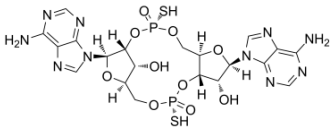
ADU-S100

Cat. No.:	HY-12885
CAS No.:	1638241-89-0
Molecular Formula:	$C_{20}H_{24}N_{10}O_{10}P_2S_2$
Molecular Weight:	690.54
Target:	STING
Pathway:	Immunology/Inflammation
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



BIOLOGICAL ACTIVITY

Description	ADU-S100 (MIW815), 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 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. 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)[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cancer Cell. 2020 Mar 16;37(3):289-307.e9.
- Biomaterials. 2018 May;163:67-75.
- J Immunother Cancer. 2019 Sep 18;7(1):252.
- Environ Int. 2020 Oct;143:105949.
- Acta Crystallogr D Struct Biol. 2020 Sep 1;76(Pt 9):889-898.

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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.

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