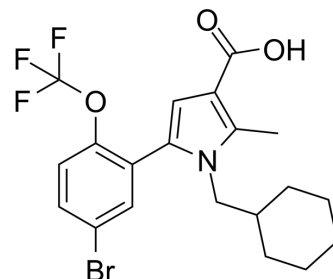


## TPC2-A1-P

<b>Cat. No.:</b>	HY-131615		
<b>CAS No.:</b>	2804595-86-4		
<b>Molecular Formula:</b>	C <sub>20</sub> H <sub>21</sub> BrF <sub>3</sub> NO <sub>3</sub>		
<b>Molecular Weight:</b>	460.28		
<b>Target:</b>	Sodium Channel		
<b>Pathway:</b>	Membrane Transporter/Ion Channel		
<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 : 50 mg/mL (108.63 mM; Need ultrasonic)				
		Solvent Concentration	Mass 1 mg	5 mg	10 mg
	<b>Preparing Stock Solutions</b>	1 mM	2.1726 mL	10.8630 mL	21.7259 mL
		5 mM	0.4345 mL	2.1726 mL	4.3452 mL
10 mM		0.2173 mL	1.0863 mL	2.1726 mL	
Please refer to the solubility information to select the appropriate solvent.					
<b>In Vivo</b>	1. Add each solvent one by one: 10% DMSO >> 90% corn oil Solubility: ≥ 2.5 mg/mL (5.43 mM); Clear solution				

## BIOLOGICAL ACTIVITY

<b>Description</b>	TPC2-A1-P is a powerful and membrane permeable agonist of two pore channel 2 (TPC2) with an EC <sub>50</sub> of 10.5 μM. TPC2-A1-P plays its role by mimicking the physiological actions of PI(3,5)P <sub>2</sub> . TPC2-A1-P also shows higher potency to induce Na <sup>2+</sup> mobilisation from TPC2 than TPC-A1-N (HY-131614). TPC2-A1-P can be used to probe different functions of TPC2 channels in intact cells <sup>[1][2][3]</sup> .
<b>IC<sub>50</sub> &amp; Target</b>	EC <sub>50</sub> : 10.5 μM (TPC2) <sup>[2]</sup>
<b>In Vitro</b>	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 <sup>[1]</sup> . 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 <sup>[1]</sup> .

TPC2-A1-P (10  $\mu\text{M}$ ) reproducibly evokes  $\text{Ca}^{2+}$  signals, and TPC2-A1-P response reaches its plateau slower than TPC2-A1-N (HY-131614). The  $\text{EC}_{50}$  in full concentration-effect relationships for the plateau response is 10.5  $\mu\text{M}$  for TPC2-A1-P in a cell line stably expressing TPC2<sup>L11A/L12A</sup>.

TPC2-A1-P (10-30  $\mu\text{M}$ ) induces  $\text{Ca}^{2+}$  signals in HeLa cells expressing TPC2 in the presence but not absence of extracellular  $\text{Ca}^{2+}$ . However, the responses are smaller and delayed compared to TPC2-A1-N (HY-131614), consistent with the results obtained in cells stably expressing TPC2<sup>L11A/L12A</sup>. TPC2-A1-P fails to induce  $\text{Ca}^{2+}$  signals in cells expressing 'pore-dead' TPC2<sup>L11A/L12A/L265P</sup> and also fails to evoke  $\text{Ca}^{2+}$  signals in cells expressing human TRPML1 re-routed to the plasma membrane (TRPML1 <sup>$\Delta\text{NC}$</sup> )<sup>[1]</sup>.

In endo-lysosomal patch-clamp experiments, TPC2-A1-P (10  $\mu\text{M}$ ) evokes currents in endo-lysosomes isolated from cells expressing TPC2 and TPC2<sup>M484L</sup>, the currents evoked by TPC2-A1-P are significantly larger than those evoked by TPC2-A1-N (HY-131614) in both wild-type and gain-of-function variant, and exhibits an  $\text{EC}_{50}$  value of 0.6  $\mu\text{M}$  for TPC2-A1-P<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.

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## REFERENCES

- [1]. Susanne Gerndt, et al. Agonist-mediated switching of ion selectivity in TPC2 differentially promotes lysosomal function. *Elife*. 2020 Mar 16;9:e54712.
- [2]. Xuhui Jin, et al. Targeting Two-Pore Channels: Current Progress and Future Challenges. *Trends Pharmacol Sci*. 2020 Aug;41(8):582-594.
- [3]. Gerndt S, et al. Discovery of lipophilic two-pore channel agonists. *FEBS J*. 2020;287(24):5284-5293.

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

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