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产品名称：HG-9-91-01
产品别名：SIK inhibitor 1

生物活性：

Description	HG-9-91-01 is a potent and highly selective salt-inducible kinase (SIK) inhibitor with IC_{50}s of 0.92 nM, 6.6 nM and 9.6 nM for SIK1, SIK2 and SIK3 respectively.
IC_{50} & Target	IC50: 0.92/6.6/9.6 nM (SIK1/2/3)[1]
In Vitro	HG-9-91-01 inhibits a number of protein tyrosine kinases that possess a threonine residue at the gatekeeper site, such as Src family members (Src, Lck, and Yes), BTK, and the FGF and Ephrin receptors[1]. HG-9-91-01 demonstrates a strong correlation between the potency of SIK2 inhibition and enhanced IL-10 production. In agreement with these reports, pretreating BMDCs with HG-9-91-01, a recently described inhibitor of SIK1-3, along with several other kinases, results in concentration-dependent potentiation of zymosan-induced IL-10 production with an EC_{50} ~200 nM and a maximum effect similar to that observed with PGE_2[2]. HG-9-91-01 has more than a 100-fold greater potency against SIKs than AMPK (IC_{50}=4.5 μM) in a cell-free assay. HG-9-91-01 treatment dose dependently increased mRNA expression of *Pck1* and *G6pc* and that effect is similar in cells treated with 4 μM HG-9-91-01. Consistent with this observation, there is also a dose-dependent increase in glucose production following HG-9-91-01 treatment[3].
Solvent&Solubility	***In Vitro:*** **DMSO : ≥ 150 mg/mL (264.23 mM)** * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.7616 mL	8.8078 mL	17.6156 mL
	5 mM	0.3523 mL	1.7616 mL	3.5231 mL
	10 mM	0.1762 mL	0.8808 mL	1.7616 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 (4.40 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (4.40 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) Solubility: ≥ 2.5 mg/mL (4.40 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (4.40 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 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 (4.40 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (4.40 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]. Clark K, et al. Phosphorylation of CRTC3 by the salt-inducible kinases controls the interconversion of classically activated andregulatory macrophages. Proc Natl Acad Sci U S A. 2012 Oct 16;109(42):16986-91. [2]. Sundberg TB, et al. Small-molecule screening identifies inhibition of salt-inducible kinases as a therapeutic strategy to enhance immunoregulatory functions of dendritic cells. Proc Natl Acad Sci U S A. 2014 Aug 26;111(34):12468-73. [3]. Patel K, et al.The LKB1-salt-inducible kinase pathway functions as a key gluconeogenic suppressor in the liver. Nat Commun. 2014 Aug 4;5:4535.
实验参考：	
Cell Assay	Bone marrow is harvested from femurs and tibias of C57BL/6 mice. Bone-marrow-derived dendritic cells (BMDCs) are differentiated DMEM. Cultures are differentiated for 7 d and routinely analyzed for >90% CD11c (allophycocyanin (APC) anti-CD11c clone HL3) positivity by flow cytometry before use in experiments. Lentiviral transduction of bone marrow cultures is conducted by addition of 293T culture supernatants containing lentiviral particles encoding the CREB-dependent luciferase reporter construct or CRTC3 targeting or control shRNAs 1 d postisolation. Stable integration of lentiviral shRNA constructs is selected by addition of puromycin (3 μg/mL) on day 4 posttransduction. After 2 d, stably transduced BMDCs are released from selection and used in subsequent assays. Unless otherwise indicated, cells are treated for 2 d with PGE2 (5 μM) or HG-9-91-01 (0.5 μM) or an equivalent concentration of DMSO (≤0.5%) and then stimulated for 18 h with LPS (100 ng/mL), R848 (10 μg/mL), or Zymosan (4 μg/mL)[2].
References	[1]. Clark K, et al. Phosphorylation of CRTC3 by the salt-inducible kinases controls the interconversion of classically activated andregulatory macrophages. Proc Natl Acad Sci U S A. 2012 Oct 16;109(42):16986-91. [2]. Sundberg TB, et al. Small-molecule screening identifies inhibition of salt-inducible kinases as a therapeutic strategy to enhance immunoregulatory functions of dendritic cells. Proc Natl Acad Sci U S A. 2014 Aug 26;111(34):12468-73. [3]. Patel K, et al.The LKB1-salt-inducible kinase pathway functions as a key gluconeogenic suppressor in the liver. Nat Commun. 2014 Aug 4;5:4535.