2’3’-cGAMP VacciGrade™

Cyclic [G(2’,5’)pA(3’,5’)p], a STING ligand

Catalog # vac-nacga23

For research use only. Not for use in humans.

Version # 15K27-MM

PRODUCT INFORMATION

Content:

• 1 mg (2 x 500 µg) lyophilized 2’3’-cGAMP VacciGrade™

• 10 ml sterile endotoxin-free physiological water (NaCl 0.9%)

Storage and stability:

- 2’3’-cGAMP VacciGrade™ is shipped at room temperature and should be stored at -20 °C. Lyophilized product is stable for 1 year when properly stored.

- Upon resuspension, prepare aliquots of 2’3’-cGAMP VacciGrade™ and store at -20 °C. Resuspended product is stable for 6 months when properly stored. Avoid repeated freeze-thaw cycles.

Quality control:

- 2’3’-cGAMP VacciGrade™ is a preclinical grade preparation of the cyclic dinucleotide 2’3’-cGAMP. It is prepared under strict aseptic conditions and is tested for the presence of endotoxins. 2’3’-cGAMP VacciGrade™ is guaranteed sterile and its endotoxin level is <0.005 EU/µg.

- Purity and structure has been determined by LC/MS and NMR: ≥ 95%

- Biological activity has been assessed by measuring induction of the interferon pathway in THP1-Blue™ ISG cells.

METHODS

Preparation of stock solution (1 mg/ml):

- Add 500 µl sterile endotoxin-free physiological water (provided) to 500 µg 2′3′-cGAMP VacciGrade™.

- Mix the solution by pipetting up and down.

Working Concentration: 5 - 50 µg/mouse

CHEMICAL PROPERTIES

Synonym: cyclic GMP-AMP; c-GpAp sodium salt

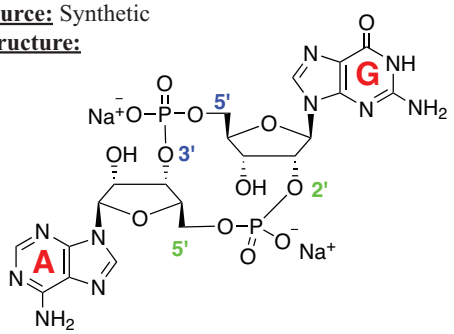
Formula: $C_{20}H_{22}N_{10}O_{13}P_2 .2Na$

Molecular weight: 718.38

Solubility: 50 mg/ml in physiological water

Source: Synthetic

Structure:



DESCRIPTION

2’3’-cGAMP (cyclic [G(2’,5’)pA(3’,5’)p]) is a cyclic dinucleotide produced in mammalian cells by cGAS (cGAMP synthase) in response to double-stranded DNA in the cytoplasm. Cyclic dinucleotides (CDNs) are a relatively new class of adjuvants that have been shown to increase vaccine potency[1]. CDNs activate innate immunity by directly binding the endoplasmic reticulum-resident receptor STING (stimulator of interferon genes), activating a signaling pathway that induces the expression of interferon-β (IFN-β) and also nuclear factor-κB (NF-κB) dependent inflammatory cytokines[1].

2’3’-cGAMP is also referred to as “noncanonical” cGAMP due to the presence of the atypical 2’-5’ phosphodiester linkage between the guanosine and the adenosine. Structural and functional studies revealed that noncanonical 2’3’-cGAMP is distinct from the canonical 3’3’-cGAMP produced by bacteria[2, 3]. Certain variants of STING are able to distinguish between noncanonical and canonical cGAMP[4].

Similar to the canonical 3’3’-cGAMP, 2’3’-cGAMP serves as a second messenger to activate innate immune responses by binding to STING and subsequently inducing the TBK1-IRF3 (TANK-binding kinase 1-IFN regulatory transcription factor3)-dependent production of IFN-β[5]. Recently, it has been reported that 2′3′-cGAMP is an effective adjuvant that boosts the production of antigen-specific antibodies and T cell responses in mice[6].

1. Dubensky TW. *et al.*, 2013. Rationale, progress and development of vaccines utilizing STING-activating cyclic dinucleotide adjuvants. Therapeutic Advances in Vaccines 1(4): 131-143. **2. Diner E. *et al.*, 2013.** The Innate Immune DNA Sensor cGAS Produces a Noncanonical Cyclic Dinucleotide that Activates Human STING. Cell Rep. 3(5):1355-61. **3. Gao P. *et al.*, 2013.** Cyclic [G(2',5')pA(3',5')p] is the metazoan second messenger produced by DNA-activated cyclic GMP-AMP synthase. Cell. 153(5):1094-107. **5. Zhang X. *et al.*, 2013.** Cyclic GMP-AMP containing mixed phosphdiester linkages is an endogenous high-affinity ligand for STING. Mol Cell.51(2):226-35. **6. Li XD. *et al.*, 2013.** Pivotal roles of cGAS-cGAMP signaling in antiviral defense and immune adjuvant effects. Science. 341(6152):1390-4.

RELATED PRODUCTS

Product	Description	Cat. Code
AddaVax™	Squalene-Oil-in-water	vac-adx-10
Alhydrogel® 2%	Al(OH)3 gel	vac-alu-250
c-di-GMP VacciGrade™	STING ligand	vac-nacdg
CFA	Complete Freund’s adjuvant	vac-cfa-10
EndoFit™ Ovalbumin	For *in vivo* use	vac-pova
Flagellin FliC VacciGrade™	TLR5 ligand	vac-fla
MPLAs VacciGrade™	TLR4 ligand	vac-mpls
ODN 2006 VacciGrade™	Human TLR9 ligand	vac-2006-1
Poly(I:C) VacciGrade™	TLR3 ligand	vac-pic

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