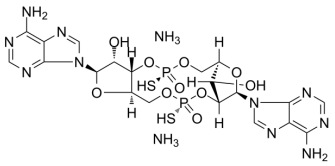
ADU-S100 ammonium salt

Cat. No.:	HY-12885B
CAS No.:	1638750-96-5
Molecular Formula:	$C_{20}H_{30}N_{12}O_{10}P_2S_2$
Molecular Weight:	724.6
Target:	STING
Pathway:	Immunology/Inflammation
Storage:	4°C, sealed storage, away from moisture * In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

H_2O : 100 mg/mL (138.01 mM; ultrasonic and warming and heat to 60°C)
DMSO : 15 mg/mL (20.70 mM; Need ultrasonic and warming)
Methanol : 5 mg/mL (6.90 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.3801 mL	6.9004 mL	13.8007 mL
	5 mM	0.2760 mL	1.3801 mL	2.7601 mL
	10 mM	0.1380 mL	0.6900 mL	1.3801 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: PBS
Solubility: 50 mg/mL (69.00 mM); Clear solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

ADU-S100 ammonium salt (MIW815 ammonium salt), an activator of stimulator of interferon genes (STING), leads to potent and systemic tumor regression and immunity[1].

IC_{50} & Target

STING[1]

In Vitro

ADU-S100 ammonium salt has several features that improve both stability and lipophilicity, promoting significantly increased STING signaling as compared to endogenous and pathogen-derived cyclic dinucleotides (CDNs)[1].
ADU-S100 shows enhanced type I IFN production over CDA in THP-1 human monocytes. In contrast, the dithio, mixed-linkage cyclic dinucleotide (CDN) derivatives (ML RR-CDA, ML RR-S2 CDG, and ML RR-S2 cGAMP) potently activate all five hSTING alleles, including the refractory $hSTING^{REF}$ and $hSTING^{Q}$ alleles. ADU-S100 induces the highest expression of IFN-β and the pro-inflammatory cytokines TNF-α, IL-6, and MCP-1 on a molar equivalent basis, as compared to endogenous ML cGAMP and the TLR3 agonist poly I:C. ADU-S100 is also found to induce aggregation of STING and induce phosphorylation of

	TBK1 and IRF3 in mouse bone marrow macrophage (BMM). ADU-S100 induces significantly higher levels of IFN-α when compared to ML cGAMP[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	ADU-S100 shows higher anti-tumor control than the endogenous ML cGAMP. A dose response of the ADU-S100 compound is performed in B16 tumor-bearing mice, which identifies an optimal antitumor dose level that also elicites maximum tumor antigen-specific $CD8^+$ T cell responses, and improves long-term survival to 50%[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	Cryopreserved hPBMCs are thawed and 1×10^6 cells per well are plated in a 96 well plate in RPMI media supplemented with 10% FBS, 1% non-essential amino acids, 1% penicillin/streptomycin, L-glutamine, 10 mM HEPES buffer, 1 mM Sodium Pyruvate, 0.055 mM β-ME at 37°C with 5% CO_2. Cells are stimulated with 10 μM ADU-S100 or ML cGAMP for 6 hours and supernatants are harvested. Supernatants are diluted 1:2 and assayed for IFN-α protein using Cytometric Bead Array (CBA) Human Flex Set. Data is collected using a FACSVerse cytometer and analyzed by FCAP Array Software[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice[1] WT C57BL/6 mice are inoculated with 5×10^4 B16.F10 cells in the left flank (n=8). When tumor volumes are 100 mm^3 mice receive three IT doses of either ML RR-S2 CDG (25 μg), ADU-S100 (50 μg), or HBSS as control. WT C57BL/6 mice are inoculated with 5×10^4 B16.F10 cells in the left flank (n=5). When tumor volumes are 100 mm^3 they received three IT doses of ADU-S100 at 5, 25, 50 or 100 μg or HBSS as control. WT C57BL/6 mice are inoculated with 5×10^4 B16.F10 cells in the left flank (n=8). When tumor volumes are 100 mm^3 they receive three IT doses of 100 μg ADU-S100 or HBSS as control. Treatments are administered on days 13, 17 and 20 and tumor measurements are taken twice weekly. Results are shown as percent survival by Log-rank (Mantel-Cox) test (A and C). MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cancer Cell. 2023 Jun 12;41(6):1073-1090.e12.
- Cancer Cell. 2020 Mar 16;37(3):289-307.e9.
- Nat Nanotechnol. 2021 Sep 30.
- Nat Commun. 2023 Mar 13;14(1):1390.
- Nat Commun. 2022 May 31;13(1):3022.

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REFERENCES

[1]. Corrales L, et al. Direct Activation of STING in the Tumor Microenvironment Leads to Potent and Systemic Tumor Regression and Immunity. Cell Rep. 2015 May 19;11(7):1018-30.

Caution: Product has not been fully validated for medical applications. For research use only.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA