

CU-CPT9a

TLR8 inhibitor

Catalog Code: inh-cc9a

<https://www.invivogen.com/cucpt9a>

For research use only

Version 19J25-ED

PRODUCT INFORMATION

Contents

- 10 mg CU-CPT9a
- 5 ml CU-CPT9a Diluent

Storage and stability

- CU-CPT9a is provided as a dried powder and shipped at room temperature. Upon receipt, store product at -20°C.
- Diluent is provided as a clear solution. Upon receipt, store at 4 °C
- Upon resuspension of CU-CPT9a in DMSO prepare aliquots and store at -20°C. Resuspended product is stable for up to 3 months when properly stored at -20°C.
- Avoid repeated freeze-thaw cycles.

Quality control

- Purity: ≥95% (UHPLC)
- Inhibition of TLR8 by CU-CPT9a has been confirmed using cellular assays.
- Absence of bacterial contamination (e.g. lipoproteins and endotoxins) has been confirmed using HEK-Blue™ TLR2 and TLR4 cellular assays.

PRODUCT DESCRIPTION

CU-CPT9a is a potent and selective inhibitor of human Toll-like receptor 8 (TLR8)^{1,2}. Normally upon the binding of a TLR8 agonist, such as R848 or ssRNA, two TLR8 protomers are brought in close proximity, which induces the necessary conformational change for activation and initiation of downstream signaling. CU-CPT9a binds to and stabilizes the TLR8 dimer in its resting state, thus preventing TLR8 activation. Therefore, antagonizes binding of any TLR8 ligands. Importantly, CU-CPT9a blocks TLR8-induced expression of NF-κB in various cultured and primary cells without having any effect on other TLRs, especially the closely related TLR7¹. Thereby, by using CU-CPT9a to specifically block TLR8 it has been established that TLR8 is a dominant sensor of pyrogenic Gram-positive bacteria (i.e. *S. aureus*) as well as having an important role in sensing Gram-negative bacteria (i.e. *E. coli* and *P. aeruginosa*)². Additionally, CU-CPT9a has been shown to exert potent anti-inflammatory effects in samples from patients with inflammatory diseases such as osteoarthritis (OA), rheumatoid arthritis (RA), and adult-onset Still's disease (AOSD)¹.

Taken together, it seems that TLR8 plays an important role in both inflammatory conditions as well as in the sensing of bacterial infection. Therefore, CU-CPT9a is a useful tool in furthering our understanding of the role of TLR8 in these pathologies.

1. Zhang, S. et al., 2018. Small-molecule inhibition of TLR8 through stabilization of its resting state. *Nat Chem Biol*, 14(1): 58-64. 2. Moen, S.H. et al., 2019. Human Toll-like Receptor 8 (TLR8) Is an Important Sensor of Pyrogenic Bacteria, and Is Attenuated by Cell Surface TLR Signaling. *Front Immunol*, 10: 1209.

TECHNICAL SUPPORT

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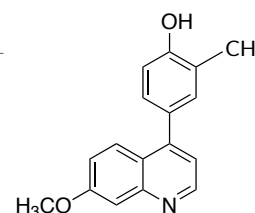
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CHEMICAL PROPERTIES

- Synonyms: 2-Methyl-4-(7-methoxy-4-quinolinyl)-phenol, Phenol,4-(7-methoxy-4-quinolinyl)-2-methyl
- CAS Number: 2165340-32-7
- Formula: C₁₇H₁₅NO₂
- Molecular weight: 265.31 g/mol
- Solubility: 100 mM DMSO



METHODS

Preparation of a 10 mM CU-CPT9a stock solution

1. Resuspend CU-CPT9a in 0.378 ml of DMSO (100 mM stock)
2. Prepare aliquots and store at -20°C until required.
3. **On the day of use**, thaw a CU-CPT9a aliquot, and perform a 1:10 dilution into the provided **CU-CPT9a Diluent**.
4. Mix well and use immediately.

Note: Subsequent dilutions into the working concentration range can be performed with sterile water.

Working concentration range: 1 - 10 μM (for cell culture assays)

Specific inhibition of TLR8 by CU-CPT9a in cellular assays

Below is a protocol for using InvivoGen's **HEK-Blue™ hTLR8 cells** for studying the specific inhibition of human TLR8 (hTLR8) by CU-CPT9a. These cells express an inducible secreted embryonic alkaline phosphatase (SEAP) reporter to readily measure the activation of the NF-κB pathway. Changes in SEAP expression due to inhibition of TLR8 can be assessed using **QUANTI-Blue™ Solution**, a SEAP detection reagent.

Note: For more information regarding this cell line please visit <https://www.invivogen.com/hek-blue-htr8>

1. Add 20 μl CU-CPT9a (10x conc) per well of a flat bottom 96-well plate.
2. Prepare a suspension of **HEK-Blue™ hTLR8 cells** (~300,000 cells per ml) in culture medium.
3. Add 160 μl of the cell suspension (~50,000 cells) to each well.
4. Incubate the plate at 37°C in a CO₂ incubator for 3 hours.
5. Add 20 μl of an inducer of TLR8 signaling (such as **R848** or **TL8-506**) and incubate the plate at 37°C in a CO₂ incubator for 24 hours.
6. Prepare **QUANTI-Blue™ Solution** and carry out the measurements following the instructions on the data sheet.

RELATED PRODUCTS

Product	Description	Cat. Code
R848	TLR7/8 agonist	tlrl-r848
TL8-506	TLR8 agonist	tlrl-tl8506
HEK-Blue™ hTLR8 cells	Human NF-κB reporter cells	hkb-htr8
Quanti-Blue™ Solution	SEAP detection reagent	rep-qbs

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