上海源叶生物科技有限公司
Shanghai yuanye Bio-Technology Co., Ltd
电话：021-61312973　　传真：021-55068248
网址：www.shyuanye.com
邮箱：shyysw@sina.com

产品名称：ML402
产品别名：ML402

生物活性：

Description	ML402 is a selective TREK-1 activator.
IC_{50} & Target	TREK-1[1]
In Vitro	Xenopus oocyte two-electrode voltage-clamp measurements show that ML335 and ML402 activate K_{2P}2.1 and K_{2P}10.1 but not K_{2P}4.1(14.3±2.7 μM, K_{2P}2.1-ML335; 13.7±7.0 μM, K_{2P}2.1-ML402; 5.2±0.5 μM, K_{2P}10.1-ML335; and 5.9±1.6 μM, K_{2P}10.1-ML402). The K_{2P} modulator pocket has a single difference among TREK subfamily members at the cation-π interaction position, K_{2P}2.1 Lys271, which is also a lysine in K_{2P}10.1 but a glutamine in K_{2P}4.1. Swapping the Lys271 equivalent between K_{2P}2.1 and K_{2P}4.1 results in a clear phenotype reversal for ML335 and M402 activation. K_{2P}2.1 (K271Q) is insensitive to ML335 and ML402, whereas K_{2P}4.1 (Q258K) responds to both with a similar EC_{50} to K_{2P}2.1 (14.3±2.7 μM, K_{2P}2.1-ML335; 16.2±3.0 μM, K_{2P}4.1(Q258K)-ML335; 13.7±7.0 μM, K_{2P}2.1-ML402; 13.6±1.5 μM, K_{2P}4.1 (Q258K)-ML402) but with a lower magnitude response than K_{2P}2.1[1].
Solvent&Solubility	***In Vitro:*** **DMSO : ≥ 100 mg/mL (338.09 mM)** * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	3.3809 mL	16.9045 mL	33.8089 mL
	5 mM	0.6762 mL	3.3809 mL	6.7618 mL
	10 mM	0.3381 mL	1.6904 mL	3.3809 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 (8.45 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (8.45 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% corn oil

Solubility: ≥ 2.5 mg/mL (8.45 mM); Clear solution

	此方案可获得 ≥ 2.5 mg/mL (8.45 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]. Lolicato M, et al. K2P2.1 (TREK-1)-activator complexes reveal a cryptic selectivity filter binding site. Nature. 2017 Jul 20;547(7663):364-368.
实验参考：	
Kinase Assay	$K_{2P}2.1_{cryst}$ ML335 and ML402 complex crystals grow in the same conditions as $K_{2P}2.1_{cryst}$, but the protein is incubated for at least 1 h with 2.5 mM of activator (including ML 402) before setting the crystal plates. ML335 and ML402 are insoluble in aqueous solutions, so they are dissolved in 100% DMSO at a concentration of 500 mM. Then each compound is diluted 1:100 in SEC buffer to 5 mM concentration, giving a milky solution. This solution is mixed 1:1 to $K_{2P}2.1_{cryst}$ previously concentrating to 12 mg/mL. The $K_{2P}2.1_{cryst}$ ML402 mixture results in a clear solution, while the mixture with ML335 is slightly milky. The samples are briefly centrifuged in a table-top centrifuge (10,000×g) to remove any insoluble material before setting the crystal plates. Dose-response experiments are carried by first preparing a DMSO stock solution of each activator (including ML402) at a concentration of 100 mM. Owing to the low solubility of the compounds the highest test concentrations in recording solution are 100 μM and 80 μM for ML335 and ML402, respectively. Other concentrations are prepared by serial dilutions of the 100 μM solution in recording buffer supplementing with 0.1% DMSO[1].
References	[1]. Lolicato M, et al. K2P2.1 (TREK-1)-activator complexes reveal a cryptic selectivity filter binding site. Nature. 2017 Jul 20;547(7663):364-368.