

Validation data for MCC950

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Version 22F07-MM

MCC950 (also known as CP-456773) is a potent and specific NLRP3 inhibitor that prevents NLRP3 (NOD-like receptor (NLR) pyrin domain-containing protein 3) 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 by microbial molecules such as lipopolysaccharide (LPS), while the second signal is provided by a wide array of stimuli including endogenous molecules or crystalline substances such as monosodium urate (MSU) crystals. The ability of MCC950 to inhibit the NLRP3 inflammasome was validated using InvivoGen's THP-1/HEK-Blue™ IL-1 β assay. This assay uses the secretion of IL-1 β by THP1-Null2 cells as an indicator of NLRP3 inflammasome induction. The IL-1 β production by these cells is measured using HEK-Blue™ IL-1 β cells. Treatment with MCC950 inhibited IL-1 β secretion in a dose-dependent manner (Figure 1).

Dose-dependent inhibition of NLRP3 activity

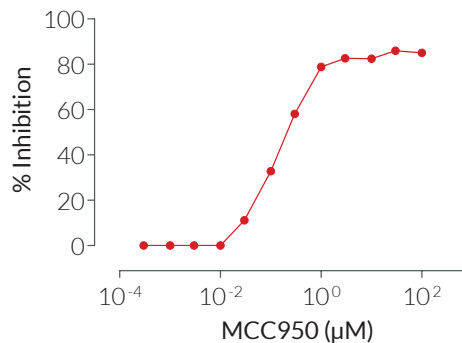


Figure 1: MCC950 inhibits the NLRP3 inflammasome response in a dose-dependent manner.

THP1-Null2 cells, primed with LPS-EK (1 μ g/ml for 3 h), were stimulated with MSU (150 μ g/ml) and increasing concentrations of MCC950. After overnight incubation, IL-1 β secretion was analyzed by adding 50 μ l of supernatant from treated THP1-Null2 cells to HEK-Blue™ IL-1 β cells. IL-1 β -induced activation of NF- κ B was assessed by measuring the levels of SEAP in the supernatant of HEK-Blue™ IL-1 β cells using QUANTI-Blue™ Solution, a SEAP detection reagent, and by reading the optical density (OD) at 655 nm. Data are shown as percentage (%) inhibition.

TECHNICAL SUPPORT

InvivoGen USA (Toll-Free): 888-457-5873
InvivoGen USA (International): +1 (858) 457-5873
InvivoGen Europe: +33 (0) 5-62-71-69-39
InvivoGen Asia: +852 3622-3480
E-mail: info@invivogen.com