MCC950
NLRP3 inflammasome inhibitor
Catalog code: inh-mcc
https://www.invivogen.com/mcc950

For research use only
Version 2011-MM

PRODUCT INFORMATION

Contents:
- 10 mg MCC950 provided as a translucent film.

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. Avoid repeated freeze-thaw cycles.

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

DESCRIPTION

MCC950 (also known as CP-456773) is a potent and specific inhibitor of the NLRP3 inflammasome. Specifically, it prevents NLRP3 inflammasome assembly in a reversible manner. The NLRP3 inflammasome is an innate immune sensor that is activated by a two-step process: a first signal ('priming') is provided mainly by bacterial components or endogenous cytokines and involves NF-κB induction, while the second signal is provided by various stimuli including endogenous molecules, crystalline substances or bacterial toxins and leads to inflammasome assembly and activation. Upon assembly, it activates caspase-1 and mediates the processing and release of interleukin-1β (IL-1β) and IL-18.

Studies have demonstrated that MCC950 blocks the release of IL-1β induced by NLRP3 activators, such as ATP, MSU crystals, and nigericin. Specifically, this small molecule directly targets the NLRP3 NATCH domain and interferes with the Walker B motif function that is crucial for ATP hydrolysis, a requirement for NLRP3 conformational change and oligomerization. In research models of inflammation, such as cryopyrin-associated periodic syndromes (CAPS) and myocardial infarction, MCC950 effectively inhibited NLRP3-induced IL-1β production. Importantly, it does not inhibit the AIM2, NLRC4, or NLRP1 inflammasomes.


RELATED PRODUCTS

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METHODS

Preparation of 20 mM (8.1 mg/ml) stock solution
1. Add 1.235 ml of DMSO to 10 mg MCC950. Mix by vortexing.
2. 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 μM (4.04 μg/ml) for cell culture assays

In vitro inhibition of the NLRP3 inflammasome:
1. Prepare a THP-1 cell suspension at 2 x 10^6 cells/ml and add 180 μl of this cell suspension per well of a 96-well plate (3 x 10^6 cells/well).
2. Prime cells by adding 1 μg/ml LPS-EK for 3 hours at 37°C in 5% CO2.
3. Gently remove medium and add 180 μl of fresh test medium.
4. Stimulate cells by adding IL-1β inducers, such as MSU crystals (100-200 mg/ml) in the presence or absence of MCC950 (300 nM-10 μM).
5. Incubate from 6 hours to overnight at 37°C in 5% CO2.
6. Determine caspase-1 inhibition by detecting mature IL-1β with Invivogen's HEK-Blue™ IL-1β cells, which are specifically engineered to detect bioactive IL-1β.

PROTOLUGS

For reference only; as described in the indicated publications.

Cell Culture Assay

Cells: Bone marrow-derived macrophages and human peripheral blood mononuclear cells
Working concentration: 100 nM-10 μM
Incubation time: 16 hours
Method: Inflammasome activation assays and Western blotting

Animal Study

Animal model: pigs
Dose: 6 or 3 mg/kg daily for 7 days
Administration: Intravenous (IV)