DMXAA

Murine STING ligand

Catalog # tlrl-dmx

For research use only. Not for use in humans.

Version # 16G19-MM

PRODUCT INFORMATION

Content:

• 5 mg of DMXAA

Storage and stability:

- DMXAA is shipped at room temperature and should be stored at -20°C. Product is stable for 1 year when properly stored.
- Upon resuspension, prepare aliquots of DMXAA and store at -20°C. Resuspended product is stable for 12 months when properly stored. Avoid repeated freeze-thaw cycles.

Quality control:

- Purity: ≥ 95% (LC/MS)
- Biological activity has been assessed by measuring induction of the interferon pathway in B16-Blue™ ISG cells.
- The absence of bacterial contamination (e.g. lipoproteins and endotoxins) has been verified using HEK-Blue™ TLR2 and HEK-Blue™ TLR4 cells.

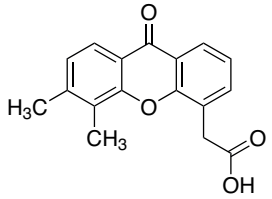
DESCRIPTION

DMXAA (also known as Vadimezan or ASA404) was initially identified as a potent tumor vascular disrupting agent in mice. The antitumor activity of DMXAA has been linked to its ability to induce a variety of cytokines and chemokines, including TNF-α, IP-10, IL-6 and RANTES[1]. DMXAA is also a potent inducer of IFN-β[1, 2]. Despite significant preclinical promise, DMXAA failed human clinical trials. Recent studies have demonstrated that DMXAA targets the STING pathway[3], and this in a mouse-specific manner; DMXAA has no effect on human STING[4,5]. A unique point mutation (S162A) located within the cyclic-dinucleotide-binding site of human STING has been identified that renders it sensitive to DMXAA.

1. Jassar AS. *et al.*, 2005. Activation of tumor-associated macrophages by the vascular disrupting agent 5,6-dimethylxanthenone-4-acetic acid induces an effective CD8+ T-cell-mediated antitumor immune response in murine models of lung cancer and mesothelioma. Cancer Res. 65(24):11752-61. **2. Roberts ZJ. *et al.*, 2007.** The chemotherapeutic agent DMXAA potently and specifically activates the TBK1-IRF-3 signaling axis. J Exp Med. 204(7):1559-69. **3. Prantner D. *et al.*, 2012.** 5,6-Dimethylxanthenone-4-acetic acid (DMXAA) activates stimulator of interferon gene (STING)-dependent innate immune pathways and is regulated by mitochondrial membrane potential. J Biol Chem. 287(47):39776-88. **4. Conlon J. *et al.*, 2013.** Mouse, but not human STING, binds and signals in response to the vascular disrupting agent 5,6-dimethylxanthenone-4-acetic acid. J Immunol. 190(10):5216-25. **5. Kim S. *et al.*, 2013.** Anticancer Flavonoids Are Mouse-Selective STING Agonists. ACS Chem Biol. 8(7): 1396-1401. **6. Gao P. *et al.*, 2013.** Structure-function analysis of STING activation by c[G(2',5')pA(3',5')p] and targeting by antiviral DMXAA. Cell. 154(4):748-62. **7. Lam E. *et al.*, 2014.** Adenovirus Detection by the cGAS/STING/TBK1 DNA Sensing Cascade. J Virol. 88(2):974-81. **8. Shirey KA. *et al.*, 2011.** The anti-tumor agent, 5,6-dimethylxanthenone-4-acetic acid (DMXAA), induces IFN-beta-mediated antiviral activity in vitro and in vivo. J Leukoc Biol. 89(3):351-7.

CHEMICAL PROPERTIES

Synonym: 5,6-dimethylxanthenone-4-acetic acid
CAS Number: 117570-53-3
Formula: $C_{17}H_{14}O_4$
Molecular weight: 282.29
Solubility: 10 mg/ml in DMSO
Source: Synthetic
Structure:



METHODS

Preparation of stock solution (10 mg/ml):

Stimulation of mSTING can be achieved with 10-100 µg/ml DMXAA.
- Reconstitute by adding 500 µl DMSO to the content of the tube.
- Mix by vortexing for several minutes until complete solubilization.
- Use cell culture medium (e.g. DMEM) to prepare serial dilutions.

Induction of type I IFNs in RAW-Lucia ISG cells

Induction of type I IFNs with DMXAA can be studied in a variety of murine cells. The murine RAW 264.7 macrophage cell line has been shown to express STING[7] and respond to DMXAA[8].

A protocol for the induction of type I IFNs using RAW-Lucia™ ISG cells, a cell line that expresses the secreted Lucia luciferase reporter gene under the control of an IRF-inducible promoter, is given below:
- Resuspend DMXAA, as described above.
- Stimulate cells with 10-100 µg/ml DMXAA for 16-48 hours.
- Monitor induction of type I IFNs by measuring the levels of IRF-induced Lucia luciferase in the supernatant using QUANTI-Luc™, a Lucia luciferase detection reagent.

RELATED PRODUCTS

Product	Catalog Code
2'3'-cGAMP	tlrl-nacga23
3'3'-cGAMP	tlrl-nacga
B16-Blue™ ISG Cells	bb-ifnabg
c-di-AMP	tlrl-nacda
c-di-GMP	tlrl-nacdg
QUANTI-Luc™	rep-qlc1
RAW-Lucia™ ISG cells	rawl-isg

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