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产品名称: **LY2409881 (trihydrochloride)**

产品别名: **LY2409881 trihydrochloride**

生物活性:	
Description	LY2409881 trihydrochloride is a selective I κ B kinase β (IKK2) inhibitor with an IC ₅₀ of 30 nM.
IC ₅₀ & Target	IKK2
	30 nM (IC ₅₀)
In Vitro	LY2409881 is an IKK2 inhibitor that inhibits TNF α -induced activation of NF- κ B. By in vitro kinase assay, LY2409881 potently inhibits IKK2, with an IC ₅₀ of 30 nM. In contrast, the IC ₅₀ for IKK1 and other common kinases is at least one log higher. The specificity of LY2409881 for NF- κ B signaling is further studied in a cell-based assay, by examining the effect of LY2409881 in the TNF α -dependent antiapoptosis function. TNF α is a well-characterized upstream stimulus of NF- κ B. In the ovarian cancer cell line SKOV3, LY2409881 demonstrates moderate cytotoxicity, whereas TNF α at 10 ng/mL does not cause any cytotoxicity. In contrast, coadministration of LY2409881 and TNF α results in markedly higher cell killing compared with LY2409881. This is because TNF α -dependent activation of antiapoptotic signals mediated by NF- κ B is blocked by LY2409881, while the proapoptotic TNF receptor-associated death domain (TRADD) and FAS-associated death domain (FADD) cascade pathways activated by TNF α are not affected by LY2409881[1].
In Vivo	A well-established xenograft model of DLBCL is used to confirm the activity of LY2409881 in vivo. SCID-beige mice implanted with LY10 cell-derived tumors are given intraperitoneal injections of LY2409881 twice weekly at three different doses: 50, 100, and 200 mg/kg. The treatments are well tolerated, resulting in no death or severe morbidity of the mice. The average tumor volume is graphed as a function of time for each treatment group. The rates of tumor volume growth of the treatment groups are all significantly slower than the untreated control group ($P \leq 0.01$)[1].
References	[1]. Deng C, et al. The novel IKK2 inhibitor LY2409881 potently synergizes with histone deacetylase inhibitors in preclinical models of lymphoma through the downregulation of NF- κ B. Clin Cancer Res. 2015 Jan 1;21(1):134-45.
实验参考:	
Cell Assay	OCI-Ly1, OCI-Ly7, and Su-DHL4 are GCB DLBCL cell lines; OCI-Ly3, OCI-Ly10, HBL1, and Su-DHL2 are ABC DLBCL lines. These cell lines are grown in Iscove Modified Dulbecco Medium with 10% FCS. Fresh medium is added every 2 to 3 days, and the cells are kept at a cell concentration of 0.1 to 1×10^6 /mL. Cytotoxicity is evaluated using the CellTiter-Glo Reagent. Experiments are carried out in 96-well plates, with each treatment in triplicate. Samples are taken at typically 24, 48, and 72 hours after treatment. Cytotoxicity is expressed by the decreasing percentage of live cells in each treatment (LY2409881; 0.01, 0.1, 1 and 10 μ M) relative to the untreated control from the same experiment, as a function of time. IC ₅₀ for each cell line is calculated using the CalcuSyn Version 2.0 software[1].
	Mice[1] Mouse experiments are carried out. Five- to 7-week-old SCID beige mice are injected with 107 Ly10 cells mixed in Matrigel in the posterior flank subcutaneously. When the tumors approach 150 mm ³ , the mice are divided into four groups of 8 mice: (i) control group, which receive 5% dextrose in



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Animal Administration	water; (ii) LY2409881 at 50 mg/kg in D5W; (iii) LY2409881 at 100 mg/kg in D5W; and (iv) LY2409881 at 200 mg/kg in D5W. LY2409881 or D5W is administered intraperitoneally on day 1 and 4 of every week for 4 weeks. The data are expressed as average tumor volume (mm ³) per group as a function of time. Tumor volume is calculated.
References	[1]. Deng C, et al. The novel IKK2 inhibitor LY2409881 potentially synergizes with histone deacetylase inhibitors in preclinical models of lymphoma through the downregulation of NF- κ B. Clin Cancer Res. 2015 Jan 1;21(1):134-45.



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