diABZI

diABZI (compound 3) trihydrochloride; non-CDN STING agonist

Catalog code: tlrl-diabzi-2, tlrl-diabzi-10

https://www.invivogen.com/diabzi

For research use only

Version 25A30-MM

PRODUCT INFORMATION

Contents: diABZI is available in two quantities:

- tlrl-diabzi-2: 2 mg (2 x 1 mg)
- tlrl-diabzi-10: 10 mg (10 x 1 mg)
- endotoxin-free water; 2 x 1.5 ml with tlrl-diabzi-2 and 10 x 1.5 ml with tlrl-diabzi-10

Storage and stability

- diABZI is provided as a lyophilized product and shipped at room temperature. Upon receipt, store product 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)
- Activation of STING has been confirmed using cellular assays.
- The absence of bacterial contamination (e.g. lipoproteins and endotoxins) has been confirmed using HEK-Blue™ cellular assays.

PRODUCT DESCRIPTION

diABZI, also known as diABZI (compound 3) trihydrochloride, is a small molecule, non-cyclic dinucleotide, that potently activates STING. Notably, diABZI (compound 3) trihydrochloride is water soluble.

Development of a non-CDN STING agonist

A series of small molecule amidobenzimidazoles (ABZI) were identified to effectively competed with the classical STING agonist, 2'3'-cGAMP. To take advantage of the symmetrical nature of STING, two molecules of the lead compound were joined to create a single dimeric ligand (diABZI; compound 2). Importantly, this afforded a 1000X increase in the STING binding affinity, when compared to 2'3'-cGAMP. This dimeric ligand was then further optimized into 'diABZI (compound 3)'[1].

Activation of STING by diABZI

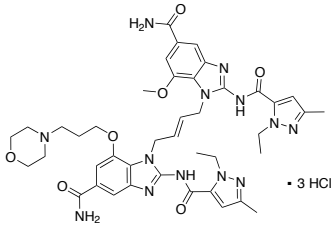
In contrast to classical CDNs, diABZI activates STING while maintaining its open conformation[1]. Further research is needed to understand the implications of this difference. However, similar to 2'3'-cGAMP, diABZI induces STING-dependent activation of type-I interferon and pro-inflammatory cytokines *in vitro* and *in vivo*[1].

diABZI has therapeutic potential in the treatment of cancer with significant inhibition of tumor growth observed in a syngeneic mouse model of colorectal cancer[1]. Furthermore, diABZI has been shown to suppress infection by diverse strains of SARS-CoV-2, including variants of concern (e.g. B.1.351), through the induction of a effective IFN response[2].

1. Ramanjulu, J.M. *et al.* 2018. Design of amidobenzimidazole STING receptor agonists with systemic activity. Nature 564, 439-443. 2. Li, M. *et al.* 2021. Pharmacological activation of STING blocks SARS-CoV-2 infection. Science 6(59), eabi9007.

CHEMICAL PROPERTIES

CAS Number: 2138299-34-8
Synonyms: diABZI (Compound 3)
Formula: $C_{42}H_{51}N_{13}O_7 \bullet 3HCl$
Molecular weight: 959.33 g/mol
Solubility: 2mg/ml H_2O



METHODS

Preparation of a stock solution (1 mg/ml; 1.04 mM)

1. Before opening the vial, centrifuge briefly and open the lid carefully to avoid any loss of product.
2. Add 1 ml of endotoxin-free water (provided) to 1 mg of diABZI to obtain a stock solution at 1 mg/ml.
3. Vortex until completely dissolved.

Working concentration: 0.01 - 30 µM

Activation of STING in THP1-Dual™ cells

Below is a protocol for monitoring the activation of STING by diABZI using InvivoGen's THP1-Dual™ cells. These cells allow the simultaneous study of the NF-κB pathway, by monitoring the activity of SEAP, and the IRF (interferon regulatory factor) pathway, by assessing the activity of the secreted Lucia luciferase. For more information, please visit https://www.invivogen.com/thp1-dual.

1. Add 20 µl of diABZI (10X final concentration) per well of a flat-bottom 96-well plate.
2. Add 20 µl of a positive control (i.e. 2'3'-cGAMP) to another well.
3. Prepare a suspension of THP1-Dual™ cells (~500,000 cells per ml) as detailed in the cell line data sheet.
4. Add 180 µl of cell suspension (~100,000 cells) per well.
5. Incubate the plate at 37°C in a 5% CO_2 incubator for 18-24 hours.
6. Prepare QUANTI-Luc™ 4 Lucia/Gaussia (IRF assessment) and/or QUANTI-Blue™ Solution (NF-κB assessment) and carry out the measurements following the instructions on the data sheet.

RELATED PRODUCTS

Product	Description	Cat. Code
2'3'-cGAMP	STING ligand	tlrl-nacga23
THP1-Dual™ cells	Reporter monocytes	thpd-nfis
QUANTI-Blue™ Solution	SEAP detection reagent	rep-qbs
QUANTI-Luc™ 4 Lucia/Gaussia	Luciferase detection reagent	rep-qlc4lg1

TECHNICAL SUPPORT
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