Product Data Sheet

Product Name: LY 303511
Cat. No.: GC12045

Chemical Properties

Cas. No.	154447-38-8		
Chemical Name	8-phenyl-2-(piperazin-1-yl)-4H-chromen-4-one		
SMILES	O=C(C1=CC=CC(C2=CC=CC=C2)=C1O3)C=C3N4CCNCC4		
Formula	$C_{19}H_{18}N_2O_2$	M.Wt	306.36
Solubility	Soluble in DMSO	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure	LY 303511		

Protocol

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com
Address: 10292 Central Ave. #205, Montclair, CA, USA

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Cell experiment:

Human neuroblastoma SHEP-1 cells are maintained in DMEM supplemented with 10% fetal bovine serum and 1% Penicillin. In a typical survival assay, SHEP-1 cells (8×104 per well) plated in 24-well plates for 24 h are exposed to LY303511 (12.5, 25, and 50 μM), TRAIL (25, 50, and 100 ng/mL), and a combination of the two (1 h preincubation with LY303511 followed by TRAIL for 4 h). Cytotoxicity is determined by the crystal violet assay. After drug exposure, cells are washed with PBS and incubated for 20 min with crystal violet solution (200 μL). The excess crystal violet solution is washed away with distilled water, and the remaining crystals are dissolved with 20% acetic acid. Viability is determined by absorbance at 595 nm wavelength using an automated ELISA reader. Cell viability experiments are performed similarly with 2,000 units/mL of catalase, 4 μM JNK inhibitor SP600125, 10 μM p38 inhibitor SB202190, 20 μM MAPK/ERK kinase (MEK) inhibitor PD98059, 50 μM of caspase-8 inhibitor Z-IETD-FMK or pan-caspase inhibitor Z-VAD-FMK, or death receptor blocking antibodies (4 μg/mL anti-DR4 or 1 μg/mL anti-DR5), or in cells transfected with small interfering RNA (siRNA) for silencing JNK and ERK expression, respectively. Cells are preincubated for 1 h with LY303511 and the respective inhibitor or catalase before the addition of TRAIL. Similar sensitizing effect of LY303511 on TRAIL-induced apoptosis is carried out with SY5Y neuroblastoma, T98G glioblastoma, Jurkat leukemia, CEM myelogenous leukemia, HeLa ovarian carcinoma, and HT29 colorectal carcinoma cell lines[2].

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Animal experiment:

Mice[4]Human prostate adenocarcinoma (PC-3) cells (ATCC CRL-1435) are cultured in vitro before harvesting and implantation of 1×106 cells in 20% Matrigel per athymic NCR nude mouse by subcutaneous injection at the flank. Inoculated mice are subdivided into four groups of 10. Administration of vehicle or LY303511, 10 mg/kg/day, is begun (day 1) when tumors reach ~150 mm3 (n=35), and tumor volumes are measured for 30 days at the indicated time points.

References:

[1]. Bodenstine TM, et al. Homotypic gap junctional communication associated with metastasis suppression increases with PKA activity and is unaffected by PI3K inhibition. Cancer Res. 2010 Dec 1;70(23):10002-11.
[2]. El-Kholy W, Macdonald PE, Lin JH, The phosphatidylinositol 3-kinase inhibitor LY294002 potently blocks K(V) currents via a direct mechanism. FASEB J. 2003

Apr;17(6):720-2.
[3]. Shenoy K, et al. LY303511 enhances TRAIL sensitivity of SHEP-1 neuroblastoma cells via hydrogen peroxide-mediated mitogen-activated protein kinase activation and up-regulation of death receptors. Cancer Res. 2009 Mar 1;69(5):1941-50.
[4]. Kristof AS, et al. LY303511 (2-piperazinyl-8-phenyl-4H-1-benzopyran-4-one) acts via phosphatidylinositol 3-kinase-independent pathways to inhibit cell proliferation via mammalian target of rapamycin (mTOR)- and non-mTOR-dependent mechanisms. J Pharmacol Exp Ther. 2005 Sep;314(3):1134-43.

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Background

Description: IC50 Value:N/A LY303511, an inactive analogue of LY294002, is a mTOR inhibitor that did not inhibit PI3-K. in vitro: 100 μM LY303511 significantly reduced the fraction of cells in S phase. The proportion of cells in G2/M remained unchanged, indicating that cells were arrested in both G1 and G2/M. In contrast, rapamycin increased the G1 population by reducing the proportion of cells in both S and G2/M. The effects of 10 μM LY303511 and rapamycin on the reduction in S phase cells were additive to that of 10 μM LY303511 alone (P = 0.056) [1]. In MIN6 insulinoma cells, wortmannin (100 nM) had no effect on whole-cell outward K+ currents, but LY294002 and LY303511 reversibly blocked currents in a dose-dependent manner (IC50=9.0+/-0.7 microM and 64.6+/-9.1 microM, respectively). Western blotting confirmed the specific inhibitory effects of LY294002 and wortmannin on insulin-stimulated PI3K activity [2]. Both LY294002 and LY303511 increased the activity of protein kinase A (PKA). Moreover, PKA blockade by the small molecule inhibitor H89 decreased the LY294002/LY303511-mediated increase in GJIC [3]. in vivo: PND4 ovaries were cultured for 8 days in control medium or medium containing VCD (30 μM) in the presence or absence of LY303511 (20 μM). Incubation with LY303511 alone caused a reduction (P < 0.05) in primordial and small primary follicle numbers. On the other hand, whereas VCD alone depleted (P < 0.05) primordial and small primary follicle numbers, this depletion was not prevented by co-incubation with LY303511 [4]. Clinical trial: N/A

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