产品名称：MCC950 (sodium)
产品别名：CP-456773 sodium; CRID3 sodium salt

生物活性：

Description	MCC950 sodium (CP-456773 sodium; CRID3 sodium salt) is a potent, selective NLRP3 inhibitor with IC_{50}s of 7.5 and 8.1 nM in BMDMs and HMDMs, respectively.
IC_{50} & Target	IC50: 7.5 nM (NLRP3, in BMDMs), 8.1 nM (NLRP3, in HMDMs)[1]
In Vitro	MCC950 blocks canonical and non-canonical NLRP3 activation at nanomolar concentrations. MCC950 specifically inhibits NLRP3 but not AIM2, NLRC4 or NLRP1 activation. The effect of MCC950 on NLRP3 inflammasome activation is tested in mouse bone marrow derived macrophages (BMDM) and human monocyte derived macrophages (HMDM). The IC50 of MCC950 in BMDM is approximately 7.5 nM, while in HMDM it has a similar inhibitory capacity (IC50=8.1 nM). MCC950 also dose dependently inhibit IL-1β but not TNF-α secretion.MCC950 specifically blocks caspase-11-directed NLRP3 activation and IL-1β secretion upon stimulation of the non-canonical pathway. NLRC4-stimulated IL-1β and TNF-α secretion (as activated by Salmonella typhimurium) are not inhibited by MCC950 even at a concentration of 10 μM. MCC950 does not inhibit caspase-1 activation or IL-1β processing in response to S. typhimurium. The expression of pro-caspase-1 and pro-IL-1β in cell lysates is not substantially affected by MCC950 treatment[1].
In Vivo	MCC950 reduces Interleukin-1p (IL-1β) production and attenuates the severity of experimental autoimmune encephalomyelitis (EAE), a disease model of multiple sclerosis. Pre-treatment with MCC950 reduces serum concentrations of IL-1β and IL-6 while it does not considerably decrease the amount of TNF-α. Treatment of mice with MCC950 delays the onset and reduced the severity of EAE. Intracellular cytokine staining and FACS analysis of brain mononuclear cells from mice sacrificed on day 22 shows modestly reduced frequencies of IL-17 and IFN-γ producing $CD3^+$ T cells in MCC950 treated mice in comparison with PBS-treated mice. IFN-γ and particularly IL-17 producing cell numbers are also reduced in both the $CD4^+$ and $γδ^+$ sub-populations of $CD3^+$ T cells[1].
Solvent&Solubility	***In Vitro:*** **DMSO : 50 mg/mL (117.24 mM;** Need ultrasonic) **H_2O : ≥ 30 mg/mL (70.35 mM)** * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.3449 mL	11.7244 mL	23.4489 mL
5 mM	0.4690 mL	2.3449 mL	4.6898 mL
10 mM	0.2345 mL	1.1724 mL	2.3449 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 (5.86 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.86 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 (5.86 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.86 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 (5.86 mM); Precipitated solution 此方案可获得 ≥ 2.5 mg/mL (5.86 mM，饱和度未知) 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]. Coll RC, et al. A small-molecule inhibitor of the NLRP3 inflammasome for the treatment of inflammatory diseases. Nat Med. 2015 Mar;21(3):248-55. [2]. Zhai Y, et al. Inhibiting the NLRP3 Inflammasome Activation with MCC950 Ameliorates Diabetic Encephalopathy in db/db Mice. Molecules. 2018 Feb 27;23(3). pii: E522.

实验参考：

Cell Assay	BMDM are seeded at 5×10^5/mL or 1×10^6/mL, HMDM at 5×10^5/mL and PBMC at 2×10^6/mL or 5×10^6/mL in 96 well plates. The following day the overnight medium is replaced and cells are stimulated with 10 ng/mL LPS from *Escherichia coli* serotype EH100 (ra) TLRgrad for 3 h. Medium is removed and replaced with serum free medium (SFM) containing DMSO (1:1,000), MCC950 (0.001-10 μM), glyburide (200 μM), Parthenolide (10 μM) or Bayer cysteinyl leukotriene receptor antagonist 1-(5-carboxy-2{3-[4-(3-cyclohexylpropoxy)phenyl]propoxy}benzoyl)piperidine-4-carboxylic acid (40 μM) for 30 min. Cells are then stimulated with inflammasome activators: 5 mM adenosine 5'-triphosphate disodium salt hydrate (ATP) (1 h), 1 μg/mL Poly(deoxyadenylic-thymidylic) acid sodium salt (Poly dA:dT) transfected with Lipofectamine 200 (3-4 h), 200 μg/mL MSU (overnight) and 10 μM nigericin (1 h) or *S. typhimurium* UK-1 strain. Cells are also stimulated with 25 μg/mL Polyadenylic-polyuridylic acid (4 h). For non-canonical inflammasome activation cells are primed with 100 ng/mL Pam3CSK4 for 4 h, medium is removed and replaced with SFM containing DMSO or MCC950 and 2 μg/mL LPS is transfected using 0.25% FuGENE for 16 h. Supernatants are removed and analysed using ELISA kits. LDH release is measured using the CytoTox96 non-radioactive cytotoxicity assay[1].
Animal Administration	Mice[1] C57BL/6 mice are immunized subcutaneously with 150 μg of MOG peptide 35-55 emulsified in CFA containing 4 mg/mL (0.4.mg/mouse) of heat-killed MTB. Mice are injected i.p. with 500 ng pertussis toxin (PT: kaketsuken) on days 0 and 2. MCC950 is administered i.p. to mice (10 mg/kg) at induction of the disease, day 0, 1 and 2 and every 2 days thereafter. Control mice are administered vehicle

	(PBS) at the same time points. Mice are observed for clinical signs of disease daily (unblinded). Disease severity is scored as follows: no clinical signs, 0; limp tail, 1; ataxic gait, 2; hind limb weakness, 3; hind limb paralysis, 4; and tetra paralysis, 5.
References	[1]. Coll RC, et al. A small-molecule inhibitor of the NLRP3 inflammasome for the treatment of inflammatory diseases. Nat Med. 2015 Mar;21(3):248-55. [2]. Zhai Y, et al. Inhibiting the NLRP3 Inflammasome Activation with MCC950 Ameliorates Diabetic Encephalopathy in db/db Mice. Molecules. 2018 Feb 27;23(3). pii: E522.