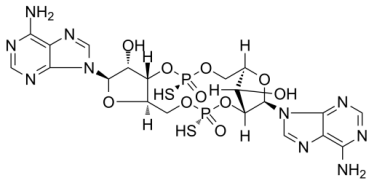
Data Sheet

Product Name:	ADU-S100
Cat. No.:	CS-4197
CAS No.:	1638241-89-0
Molecular Formula:	C20H24N10O10P2S2
Molecular Weight:	690.54
Target:	STING
Pathway:	Immunology/Inflammation
Solubility:	H2O : 300 mg/mL (434.44 mM; Need ultrasonic); DMSO : 2 mg/mL (2.90 mM; Need ultrasonic)



BIOLOGICAL ACTIVITY:

ADU-S100 (ML RR-S2 CDA; MIW815), an activator of stimulator of interferon genes (**STING**), leads to potent and systemic tumor regression and immunity[1]. IC50 & 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]. **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].

PROTOCOL (Extracted from published papers and Only for reference)

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]. **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].

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.

CAIndexNames:

Adenosine, [P(R)]-5'-O-[(R)-hydroxymercaptophosphinyl]-P-thioadenylyl-(2'→5')-, cyclic nucleotide

SMILES:

OC1([H])[C@](O[P@](S)(OC[C@](O[C@@H](N2C3=NC=NC(N)=C3N=C2)[C@@H]4O)([H])[C@@]4([H])O5)=O)([H])[C@H](N6C7=NC=NC(N)=C7N=C6)O[C@]1([H])CO[P@]5(S)=O

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

Tel: 732-484-9848 Fax: 888-484-5008 E-mail: sales@ChemScene.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA