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产品名称：ML RR-S2 CDA (ammonium salt)
产品别名：ADU-S100 ammonium salt ；MIW815 ammonium salt

生物活性：

Description	ADU-S100 ammonium salt (ML RR-S2 CDA 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 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].
Solvent&Solubility	***In Vitro:*** **DMSO : 15 mg/mL (20.70 mM;** Need ultrasonic and warming) **H_2O : 12.5 mg/mL (17.25 mM;** Need ultrasonic and warming)

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

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

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.

实验参考：

Cell Assay	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].
Animal Administration	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).
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.