

TDI-6570

cGAS inhibitor - InvitroFit™

Catalog codes: inh-tdi6570-1, inh-tdi6570-2

<https://www.invivogen.com/tdi-6570-cGAS-inhibitor>

For research use only

Version 24D15-AK

PRODUCT INFORMATION

Contents: TDI-6570 is available in two quantities:

- **inh-tdi6570-1:** 2 mg of TDI-6570 - InvitroFit™
- **inh-tdi6570-2:** 50 mg of TDI-6570 - InvitroFit™

Storage and stability

- TDI-6570 is provided dried and shipped at room temperature. Upon receipt, store at -20°C.
- Upon resuspension, prepare aliquots and store at -20°C. Resuspended product is stable for 6 months when properly stored.
- Avoid repeated freeze-thaw cycles.
- *Note:* Crystallization may occur at temperatures below 15°C. Reheat product at 37°C until completely dissolved.

Quality Control

- Purity: ≥95% (UHPLC)
- The inhibitory function of TDI-6570 has been confirmed using 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

TDI-6570 is described as a small molecule inhibitor of the murine cytosolic double-stranded (ds)DNA sensor cyclic GMP-AMP synthase (cGAS)¹. cGAS is the primary sensor of cytosolic dsDNA, a danger signal indicating possible disturbances in homeostasis caused by infection, sterile tissue damage, or cancer¹⁻³. TDI-6570 is described as one of the most potent inhibitors for mouse cGAS³. It possesses high gastrointestinal absorption and good brain permeability¹⁻². TDI-6570 has been used to determine the effects of cGAS inhibition on the cGAS-STING pathway in a mouse model of tauopathy¹. Even high concentrations of TDI-6570 show no substantial toxicity¹. TDI-6570 can be formulated into chow diet and is orally administrable¹⁻². Inhibition of cGAS using TDI-6570 represents a promising therapeutic strategy to treat multiple neurodegenerative diseases, including Huntington's, or Parkinson's disease³.

InvivoGen's TDI-6570 efficiently inhibits mouse cGAS, but not human cGAS, as assessed using InvivoGen's reporter cell lines J774-Dual™ and THP1-Dual™, respectively (see validation data sheet).

1. Lo I, et al. 2023. Tau activation of microglial cGAS-IFN reduces MEF2C-mediated cognitive resilience. Nat Neurosci. 26(5):737-750. 2. Lama L, et al. 2019. Development of human cGAS-specific small-molecule inhibitors for repression of dsDNA-triggered interferon expression. Nat Commun.10(1):2261. 3. Huang Y, et al. 2023. Mechanism and therapeutic potential of targeting cGAS-STING signaling in neurological disorders. Mol Neurodegener.18(1):79.

CHEMICAL PROPERTIES

CAS number: 2287331-29-5

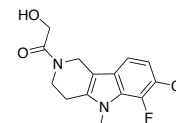
Synonyms: 1-(7-chloro-6-fluoro-5-methyl-1,3,4,5-tetrahydro-2H-pyrido[4,3-b]indol-2-yl)-2-hydroxyethan-1-one

Formula: C₁₄H₁₄ClFN₂O₂

Molecular weight: 296.7 g/mol

Solubility: 16.85 mM (5 mg/ml) in DMSO

Chemical structure:



METHODS

Preparation of 16.85 mM stock solution (5 mg/ml)

1. Add 400 µl of DMSO to 2 mg of TDI-6570 and vortex.
2. Heat up to 37°C until completely dissolved.
3. Prepare aliquots and store at -20°C. Once TDI-6570 has been resuspended, dilutions can be prepared in cell culture medium.

PROTOCOLS

Below is a protocol using J774-Dual™ cells for studying the specific inhibition of mouse cGAS signaling by TDI-6570. J774-Dual™ cells were generated from the J774 murine macrophage cell line by stable integration of two inducible reporter constructs for SEAP (secreted embryonic alkaline phosphatase) and Lucia luciferase. These cells allow the monitoring of the cGAS-dependent IRF activation by determining the activity of Lucia luciferase in the supernatant. For more information, visit <https://www.invivogen.com/j774-dual>

1. Add 20 µl of TDI-6570 at 1 nM -1 µM (final concentration) per well of a flat-bottom 96-well plate.
2. Add 160 µl of cell suspension (~50,000 cells) per well.
3. Incubate at 37°C for 3 hours.
4. Add 20 µl of a test sample or a cGAS ligand (positive control) such as G3-YSD, complexed with LyoVec™ at 1 µg/ml (final concentration) per well of a flat-bottom 96-well plate.
5. Incubate the plate at 37°C in a 5% CO₂ incubator for 18-24 hours.
6. Monitor Lucia luciferase reporter protein production using a luciferase detection reagent, such as QUANTI-Luc™ 4 Lucia/Gaussia.

RELATED PRODUCTS

Product	Cat.Code
J774-Dual™ Cells	j774d-nfis
THP1-Dual™ Cells	thpd-nfis
G3-YSD	tlrl-ydna
Poly(dA:dT) / LyoVec™	tlrl-patc
RU.521	inh-ru521-2
QUANTI-Luc™ 4 Lucia/Gaussia	rep-qlc4lg1

TECHNICAL SUPPORT

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