产品名称：**ESI-09**
产品别名：**ESI-09**

生物活性：

Description	ESI-09 is a novel noncyclic nucleotide EPAC antagonist with IC50 values of 3.2 and 1.4 μM for EPAC1 and EPAC2, respectively.
IC_{50} & Target	IC50: 3.2 μM (EPAC1), 1.4 μM (EPAC2)[1]
In Vitro	While cAMP competes with 8-NBD-cAMP binding with an IC50 of 39 μM, ESI-09 shows an increased potency with an apparent IC50 of 10 μM. ESI-09 inhibis cAMP-mediated EPAC2 and EPAC1 GEF activity with an IC50 of 1.4 and 3.2μM, respectively. ESI-09 could fit well into the functional cAMP-binding pocket of EPAC1, establishing favorable hydrophobic and hydrogen bonding interactions with the protein's active-site residues. ESI-09 inhibits 007-AM-stimulated Akt phosphorylation at T308 and S473 in a dose-dependent manner. ESI-09 inhibits pancreatic cancer cells AsPC-1 and PANC-1 migration. ESI-09 inhibits EPAC1-mediated adhesion of PDA cells on collagen I[1]. Exposure to ESI-09 significantly reduces intracellular and total bacterial counts in HUVECs at 30 min postinfection with 10 multiplicities of infection (MOI) of R. australis compared with similarly infected controls[2].
In Vivo	Treatment with ESI-09 dramatically protects WT mice against R. australis infection with much milder disease manifestations and significantly improves survival[2].

Solvent&Solubility

In Vitro:

DMSO : ≥ 47 mg/mL (142.09 mM)

H_2O : < 0.1 mg/mL (insoluble)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	3.0232 mL	15.1162 mL	30.2325 mL
	5 mM	0.6046 mL	3.0232 mL	6.0465 mL
	10 mM	0.3023 mL	1.5116 mL	3.0232 mL

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

In Vivo:

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 **In Vitro** 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline

Solubility: ≥ 2.5 mg/mL (7.56 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (7.56 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀；向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。

2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline)

源叶生物

	Solubility: 2.5 mg/mL (7.56 mM); Precipitated solution; Need ultrasonic 此方案可获得 2.5 mg/mL (7.56 mM) 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (7.56 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (7.56 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Almahariq M, et al. A novel EPAC-specific inhibitor suppresses pancreatic cancer cell migration and invasion. Mol Pharmacol. 2013 Jan;83(1):122-8. [2]. Gong B, et al. 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.

实验参考：

Cell Assay	INS-1 cells are plated in 96-well plates precoated with polylysine. After overnight incubation, the medium is replaced with Krebs-Ringer bicarbonate (KRB) containing 2.9 mM glucose. After an additional 2-hour incubation, the cells are treated with ESI-09 or DMSO vehicle as a control in fresh KRB containing 11.8 mM glucose for 10 minutes, followed by a 30-minute stimulation with 10 μM 007-AM. The supernatant is collected, and insulin is quantified using an Ultra Sensitive Rat Insulin ELISA kit from Crystal Chem Inc[1].
Animal Administration	Mice: ESI-09 is dissolved in buffered saline containing 10% (vol/vol) ethanol and 10% (vol/vol) Tween-80. Thirty-three WT C57BL/6 mice are divided into four groups [11 mice (group A), 10 mice (group B), 6 mice each (groups C and D)]. Groups A and C are treated with the Epac-specific inhibitor ESI-09 [10 mg/kg] via i.p. injection for 5 d before infection, whereas groups B and D are treated with vehicle, followed by i.v. inoculation of R. australis for groups A and B or mock inoculation for groups C and D. ESI-09 or vehicle treatment is continued for another 7 d until mice are killed on day 8. During the course of the experiments, animals are monitored daily for signs of illness and mortality[2].
References	[1]. Almahariq M, et al. A novel EPAC-specific inhibitor suppresses pancreatic cancer cell migration and invasion. Mol Pharmacol. 2013 Jan;83(1):122-8. [2]. Gong B, et al. 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.