MPLA-SM* VacciGrade™

Monophosphoryl Lipid A from *S. minnesota* R595; TLR4-based adjuvant

Catalog code: vac-mpla2

https://www.invivogen.com/mpla-vaccigrade

For research use only. Not for use in humans.

Version 22L01-NJ

PRODUCT INFORMATION

Contents

- 1 mg Monophosphoryl Lipid A (MPLA-SM*) VacciGrade™
- 10 ml sterile endotoxin-free physiological water (NaCl 0.9%)

Storage and Stability

- MPLA-SM* VacciGrade™ is provided as a lyophilized clear lipidic film, and is shipped at room temperature. Store at -20°C. Lyophilized product is stable for 1 year when properly stored.
- Upon resuspension, prepare aliquots of MPLA-SM* and store at -20°C. Resuspended product is stable for 6 months when properly stored. Avoid repeated freeze-thaw cycles.

Quality control

- Biological activity has been tested using HEK-Blue™ hTLR4 cells.
- The presence of other bacterial components (e.g. lipoproteins) is controlled using HEK-Blue™ TLR2 cells.
- MPLAs VacciGrade™ is guaranteed sterile.

PRODUCT DESCRIPTION

Monophosphoryl Lipid A (MPLA-SM) VacciGrade™ is a pre-clinical grade preparation extracted from the lipopolysaccharide (LPS) of *Salmonella minnesota* Re595 (Re mutant), a rough strain of Gram-negative bacteria. It is prepared under strict aseptic conditions.
MPLA has been tested as an adjuvant in mice and reported to induce a strong Th1 response[1-2]. Although the mechanism of action of MPLA has not been fully eludicated, it has been suggested that MPLA improves vaccine immunogenicity by enhancing antigen presenting cell maturation[3].
The preparation is a mix of MPLA congeneric forms differing in the number of acyl chains. It has been suggested that this mix is responsible for the partial TLR4 agonist function of some preparations[4]. MPLA-SM* is a new reference in our catalog. It results from an improved process of MPLA-SM extraction. While MPLA-SM* and MPLA-SM have the same ability to activate murine TLR4, MPLA-SM* is more potent than MPLA-SM at inducing human TLR4 responses.

Note: Due to the intrinsic structural complexity of lipid A, some batch-to-batch variation may occur.

BACKGROUND

Monophosphoryl Lipid A (MPLA) is a natural compound extracted from the lipopolysaccharide (LPS) component of the cell wall of Gram-negative bacteria. LPS is a potent activator of the immune system. Its recognition by Toll-like receptor 4 (TLR4) leads to NF-κB and IRF activation and the production of proinflammatory cytokines and interferons, respectively[5]. Thus, LPS features many characteristics needed for an effective vaccine adjuvant. However, large uncontrolled amounts of LPS are extremely toxic and can cause devastating diseases[6].

Wild-type LPS, referred to as smooth (sLPS) comprises three covalently linked regions: a Lipid A backbone, an oligosaccharide core, and O-polysaccharide chains. Some bacteria produce a truncated LPS, without O-side chains, referred to as rough (rLPS)[7].

LPS biological activity is mediated through Lipid A recognition by TLR4 and is commensurate to Lipid A number of fatty acyl chains[6]. Hexa-acylated (6 chains) Lipid A is a highly potent TLR4 agonist, while under-acylated (4-5 chains) Lipid A induces lower or antagonistic responses[8].

Acidic extraction of Lipid A from LPS produces MPLA, which displays reduced toxicity while retaining the ability to activate TLR4[9,10]. The reduced toxicity of MPLA is attributed to the preferential triggering of the IRF pathway upon TLR4 activation, resulting in decreased induction of inflammatory cytokines[11].

METHODS

Preparation of sterile stock solution (1 mg/ml)

- Add 1 ml of DMSO to 1 mg of MPLA-SM* VacciGrade™ and vortex until complete solubilization, then sonicate.
- Prepare aliquots of stock solution and store at -20°C. Further dilutions can be prepared with endotoxin-free physiological water (provided).

Notes:

- *The suspension may appear to contain floating fine particles. Sonication may help to disperse these particles. Difficulties may be encountered for solubilization at higher concentrations.*
- *Alternatively, MPLA-SM* VacciGrade™ can be resuspended in DMSO containing 0.2 % triethylamine.*

Working Concentration: 2 - 20 µg/mouse

TECHNICAL SUPPORT
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1. Fransen F. *et al.*, 2007. Agonists of Toll-like receptors 3, 4, 7, and 9 are candidates for use as adjuvants in an outer membrane vaccine against *Neisseria meningitidis* serogroup. Infect Immun. 75(12) :5939. **2. Rhee EG. *et al.*, 2010.** TLR4 Ligands Augment Antigen-Specific CD8+ T Lymphocyte Responses Elicited by a Viral Vaccine Vector. J. Virol. 84: 10413. **3. Didierlaurent A. *et al.*, 2009.** AS04, an aluminum salt- and TLR4 agonist-based adjuvant system, induces a transient localized innate immune response leading to enhanced adaptive immunity. J Immunol 183(10): 6186. **4. Wang YQ. *et al.*, 2020**. MPL Adjuvant Contains Competitive Antagonists of Human TLR4. Front. Immunol. 11:577823. **5. Kuzmich, NN. *et al.*, 2017.** TLR4 Signaling Pathway Modulators as Potential Therapeutics in Inflammation and Sepsis. Vaccines (Basel) 5unol. 165(2):618. **6. Steimle, A. *et al.* 2016.** Structure and function: Lipid A modifications in commensals and pathogens. Int J Med Microbiol 306, 290. **7. Raetz CR. 1990.** Biochemistry of endotoxins. Annu. Rev. Biochem. 59, 129. **8. Cochet, F. & Peri, F. 2017.** The role of carbohydrates in the lipopolysaccharide (LPS)/Toll-Like Receptor 4 (TLR4) Signalling. Int J Mol Sci 18. **9. Qureshi N. *et al.*, 1982.** Purification and structural determination of nontoxic lipid A obtained from the lipopolysaccharide of *Salmonella typhimurium*. J. Biol. Chem., 257:11808. **10. Romero CD. *et al.*, 2011.** The Toll-Like Receptor 4 agonist monophosphoryl Lipid A augments innate host resistance to systemic bacterial infection. Infect Immun. 79: 3576. **11. Mata-Haro V. *et al.*, 2007.** The vaccine adjuvant monophosphoryl lipid A as a TRIF-biased agonist of TLR4. Science. 316(5831):1628.

RELATED PRODUCTS

Product	Description	Catalog Code
Adjuvants		
MPLAs VacciGrade™ (Synthetic MPLA)	TLR4 agonist	vac-mpls
AddaVax™	Squalene-Oil-in-water	vac-adx-10
AddaS03™	AS03-like vaccine adjuvant	vac-as03-10
Allhydrogel® adjuvant 2%	Aluminum hydroxide gel	vac-alu-50
Adju-Phos® adjuvant	Aluminum phosphate gel	vac-phos-250
Quil-A® adjuvant	Saponon vaccine adjuvant	vac-quil
CFA	Complete Freund's adjuvant	vac-cfa-10
IFA	Incomplete Freund's adjuvant	vac-ifa-10
c-di-GMP VacciGrade™	STING agonist	vac-nacdg
Flagellin FliC VacciGrade™	TLR5 agonist	vac-fla
Imiquimod VacciGrade™	TLR7 agonist	vac-imq
ODN 1585 VacciGrade™	murine TLR9 agonist	vac-1585-1
ODN 1826 VacciGrade™	murine TLR9 agonist	vac-1826-1
ODN 2395 VacciGrade™	human/murine TLR9 agonist	vac-2395-1
ODN 2006 VacciGrade™	human TLR9 agonist	vac-2006-1
Pam3CSK4 VacciGrade™	TLR2 agonist	vac-pms
Poly(I:C) (HMW) VacciGrade™	TLR3 agonist	vac-pic
R848 VacciGrade™	TLR7/8 agonist	vac-r848
TDB VacciGrade™	Mincle agonist	vac-tdb
Conjugatable PRRs		
STG-982	conjugatable STING agonist	vac-stg982
STG-968	conjugatable STING agonist	vac-stg968
TL7-887	conjugatable TLR7 agonist	vac-tl7887
TL7-975	conjugatable TLR7 agonist	vac-tl7975
OVA Antigen		
EndoFit™ Ovalbumin	For *in vivo* use; endotoxin level <1EU/mg	vac-pova