

MCC950

NLRP3-inflammasome inhibitor

Catalog # inh-mcc

<http://www.invivogen.com/mcc950>

For research use only

Version # 17F02-MM

PRODUCT INFORMATION

Contents:

- 10 mg MCC950

Storage and stability:

- MCC950 is shipped at room temperature. Store at -20 °C.
- Upon resuspension, prepare aliquots of MCC950 and store at -20 °C. Resuspended MCC950 is stable for 6 months when properly stored.

Quality control:

- Purity ≥98% (UHPLC)
- The absence of bacterial contamination (e.g. lipoproteins and endotoxins) is confirmed using HEK-Blue™ TLR2 and HEK-Blue™ TLR4 cells.
- The inhibitory activity of the product has been validated using cellular assays.

DESCRIPTION

MCC950 is a potent and selective inhibitor of the NLRP3 (NOD-like receptor (NLR) pyrin domain-containing protein 3) inflammasome. The NLRP3 inflammasome is an innate immune sensor that upon assembly activates caspase-1 and mediates the processing and release of IL-1 β . MCC950 blocks the release of IL-1 β induced by NLRP3 activators, such as ATP, MSU and nigericin, by preventing oligomerization of the inflammasome adaptor protein ASC (apoptosis-associated speck-like protein containing the a CARD)^{1,2}. In research models of inflammation, such as cryopyrin associated periodic syndromes (CAPS) and myocardial infarction, it effectively inhibited NLRP3-induced IL-1 β production¹⁻³. Importantly, MCC950 does not inhibit the AIM2, NLRC4 or NLRP1 inflammasomes¹.

1. Coll RC. *et al.*, 2015. A small-molecule inhibitor of the NLRP3 inflammasome for the treatment of inflammatory diseases. *Nature Med* 21(3), 248-255. 2. Guo H. *et al.*, 2015. Inflammasomes: mechanism of action, role in disease, and therapeutics. *Nat Med*. 21(7):677-87. 3. van Hout GP. *et al.*, 2016. The selective NLRP3-inflammasome inhibitor MCC950 reduces infarct size and preserves cardiac function in a pig model of myocardial infarction. *Eur Heart J*. ehw247.

CHEMICAL PROPERTIES

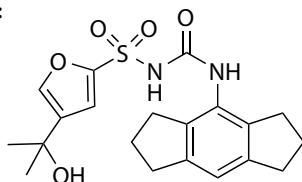
Solubility: 10 mg/ml (24.72 mM) in DMSO

CAS number: 210826-40-7

Formula: C₂₀H₂₄N₂O₅S

Molecular weight: 404.48 g/mol

Structure:



METHODS

Preparation of 20 mM (8.1 mg/ml) stock solution

- Add 1.235 ml of DMSO to 10 mg MCC950. Mix by vortexing.
- Prepare further dilutions by adding the appropriate amount using sterile endotoxin-free water or an aqueous buffer.

Working concentration: 300 nM (121.34 ng/ml) to 10 μ M (4.04 μ g/ml) for cell culture assays

Inflammasome inhibition assay:

The following protocol describes the monitoring of inflammasome inhibition by MCC950 in the human monocytic THP1-Null cell line by measuring the inhibition of IL-1 β production. The cells are grown in suspension to a density of 1.0 x 10⁶ cells/ml in RPMI 1640 medium supplemented with 10% heat inactivated fetal bovine serum.

1. Prime cells by adding 1 mg/ml LPS for 3 hours at 37 °C in 5% CO₂.
2. Wash cells gently with PBS and add fresh culture medium.
3. Stimulate cells with IL-1 β inducers such as ATP (5 mM) or MSU crystals (100-200 mg/ml) in the presence or absence of MCC950 (300 nM-10 μ M).
4. Incubate from 6 hours to overnight at 37°C in 5% CO₂.
5. Determine caspase-1 inhibition by detecting mature IL-1 β in the supernatant of THP-1 cells by Western blot, ELISA or with InvivoGen's HEK-Blue™ IL-1 β cells, which are specifically engineered to detect bioactive IL-1 β .

PROTOCOLS

For reference only; as described in the indicated publications.

Cell Culture Assay¹

Cells: Bone marrow derived macrophages and human peripheral blood mononuclear cells

Working concentration: 100 nM-10 μ M

Incubation time: 16 hours

Method: Inflammasome activation assays and Western blotting

Cell Culture Assay³

Cells: Porcine peripheral blood mononuclear cells

Working concentration: 300 nM-450 μ M

Incubation time: 3 hours

Method: Immunoassay specific for IL-1 β

Animal Study³

Animal model: pigs

Dose: 6 or 3 mg/kg daily for 7 days

Administration: Intravenous (IV)

RELATED PRODUCTS

Product	Description	Cat. Code
ATP	Adenosine 5'-triphosphate	tlrl-atp
HEK-Blue™ IL-1 β cells	IL-1 β reporter cells	hkb-il1b
Nigericin	NLRP3 inflammasome inducer	tlrl-nig
MSU Crystals	Monosodium urate crystal	tlrl-msu
THP1-Null Cells	Human monocytes	thp-null

TECHNICAL SUPPORT

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