产品名称：QNZ (EVP4593)
产品别名：QNZ

生物活性：

Description	QNZ (EVP4593) shows strong inhibitory effects on NF-κB transcriptional activation and TNF-α production with IC_{50}s of 11 and 7 nM, respectively. QNZ (EVP4593) is a neuroprotective inhibitor of SOC channel.
IC_{50} & Target [1]	NF-κB
	11 nM (IC_{50}, in human Jurkat cells transfected with pNFκB-Luc)
	TNF-α
	7 nM (IC_{50}, in murine splenocytes stimulated with LPS)
In Vitro	QNZ (Compound 11q) has a suppressing effect of the NF-κB mediated-inflammatory response. QNZ inhibits edema formation dose-dependently[1]. QNZ (EVP4593) reduces the number of lysosomes/autophagosomes and store-operated channel (SOC) currents in Huntington's disease (HD). Normalization of calcium transport within neurons in response to QNZ is expect to reduce pathology manifestation. A number of lysosomes/autophagosomes are evaluated in HD and WT neurons treated with QNZ using transmission electron microscopy (TEM). Incubation with QNZ reduces the number of lysosomes/autophagosomes in HD GABAergic medium spiny (GABA MS)-like neurons (GMSLNs) by almost two-fold (from 0.41±0.04 to 0.23±0.04; $p<0.05$), while WT neurons are not affected. This observation is confirmed by examining lysosome content by flow cytometry (FC) analysis. The median fluorescence intensity is reduced by 34±6 % in HD GMSLNs upon QNZ treatment ($p<0.05$)[2].

Solvent&Solubility

In Vitro:

DMSO : ≥ 37 mg/mL (103.81 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.8057 mL	14.0284 mL	28.0568 mL
	5 mM	0.5611 mL	2.8057 mL	5.6114 mL
	10 mM	0.2806 mL	1.4028 mL	2.8057 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。

In Vivo:

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: ≥ 2.5 mg/mL (7.01 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (7.01 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀；向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。

	2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline) Solubility: ≥ 2.5 mg/mL (7.01 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (7.01 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 25.0 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。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (7.01 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (7.01 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。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Tobe M, et al. Discovery of quinazolines as a novel structural class of potent inhibitors of NF-kappa B activation. [2]. Nekrasov ED, et al. Manifestation of Huntington's disease pathology in human induced pluripotent stem cell-derived neurons. Mol Neurodegener. 2016 Apr 14;11:27. [3]. Wu J, et al. Enhanced Store-Operated Calcium Entry Leads to Striatal Synaptic Loss in a Huntington's Disease Mouse Model. J Neurosci. 2016 Jan 6;36(1):125-41.

实验参考：

Cell Assay	iPSHD22 cells are cultured in K-4 medium in a 96-well black plates with clear flat bottom. Next, cells are treated with chemical compounds (e.g., QNZ 100 nM) for 24 h prior to analysis. Fluorescent assay MultiTox-Fluor Multiplex Cytotoxicity Assay is used to measure simultaneously the relative number of live (viability) and dead (cytotoxicity) cells in each well. Fluorescence is detected by DTX 880 Multimode Microplate Reader. To evaluate the level of cell death (LoCD), the following equation is employed: ([cytotoxicity in a well with cells]-[cytotoxicity in a well without cells])/([viability in a well with cells]-[viability in a well without cells])[2].
References	[1]. Tobe M, et al. Discovery of quinazolines as a novel structural class of potent inhibitors of NF-kappa B activation. [2]. Nekrasov ED, et al. Manifestation of Huntington's disease pathology in human induced pluripotent stem cell-derived neurons. Mol Neurodegener. 2016 Apr 14;11:27. [3]. Wu J, et al. Enhanced Store-Operated Calcium Entry Leads to Striatal Synaptic Loss in a Huntington's Disease Mouse Model. J Neurosci. 2016 Jan 6;36(1):125-41.