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产品名称: **CAL-130 (Hydrochloride)**  
产品别名: **CAL-130 Hydrochloride**

生物活性:				
Description	CAL-130 is a PI3K $\delta$ and PI3K $\gamma$ inhibitor with IC <sub>50</sub> s of 1.3 and 6.1 nM, respectively.			
IC <sub>50</sub> & Target	p110 $\delta$	p110 $\gamma$	p110 $\beta$	p110 $\alpha$
	1.3 nM (IC <sub>50</sub> )	6.1 nM (IC <sub>50</sub> )	56 nM (IC <sub>50</sub> )	115 nM (IC <sub>50</sub> )
In Vitro	CAL-130 preferentially inhibits the function of both p110 $\gamma$ and p110 $\delta$ catalytic domains. IC <sub>50</sub> values of CAL-130 are 1.3 and 6.1 nM for p110 $\delta$ and p110 $\gamma$ , respectively, as compared to 115 and 56 nM for p110 $\alpha$ and p110 $\beta$ . CAL-130 does not inhibit additional intracellular signaling pathways (i.e., p38 MAPK or insulin receptor tyrosine kinase) that are critical for general cell function and survival <sup>[1]</sup> .			
In Vivo	The clinical significance of interfering with the combined activities of PI3K $\gamma$ and PI3K $\delta$ is determined by administering CAL-130 to <i>Lck/Pten<sup>fl/fl</sup></i> mice with established T cell acute lymphoblastic leukemia (T-ALL). Candidate animals for survival studies are ill appearing, have a white blood cell (WBC) count above 45,000 $\mu\text{L}^{-1}$ , evidence of blasts on peripheral smear, and a majority of circulation cells (>75%) staining double positive for Thy1.2 and Ki-67. Mice receive an oral dose (10 mg/kg) of CAL-130 every 8 hr for a period of 7 days and are then followed until moribund. Despite the limited duration of therapy, CAL-130 is highly effective in extending the median survival for treated animals to 45 days as compared 7.5 days for the control group <sup>[1]</sup> .			
Solvent&Solubility	<b>In Vitro:</b> DMSO : 50 mg/mL (108.01 mM; Need ultrasonic)			
	Preparing Stock Solutions	Solvent Mass Concentration	1 mg	5 mg
		1 mM	2.1602 mL	10.8008 mL
		5 mM	0.4320 mL	2.1602 mL
		10 mM	0.2160 mL	1.0801 mL
	*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液; 一旦配成溶液, 请分装保存, 避免反复冻融造成的产品失效。 储备液的保存方式和期限: -80°C, 6 months; -20°C, 1 month。 -80°C 储存时, 请在 6 个月内使用, -20°C 储存时, 请在 1 个月内使用。			
	<b>In Vivo:</b> 请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 In Vitro 方式配制澄清的储备液, 再依次添加助溶剂: ——为保证实验结果的可靠性, 澄清的储备液可以根据储存条件, 适当保存; 体内实验的工作液, 建议您现用现配, 当天使用; 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比; 如在配制过程中出现沉淀、析出现象, 可以通过加热和/或超声的方式助溶 1.请依序添加每种溶剂: 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline Solubility: $\geq 3$ mg/mL (6.48 mM); Clear solution 此方案可获得 $\geq 3$ mg/mL (6.48 mM, 饱和度未知) 的澄清溶液。 以 1 mL 工作液为例, 取 100 $\mu\text{L}$ 30.0 mg/mL 的澄清 DMSO 储备液加到 400 $\mu\text{L}$ PEG300 中, 混合均匀, 向上述体系中加入 50 $\mu\text{L}$ Tween-80, 混合均匀; 然后继续加入 450 $\mu\text{L}$ 生理盐水定容至 1 mL。			



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	<p>2.请依序添加每种溶剂: 10% DMSO→ 90% (20% SBE-β-CD in saline)</p> <p>Solubility: ≥ 3 mg/mL (6.48 mM); Clear solution</p> <p>此方案可获得 ≥ 3 mg/mL (6.48 mM, 饱和度未知) 的澄清溶液。</p> <p>以 1 mL 工作液为例, 取 100 μL 30.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中, 混合均匀。</p> <p>3.请依序添加每种溶剂: 10% DMSO →90% corn oil</p> <p>Solubility: ≥ 3 mg/mL (6.48 mM); Clear solution</p> <p>此方案可获得 ≥ 3 mg/mL (6.48 mM, 饱和度未知) 的澄清溶液, 此方案不适用于实验周期在半个月以上的实验。</p> <p>以 1 mL 工作液为例, 取 100 μL 30.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中, 混合均匀。</p>
References	[1]. Subramaniam Prem S, et al. Targeting nonclassical oncogenes for therapy in T-ALL. Cancer cell (2012), 21(4), 459-72.
实验参考:	
Cell Assay	<p>Cell proliferation of CCRF-CEM cells or shRNA-transfected CCRF-CEM cells, in presence or absence of CAL-130 (1, 2.5 and 5 μM), is followed by cell counting of samples in triplicate using a hemocytometer and trypan blue. For apoptosis determinations of untransfected or shRNA-transfected CCRF-CEMs, cells are stained with APC-conjugated Annexin-V in Annexin Binding Buffer and analyzed by flow cytometry. For primary T-ALL samples, cell viability is assessed using the BD Cell Viability kit coupled with the use of fluorescent counting beads. For this, cells are plated with MS5-DL1 stroma cells, and after 72 hr following CAL-130 treatment, cells are harvested and stained with an APC-conjugated antihuman CD45 followed by a staining with the aforementioned kit<sup>[1]</sup>.</p>
Animal Administration	<p>Mice<sup>[1]</sup></p> <p>For subcutaneous xenograft experiments, luminescent CCRF-CEM (CEM-luc) cells are generated by lentiviral infection with FUW-luc and selection with Neomycin. Luciferase expression is verified with the Dual-Luciferase Reporter Assay kit. 2.5×10<sup>6</sup> CEM-luc cells embedded in Matrigel are injected in the flank of NOD.Cg-Prkdc<sup>scid</sup> Il2rg<sup>tm1Wjl</sup>/Sz mice. After 1 week, mice are treated by oral gavage with vehicle (0.5% methyl cellulose, 0.1% Tween 80), or CAL-130 (10 mg/kg) every 8 hr daily for 4 days, and then tumors are imaged as follows: mice anesthetized by isoflurane inhalation are injected intraperitoneally with D-luciferin (50 mg/kg). Photonic emission is imaged with the in vivo imaging system. Tumor bioluminescence is quantified by integrating the photonic flux (photons per second) through a region encircling each tumor using the Living Image software package. Administration of D-luciferin and detection of tumor bioluminescence in <i>Lck/Pten<sup>fl/fl</sup>/Gt(ROSA)26Sor<sup>tm1(Luc)Kael</sup>/J</i> mice are performed in a similar manner.</p>
Kinase Assay	<p>IC<sub>50</sub> values for CAL-130 inhibition of PI3K isoforms are determined in ex vivo PI3 kinase assays using recombinant PI3K. A ten-point kinase inhibitory profile is determined with ATP at a concentration consistent with the K<sub>M</sub> for each enzyme<sup>[1]</sup>.</p>
References	[1]. Subramaniam Prem S, et al. Targeting nonclassical oncogenes for therapy in T-ALL. Cancer cell (2012), 21(4), 459-72.