

# DMXAA

Murine STING ligand

Catalog code: tlr1-dmx

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

For research use only. Not for use in humans.

Version 20D23-MM

## PRODUCT INFORMATION

### Contents

- 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: ≥ 97% (UHPLC)
- Biological activity has been assessed by measuring induction of the interferon pathway in cellular assays.
- 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- $\alpha$ , IP-10, IL-6 and RANTES<sup>1</sup>. DMXAA is also a potent inducer of IFN- $\beta$ <sup>1, 2</sup>. Despite significant preclinical promise, DMXAA failed human clinical trials. Recent studies have demonstrated that DMXAA targets the STING pathway<sup>3</sup>, and this in a mouse-specific manner; DMXAA has no effect on human STING<sup>4,5</sup>. 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 potentially 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

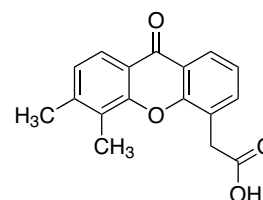
Formula: C<sub>17</sub>H<sub>14</sub>O<sub>4</sub>

Molecular weight: 282.29 g/mol

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  $\mu$ g/ml DMXAA.

- Reconstitute by adding 500  $\mu$ l DMSO to the content of the tube.
- Mix by vortexing for several minutes until completely dissolved.

*Note:* The suspension may appear to contain floating fine particles. If this occurs, heat the product at 37°C for 1 to 2 minutes to obtain a clear solution.

- Use cell culture medium (e.g. DMEM) to prepare serial dilutions.

### Induction of type I IFNs in RAW-Blue 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<sup>7</sup> and respond to DMXAA<sup>8</sup>.

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  $\mu$ g/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
293-Dual™ hSTING-A162 Cells	293d-a162
RAW-Lucia™ ISG Cells	rawl-isg
THP1-Dual™ KI-hSTING-A162 Cells	thpd-a162
QUANTI-Luc™	rep-qlc1
2'3'-cGAMP	tlr1-nacga23
3'3'-cGAMP	tlr1-nacga

## TECHNICAL SUPPORT

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