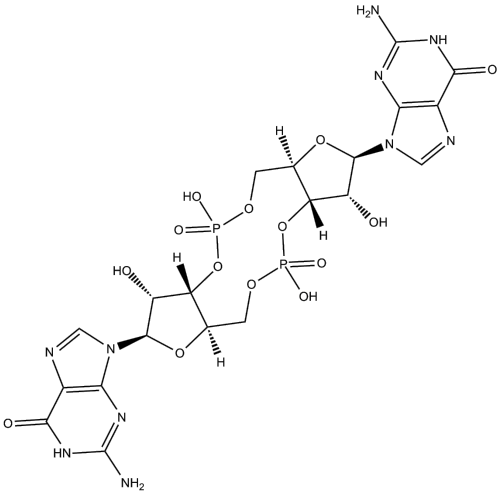
Product Data Sheet

Product Name: Cyclic di-GMP
Cat. No.: GC15048

Chemical Properties

Cas. No.	61093-23-0		
Chemical Name	9,9'-((2R,3R,3aS,7aR,9R,10R,10aS,14aR)-3,5,10,12-tetrahydroxy-5,12-dioxidodecahydrodifuro[3,2-d:3',2'-j][1,3,7,9,2,8]tetraoxadiphosphacyclododecine-2,9-diyl)bis(2-amino-1H-purin-6(9H)-one)		
SMILES	O=C1NC(N)=NC2=C1N=CN2[C@H](O[C@@]([C@@]3([H])OP(O)(OC[C@]([C@@]4([H])OP5(O)=O)(O[C@@H](N6C(N=C(N)NC7=O)=C7N=C6)[C@@H]4O)[H])=O)(CO5)[H])[C@@H]3O		
Formula	$C_{20}H_{24}N_{10}O_{14}P_2$	M.Wt	690.41
Solubility	Soluble in Water	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		

Structure



Protocol

Cell experiment [1]:

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Cell lines	Human cecal adenocarcinoma (H508 cells)
Preparation Method	H508 cells were incubated in the absence or presence of a growth stimulant [acetylcholine (300μM) and epidermal growth factor (EGF) (1ng/mL)] for 5 days alone or with increasing concentrations of Cyclic di-GMP (0.5–50μM). Cell proliferation was determined by the sulforhodamine blue (SRB) colorimetric assay.
Reaction Conditions	0.5–50μM; 5 days
Applications	Increasing concentrations of Cyclic di-GMP inhibit basal, and acetylcholine- and EGF-stimulated colon cancer cell proliferation.

Animal experiment [2]:

Animal models	C57BL/6 mice
Preparation Method	Mice (five per group) were subcutaneously injected with 4×10^5 B16F10 cells in the shaved rear flank. Eight days later, they received the first vaccine (prime) intravenously (200μL/injection via tail vein), TriVax consisted of a mixture of 120μg Pam-hgp100, 100μg hgp100 or 100μg Ova, 50μg anti CD40 antibody, and 25μg Poly-IC. Nine days after priming, a booster was administered with the same components except for a reduced anti-CD40 dose (25μg). In some experiments, 100μg Cyclic di-GMP was added to both prime and boost. Tumor growth was monitored every 2-3 days by measuring two perpendicular diameters, and mice were euthanized when the tumor area exceeded $400mm^2$ or if ulceration or >20% weight loss occurred.

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Dosage form	100μg; given two sequential vaccinations 9 days apart (prime and boost); i.v.
Applications	The administration of Cyclic di-GMP is effective in potentiating the magnitude of the immune responses generated by TriVax. TriVax in combination with Cyclic di-GMP induced significantly higher numbers of antigen-specific CD8 T cells as compared to TriVax w/o Cyclic di-GMP.

References:
[1] Karaolis D K R, Cheng K, Lipsky M, et al. 3?, 5?-Cyclic diguanylic acid (c-di-GMP) inhibits basal and growth factor-stimulated human colon cancer cell proliferation[J]. Biochemical and biophysical research communications, 2005, 329(1): 40-45.
[2]Wang Z, Celis E. STING activator c-di-GMP enhances the anti-tumor effects of peptide vaccines in melanoma-bearing mice[J]. Cancer Immunology, Immunotherapy, 2015, 64: 1057-1066.

Background

Cyclic di-GMP is a stimulator of interferon genes (STING) agonist[1]. Cyclic di-GMP is a cyclic dinucleotide and a bacterial second messenger that regulates biofilm formation, motility and virulence of different bacteria[2]. Cyclic di-GMP has anti-cancer cell proliferation activity and can also induce increased CD4 receptor expression and cell cycle arrest[3].

In vitro, treatment of human cecal adenocarcinoma H508 cells with Cyclic di-GMP (0.5-50μM) for 5 days inhibited basal cell proliferation as well as cell proliferation stimulated by acetylcholine and epidermal growth factor (EGF)[4]. Treatment of lymphoblastoid $CD4^+$ Jurkat cell line with Cyclic di-GMP (50μM) significantly increased intracellular CD4 expression and led to S phase arrest of the cell cycle[5].

In vivo, Cyclic di-GMP (100μg) was administered intravenously to mice bearing B16F10 cell xenografts, which effectively enhanced the immune response produced by the TriVax vaccine and induced the production of more antigen-specific CD8 T cells in mice[6].

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References:

[1] Burdette D L, Monroe K M, Sotelo-Troha K, et al. STING is a direct innate immune sensor of cyclic di-GMP[J]. Nature, 2011, 478(7370): 515-518.
[2] Jenal U, Reinders A, Lori C. Cyclic di-GMP: second messenger extraordinaire[J]. Nature Reviews Microbiology, 2017, 15(5): 271-284.
[3] Li A, Yi M, Qin S, et al. Activating cGAS-STING pathway for the optimal effect of cancer immunotherapy[J]. Journal of hematology & oncology, 2019, 12: 1-12.
[4] Karaolis D K R, Cheng K, Lipsky M, et al. 3′, 5′-Cyclic diguanylic acid (c-di-GMP) inhibits basal and growth factor-stimulated human colon cancer cell proliferation[J]. Biochemical and biophysical research communications, 2005, 329(1): 40-45.
[5] Steinberger O, Lapidot Z, Ben-Ishai Z, et al. Elevated expression of the CD4 receptor and cell cycle arrest are induced in Jurkat cells by treatment with the novel cyclic dinucleotide 3′, 5′-cyclic diguanylic acid[J]. FEBS letters, 1999, 444(1): 125-129.
[6] Wang Z, Celis E. STING activator c-di-GMP enhances the anti-tumor effects of peptide vaccines in melanoma-bearing mice[J]. Cancer Immunology, Immunotherapy, 2015, 64: 1057-1066.

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