 mL	2.3653 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
 Solubility: ≥ 2.5 mg/mL (5.91 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% corn oil
 Solubility: ≥ 2.5 mg/mL (5.91 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

LXR-623 is a brain-penetrant partial LXR α and full LXR β agonist, with IC₅₀s of 24 nM and 179 nM, respectively.

IC₅₀ & Target

IC₅₀: 24 nM (LXR- α), 179 nM (LXR- β)^{[2][3]}

In Vitro

LXR-623 potently kills U87EGFRvIII and GBM39 cells in vitro while completely sparing NHAs. LXR-623 also increases ABCA1 protein and decreases LDLR protein levels in all three cell lines. LXR-623 suppresses LDLR expression, increases expression of the ABCA1 efflux transporter, and induces substantial cell death in all of the GBM samples tested. LXR-623 (5 μ M) also induces GBM cell death through activation of LXR β ^[1]. LXR-623 treatment of human PBMC in vitro significantly increases transcription of ABCA1 and ABCG1^[4].

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

In Vivo

LXR-623 (400 mg/kg, p.o.) crosses the blood-brain barrier, induces target gene expression, and achieves therapeutic levels in GBM cells in the brain with minimal activity in the periphery. LXR-623 inhibits tumor growth, promotes tumor cell death, and prolongs the survival of mice bearing intracranial patient-derived GBMs^[1]. LXR-623 (1.5, 5 mg/kg/day) significantly reduces progression of atherosclerosis in animals compared with the placebo group^[2]. WAY-252623 (15 and 50 mg/kg) results in a significant reduction of atherosclerosis in a dose-dependent manner. WAY-252623 (20, 60, and 120 mg/kg/day, p.o.) displays neutral lipid effects in this CETP-expressing Syrian hamster^[3]. Moreover, LXR-623 (50 mg/kg) induces gene expression in rodent peripheral blood cells in rat. LXR-623 (0, 15 and 50 mg/kg) dose-dependently upregulates transcription of ABCA1 and ABCG1 in monkey whole blood cells proportional to dose^[4].

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

PROTOCOL

Animal Administration ^[1]

Five-week-old female athymic nu/nu mice are used in the experiment. A total of 1×10^5 U87EGFR^{vIII} IRFP720 or GBM39 IRFP720 cells in 5 μ L of PBS is intracranially injected into the mouse brain. Tumors are allowed to establish over the course of 7-10 days and engraftment of tumors is quantitatively confirmed via FMT signal intensity. Tumor growth is monitored using an FMT 2500 fluorescence tomography system. For drug treatment studies, vehicle (0.5% methylcellulose, 2% Tween 80 in water) or LXR-623 (400 mg/kg) resuspended in vehicle are administered to mice via oral gavage daily starting at day 7 postinjection.

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

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

CUSTOMER VALIDATION

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

- Cell Death Dis. 2019 May 28;10(6):416.
- Cell Death Dis. 2019 Mar 13;10(3):248.
- Nutrients. 2020 Oct 11;12(10):3088.
- Metabolites. 2021 Aug 23;11(8):562.
- Viruses. 2022, 14(3), 514.

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REFERENCES

[1]. Villa GR, et al. An LXR-Cholesterol Axis Creates a Metabolic Co-Dependency for Brain Cancers. *Cancer Cell*. 2016 Nov 14;30(5):683-693.

[2]. Giannarelli C, et al. Synergistic effect of liver X receptor activation and simvastatin on plaque regression and stabilization: an magnetic resonance imaging study in a model of advanced atherosclerosis. *Eur Heart J*. 2012 Jan;33(2):264-73.

[3]. Quinet EM, et al. LXR ligand lowers LDL cholesterol in primates, is lipid neutral in hamster, and reduces atherosclerosis in mouse. *J Lipid Res*. 2009 Dec;50(12):2358-70.

[4]. DiBlasio-Smith EA, et al. Discovery and implementation of transcriptional biomarkers of synthetic LXR agonists in peripheral blood cells. *J Transl Med*. 2008 Oct 16;6:59.