

Product Data Sheet

Product Name: TPC2-A1-N

Cat. No.: GC61342

Chemical Properties

Cas. No. 136186-07-7

SMILES O=C(NC1=CC=C(C(F)(F)F)C=C1)/C(C#N)=C(C2=CC(Cl)=CC(Cl)=C2)\O

Formula $C_{17}H_9Cl_2F_3N_2O_2$ M.Wt 401.17

Solubility DMSO : 250 mg/mL (623.18 mM; Storage Store at -20°C
Need ultrasonic)

General tips For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.

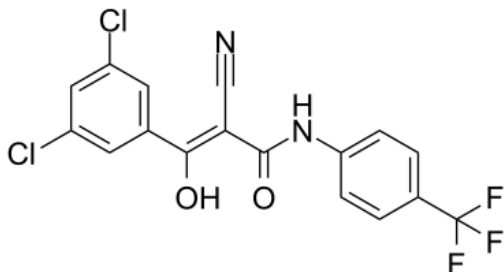
Caution: Product has not been fully validated for medical applications. For research use only.

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Structure



Background

TPC2-A1-N is a novel, lipophilic, membrane permeable isoform-selective small molecule agonist of two-pore channel 2 (TPC2). TPC2-A1-N plays its role by mimicking the physiological actions of NAADP and PI(3,5)P2 through independent binding sites. TPC2-A1-N has inverse effects on key lysosomal activities and increases the pH in the lysosomal lumen in a TPC2-dependent manner[1].

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

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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 μ M) reproducibly evokes Ca^{2+} signals, and TPC2-A1-N response reaches its plateau faster than TPC2-A1-P. The EC_{50} in full concentration-effect relationships for the plateau response is 7.8 μ M for TPC2-A1-N in a cell line stably expressing TPC2L11A/L12A. TPC2-A1-N (10 μ M) evokes Ca^{2+} influx through the TPC2 pore evokes Ca^{2+} signals in cells expressing TPC2L11A/L12A but not TPC2L11A/L12A/L265P. Additionally, the responses to TPC2-A1-N can be selectively blocked by the identified TPC2 blockers Tetrandrine, Raloxifene, and Fluphenazine by removal of extracellular Ca^{2+} [1]. In endo-lysosomal patch-clamp experiments, TPC2-A1-N (30 μ M) elicits currents using Na^{+} as the major permeant ion, in vacuolin-enlarged endo-lysosomes isolated from isolated from HEK293 cells transiently expressing human TPC2 (hTPC2) but not in cells expressing TPC1 [1]. In endo-lysosomal patch-clamp experiments, TPC2-A1-N (30 μ M) induces larger currents in endo-lysosomes isolated from cells expressing a gain-of-function variant of TPC2 (TPC2M484L) compared to the wild-type isoform, and exhibits an EC_{50} value of 0.6 μ M for TPC2-A1-N [1].

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

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