Product Data Sheet

Product Name: TASIN-1
Cat. No.: GC11469

Chemical Properties

Cas. No.	792927-06-1		
Chemical Name	1'-((4-methoxyphenyl)sulfonyl)-4-methyl-1,4'-bipiperidine		
SMILES	CC1CCN(C2CCN(S(C3=CC=C(OC)C=C3)(=O)=O)CC2)CC1		
Formula	$C_{18}H_{28}N_2O_3S$	M.Wt	352.49
Solubility	≥ 35.2mg/mL in DMSO	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure	TASIN-1		

Protocol

Cell experiment [1]:

Cell lines	HCT116 (WT APC) and DLD1 (truncated APC1417) cell lines
Preparation method	This compound is soluble in DMSO. General tips for obtaining a higher concentration: Please warm the tube at 37℃ for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20℃ for several months.

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Reacting condition	0.0001-100 μM; 48 h
Applications	TASIN-1 exhibited potent and selective toxicity toward DLD1 cells with IC50 value of 70 nM. TASIN-1 inhibited soft agar growth only in DLD1 cells. When cultured in medium with 0.1% serum for 7 days, HCT116 cells showed similar sensitivity to TASIN-1 as DLD1 cells.

Animal experiment [1]:

Animal models	genetically engineered colorectal cancer (CRC) mouse model
Dosage form	20 mg/kg twice per week for 90 days or 40 mg/kg per week for 100 days (dissolved in 0.2 ml of solvent containing 10% DMSO and 10% cremophor); intraperitoneal injection
Application	In genetically engineered colorectal cancer (CRC) mouse model, TASIN-1 had a long retention time in mouse large intestinal tissue. TASIN-1 significantly reduced tumor formation in the colons. TASIN-1 did not induce obvious histological changes in livers, kidneys, or spleens of treated animals.

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Other notes	Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

References:

[1] Lu Zhang, Panayotis C. Theodoropoulos, Ugur Eskiocak, et al. Selective targeting of mutant adenomatous polyposis coli (APC) in colorectal cancer. Science Translational Medicine 19 Oct 2016: Vol. 8, Issue 361, pp. 361ra140.

Background

TASIN-1 is a small molecule inhibitor of mutant adenomatous polyposis coli (APC) [1].

Adenomatous polyposis coli (APC) is a multifunctional tumor suppressor gene that is mutated in more than 80% of colon tumors. APC plays an important role in the negative regulation of canonical WNT signaling pathway through proteasomal degradation of b-catenin. APC is involved in cell cycle control, migration, differentiation, and apoptosis [1].

TASIN-1 is a selective inhibitor of mutant APC. In two authentic human CRC cell lines HCT116 (WT APC) and DLD1 (truncated APC1417), TASIN-1 exhibited potent and selective toxicity toward DLD1 cells with IC50 value of 70 nM but not toward HCT116 cells (IC50 >50 μM). TASIN-1 also reduced the endogenous cholesterol biosynthesis rate. TASIN-1 exerted its killing effects primarily by depleting cholesterol through inhibition of emopamil-binding protein (EBP) activity. However, knockdown of truncated APC (>90%) expression desensitized DLD1 cells to TASIN-1, suggesting that APC is required for TASIN-1's cytotoxicity [1].

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In nude mice with established DLD1 and HT29 tumors, intraperitoneal injection of TASIN-1 twice daily for 18 days reduced the size of tumor xenografts and tumor growth rates. TASIN-1 resulted in the appearance of apoptotic cells with fragmented nuclei and induced an increase in cleaved caspase 3 and cleaved PARP1. However, TASIN-1 did not inhibit tumor growth in HCT116 (WT APC) xenografts. In a genetically engineered CRC mouse model, TASIN-1 significantly reduced tumor formation in the colons of CPC;Apc mice [1].

Reference:

1.Lu Zhang, Panayotis C. Theodoropoulos, Ugur Eskiocak, et al. Selective targeting of mutant adenomatous polyposis coli (APC) in colorectal cancer. Science Translational Medicine 19 Oct 2016: Vol. 8, Issue 361, pp. 361ra140.

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