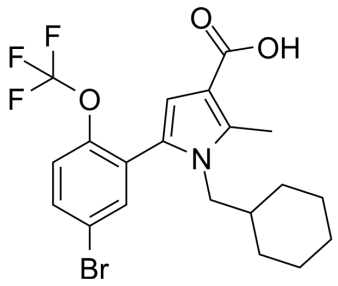
TPC2-A1-P

Cat. No.:	HY-131615
CAS No.:	2804595-86-4
Molecular Formula:	$C_{20}H_{21}BrF_3NO_3$
Molecular Weight:	460.28
Target:	Sodium Channel
Pathway:	Membrane Transporter/Ion Channel
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (108.63 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	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.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.43 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

TPC2-A1-P is a powerful and membrane permeable agonist of two pore channel 2 (TPC2) with an EC_{50} of 10.5 μM. TPC2-A1-P plays its role by mimicking the physiological actions of PI(3,5)P2. TPC2-A1-P also shows higher potency to induce Na^{2+} 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[1][2][3].

IC_{50} & Target

EC50: 10.5 μM (TPC2)[2]

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[1].
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[1].

TPC2-A1-P (10 μM) reproducibly evokes Ca^{2+}?signals, and TPC2-A1-P response reachs its plateau slower than TPC2-A1-N (HY-131614). The EC_{50}?in full concentration-effect relationships for the plateau response is 10.5 μM for TPC2-A1-P in a cell line stably expressing $TPC2^{L11A/L12A}$.

TPC2-A1-P (10-30 μM) induces Ca^{2+}?signals in Hela cells expressing TPC2 in the presence but not absence of extracellular 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 $TPC2^{L11A/L12A}$. TPC2-A1-P fails to induce Ca^{2+}?signals in cells expressing 'pore-dead' $TPC2^{L11A/L12A/L265P}$ and also fails to evoke Ca^{2+}?signals in cells expressing human TRPML1 re-routed to the plasma membrane ($TRPML1^{\Delta NC}$)[1].

In endo-lysosomal patch-clamp experiments, TPC2-A1-P (10 μM) evokes currents in endo-lysosomes isolated from cells expressing TPC2 and $TPC2^{M484L}$, 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 EC_{50}?value of 0.6 μM for TPC2-A1-P[1].

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.

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