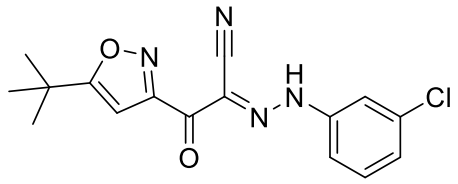
Product data sheet

MedKoo Cat#: 406603 Name: ESI-09 CAS#: 263707-16-0 Chemical Formula: $C_{16}H_{15}ClN_4O_2$ Exact Mass: 330.08835 Molecular Weight: 330.77	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:
ESI-09 is a novel noncyclic nucleotide EPAC antagonist that is capable of specifically blocking intracellular EPAC-mediated Rap1 activation and Akt phosphorylation, as well as EPAC-mediated insulin secretion in pancreatic β cells. EPAC1 plays an important role in pancreatic cancer cell migration and invasion, and thus represents a potential target for developing novel therapeutic strategies for pancreatic cancer.

2. CoA, QC data, SDS, and handling instruction
SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	66	199.53
Ethanol	20	60.46

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	3.02 mL	15.12 mL	30.23 mL
5 mM	0.60 mL	3.02 mL	6.05 mL
10 mM	0.30 mL	1.51 mL	3.02 mL
50 mM	0.06 mL	0.30 mL	0.60 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator
Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study
In vitro study

1. Almahariq M, Tsalkova T, Mei FC, Chen H, Zhou J, Sastry SK, Schwede F, Cheng X. A novel EPAC-specific inhibitor suppresses pancreatic cancer cell migration and invasion. Mol Pharmacol. 2013 Jan;83(1):122-8. doi: 10.1124/mol.112.080689. Epub 2012 Oct 11. PMID: 23066090; PMCID: PMC3533471.

2. Wang X, Luo C, Cheng X, Lu M. Lithium and an EPAC-specific inhibitor ESI-09 synergistically suppress pancreatic cancer cell proliferation and survival. Acta Biochim Biophys Sin (Shanghai). 2017 Jul 1;49(7):573-580. doi: 10.1093/abbs/gmx045. PMID: 28475672.

In vivo study

1. Gong B, Shelite T, Mei FC, Ha T, Hu Y, Xu G, Chang Q, Wakamiya M, Ksiazek TG, Boor PJ, Bouyer DH, Popov VL, Chen J, Walker DH, Cheng X. Exchange protein directly activated by cAMP plays a critical role in bacterial invasion during fatal rickettsioses. Proc Natl Acad Sci U S A. 2013 Nov 26;110(48):19615-20. doi: 10.1073/pnas.1314400110. Epub 2013 Nov 11. PMID: 24218580; PMCID: PMC3845138.

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7. Bioactivity

Biological target:

ESI-09 is a specific exchange protein directly activated by cAMP (EPAC) inhibitor with IC50 of 3.2 μM and 1.4 μM for EPAC1 and EPAC2, respectively, >100-fold selectivity over PKA.

In vitro activity

To test whether our newly identified EPAC antagonist ESI-09 is capable of modulating EPAC activation in living cells, its ability to suppress Akt phosphorylation was monitored as EPAC proteins are also known to activate Akt signaling, whereas PKA inhibits it. To determine whether ESI-09 is capable of blocking EPAC-mediated Akt activation, the phosphorylation status of T308 and S473 of Akt in the pancreatic cancer cell line AsPC-1, which overexpresses EPAC1, was followed using anti-phospho-Akt antibodies. As shown in Fig. 4, ESI-09 inhibited 007-AM-stimulated Akt phosphorylation at T308 and S473 in a dose-dependent manner. Similar results were observed in the rat pancreatic β-cell line INS-1 (Supplemental Fig. 3). On the other hand, ESI-09 failed to suppress epidermal growth factor (EGF)-induced phosphorylation of Akt in AsPC1 cells (Fig. 4).

Reference: Mol Pharmacol. 2013 Jan;83(1):122-8. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/23066090/

In vivo activity

WT C57BL/6 mice, randomly divided into two groups, were treated with ESI-09 (10 mg·kg−1·d−1) or vehicle via i.p. injection for 5 d, followed by i.v. inoculation of R. australis. ESI-09 treatment was continued for another 7 d. As shown in Fig. 5, treatment with ESI-09 dramatically protected WT mice against R. australis infection with much milder disease manifestations (Fig. 5A) and significantly improved survival (Fig. 5B). Only 1 of 11 ESI-09–treated mice died (9% mortality), compared with those of the vehicle-only group, in which 6 of 10 WT mice died (60% mortality) at the end of experiment. Histological evaluation confirmed that pharmacological inhibition of Epac significantly attenuated the pathological responses, resulting in milder vasculitis in the testis, occasional microvesicular hepatocellular fatty change, less interstitial inflammation in the lung, and immunohistochemical evidence of significantly less rickettsial antigen in tissues compared with the control group (Fig. 5C).

Reference: Proc Natl Acad Sci U S A. 2013 Nov 26;110(48):19615-20. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/24218580/

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.