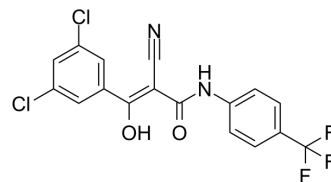


## TPC2-A1-N

<b>Cat. No.:</b>	HY-131614		
<b>CAS No.:</b>	136186-07-7		
<b>Molecular Formula:</b>	C <sub>17</sub> H <sub>9</sub> Cl <sub>2</sub> F <sub>3</sub> N <sub>2</sub> O <sub>2</sub>		
<b>Molecular Weight:</b>	401.17		
<b>Target:</b>	Calcium Channel		
<b>Pathway:</b>	Membrane Transporter/Ion Channel; Neuronal Signaling		
<b>Storage:</b>	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	2 years
		-20°C	1 year



## SOLVENT & SOLUBILITY

<b>In Vitro</b>	DMSO : 250 mg/mL (623.18 mM; Need ultrasonic)			
		Solvent Concentration	Mass	
			1 mg	5 mg
	<b>Preparing Stock Solutions</b>	1 mM	2.4927 mL	12.4635 mL
		5 mM	2.4927 mL	12.4635 mL
		10 mM	1.2464 mL	6.2317 mL
Please refer to the solubility information to select the appropriate solvent.				
<b>In Vivo</b>	<ol style="list-style-type: none"> <li>Add each solvent one by one: 10% DMSO &gt;&gt; 40% PEG300 &gt;&gt; 5% Tween-80 &gt;&gt; 45% saline Solubility: ≥ 2.08 mg/mL (5.18 mM); Clear solution</li> <li>Add each solvent one by one: 10% DMSO &gt;&gt; 90% (20% SBE-β-CD in saline) Solubility: ≥ 2.08 mg/mL (5.18 mM); Clear solution</li> <li>Add each solvent one by one: 10% DMSO &gt;&gt; 90% corn oil Solubility: ≥ 2.08 mg/mL (5.18 mM); Clear solution</li> </ol>			

## BIOLOGICAL ACTIVITY

<b>Description</b>	TPC2-A1-N is a powerful and Ca <sup>2+</sup> -permeable agonist of two pore channel 2 (TPC2), which plays its role by mimicking the physiological actions of NAADP. TPC2-A1-P reproducibly evokes significant Ca <sup>2+</sup> responses from TPC2 (EC <sub>50</sub> =7.8 μM), and the effect can be blocked by several TPC blockers. TPC2-A1-N can be used to probe different functions of TPC2 channels in intact cells <sup>[1][2]</sup> .
<b>IC<sub>50</sub> &amp; Target</b>	EC <sub>50</sub> : 10.5 μM (Ca <sup>2+</sup> current response from TPC2) <sup>[1]</sup>

## In Vitro

Two-pore channels (TPC1-3) are ancient members of the voltage-gated ion channel superfamily. TPCs are expressed throughout the endo-lysosomal system and regulates the trafficking of various cargoes.

TPC2 can mediate different physiological and possibly pathophysiological effects depending on how it is activated. The ion selectivity of TPC2 is not fixed but rather agonist-dependent. TPC2 is a unique example of an ion channel that conducts different ions in response to different activating ligands.

TPC2-A1-N (10  $\mu\text{M}$ ) reproducibly evokes  $\text{Ca}^{2+}$  signals, and TPC2-A1-N response reaches its plateau faster than TPC2-A1-P. The  $\text{EC}_{50}$  in full concentration-effect relationships for the plateau response is 7.8  $\mu\text{M}$  for TPC2-A1-N in a cell line stably expressing TPC2<sup>L11A/L12A</sup>.

TPC2-A1-N (10  $\mu\text{M}$ ) evokes  $\text{Ca}^{2+}$  influx through the TPC2 pore evokes  $\text{Ca}^{2+}$  signals in cells expressing TPC2<sup>L11A/L12A</sup> but not TPC2<sup>L11A/L12A/L265P</sup>. Additionally, the responses to TPC2-A1-N can be selectively blocked by the identified TPC2 blockers Tetrandrine (HY-13764, Tet), Raloxifene (HY-13738, Ral), and Fluphenazine (HY-A0081, Flu) by removal of extracellular  $\text{Ca}^{2+}$ [1].

In endo-lysosomal patch-clamp experiments, TPC2-A1-N (30  $\mu\text{M}$ ) elicits currents using  $\text{Na}^+$  as the major permeation, in vacuolin-enlarged endo-lysosomes isolated from HEK293 cells transiently expressing human TPC2 (hTPC2) but not in cells expressing TPC1<sup>[1]</sup>.

In endo-lysosomal patch-clamp experiments, TPC2-A1-N (30  $\mu\text{M}$ ) induces larger currents in endo-lysosomes isolated from cells expressing a gain-of-function variant of TPC2 (TPC2<sup>M484L</sup>) compared to the wild-type isoform, and exhibits an  $\text{EC}_{50}$  value of 0.6  $\mu\text{M}$  for TPC2-A1-N<sup>[1]</sup>.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

## CUSTOMER VALIDATION

- Nat Commun. 2022 Aug 2;13(1):4481.
- University of Milan. 2023 Mar 30.

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## REFERENCES

[1]. Susanne Gerndt, et al. Agonist-mediated switching of ion selectivity in TPC2 differentially promotes lysosomal function. Elife

[2]. Xuhui Jin, et al. Targeting Two-Pore Channels: Current Progress and Future Challenges. Trends Pharmacol Sci. 2020 Aug;41(8):582-594.

**Caution: Product has not been fully validated for medical applications. For research use only.**

Tel: 609-228-6898

Fax: 609-228-5909

E-mail: [tech@MedChemExpress.com](mailto:tech@MedChemExpress.com)

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA