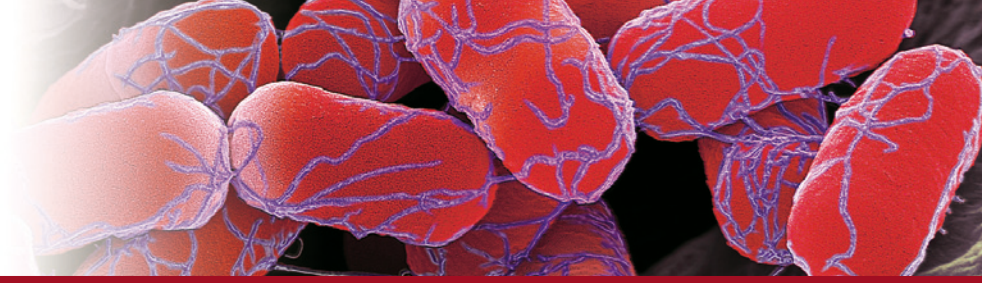
AdipoGen®
LIFE SCIENCES



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Innate Immunity

Focus Toll-like Receptor (TLR) Agonists

The innate immune system plays an essential role in the host's first line of defense against microbial invasion and involves the recognition of pathogen-associated molecular patterns **(PAMPs)** or endogenous danger signals through the sensing of danger-associated molecular patterns **(DAMPs)** by pattern recognition receptors (PRRs). Activation of PRRs triggers cell signaling leading to the production of proinflammatory cytokines, chemokines and type 1 interferons, the induction of antimicrobial and inflammatory responses, pyroptotic cell death and the recruitment of phagocytic cells. These innate responses are responsible for efficient destruction and clearance of invading pathogens and other molecular threats and instructing the development of an appropriate pathogen-specific adaptive immune response.

The innate immune system comprises several classes of PRRs that allow the early detection of pathogens at the site of infection. The membrane-bound **Toll-like receptors (TLRs)** and **C-type lectin receptors (CLRs)** detect PAMPs in extracellular milieu and endosomal compartments. TLRs and CLRs cooperate with PRRs sensing the presence of cytosolic nucleic acids, like RNA-sensing **RIG-I (retinoic acid-inducible gene I)-like receptors** (RLRs; RLHs) or the DNA-sensing AIM2. Another set of intracellular sensing PRRs are the **NOD-like receptors** (NLRs; nucleotide-binding domain leucine-rich repeat containing receptors), which not only recognize PAMPs but also DAMPs. Upon stress (including infections and metabolic deregulation), certain NLRs form high molecular weight complexes called **inflammasomes.** These complexes and the self-degrading process autophagy play central roles in controlling innate and adaptive immunity.

Toll-like receptors (TLRs)

Toll-like receptors (TLRs) are a family of evolutionally conserved pattern recognition receptors (PRRs) expressed by a variety of cell types, particularly those of the innate immune system. TLRs are type I membrane glycoproteins, characterized by a cytoplasmic TIR (Toll/interleukin-1 receptor (IL- 1R)) domain and a leucine-rich repeat domain. They are capable of detecting exogenous **PAMPs** such as lipopolysaccharide (LPS), lipopeptides, flagellin, bacterial DNA and viral dsRNA, as well as endogenous, host-derived DAMPs, including HMGB1 and β-defensins.

The activation of TLR signaling pathways results in the production and release of various cytokines and chemokines. TLRs play a crucial role in host defence and inflammation and are implicated in the pathogenesis of immune diseases and cancer. TLR agonists are being tested as vaccines, enhancing tumor immunity by targeting immune checkpoints or inducing the expansion of T cells by potent adjuvants. Therefore, TLR agonists can activate both the innate and adaptive immune systems, play an important role in antiviral and antitumor immunity and are exploited as potent adjuvants to enhance tumor immunity.

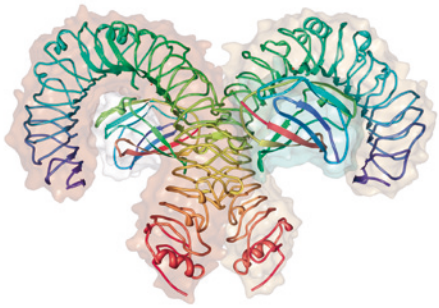


FIGURE: TLR4/MD2 complex.

SELECTED REVIEW ARTICLES

Toll-like receptors: Activation, signalling and transcriptional modulation: D. De Nardo; Cytokine **74,** 181 (2015) • Characterization of innate immune signalings stimulated by ligands for pattern recognition receptors: T. Kameyama & A. Takaoka; Methods Mol. Biol. **1142,** 19 (2014) • Newly described pattern recognition receptors team up against intracellular pathogens: P. Broz & D.M. Monack; Nat. Rev. Immunol. **13,** 551 (2013) • Toll-like receptor signaling: K.H. Lim & L.M. Staudt; Cold Spring Harb. Perspect. Biol. **5,** a011247 (2013) • Adjuvants for immunotherapy: O. Pfaar, et al.; Curr. Opin. Allergy Clin. Immunol. **12,** 648 (2012) • Pharmacology and therapeutic potential of pattern recognition receptors: M.J. Paul-Clark, et al.; Pharmacol. Ther. **135,** 200 (2012)

See Page 2 for Content Overview

Angonists/Antagonists Overview & Highlights

TLR Receptors Agonists		See Page
TLR1/TLR2	Pam_3Cys-Ser-$(Lys)_4$	2
TLR3	Poly(I:C)	2
TLR4/CD14	R-form (mutant) LPS	4–5
	S-form (wild-type) LPS	4–5
	MPLA [Monophosphorylated Lipid A]	4–5
	Lipid A (Diphosphorylated)	4–5
	*Mega*Vax™ & TLR4 Agonist Arrays	8
	Synthetic MPLA	2
	Kdo2-Lipid A (Re)	2
TLR5	Flagellin	3
TLR6/TLR2	FSL-1, (R)-FSL-1	3
TLR7	Gardiquimod, Imiquimod, Loxoribine	3
TLR7/8	R-848	3
TLR9	CpG ODNs	6
TLR11	Flagellin	3
TLR11/12	Profilin	2
Nod-like Receptor Activators/Inducers		

See
Inflammasome Signaling Brochure

RIG-I-like Receptors & Cytosolic DNA Sensor Agonists		
MDA5	Poly(I:C)	2
STING	cyclic-GMP-AMP (cGAMP)	7
TLR4 and TLR9 Antagonists		
Small Molecule TLR4/CD14 Antagonists	IAXO Compounds (synthetic) IAXO-101 IAXO-102, IAXO-103	3
Unique iODNs	iODN (Class I-IV)	7

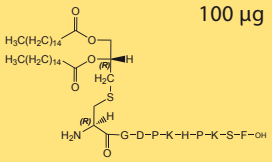
NLRC3 – Negative Regulator of Innate Immunity		
	anti-NLRC3 (mouse), mAb (Eowyn-1)	7

FSL-1 – The MALP-2 Alternative

TLR6/TLR2 Agonists

(R)-FSL-1
AG-CP3-0010 — 100 µg

Formula: $C_{84}H_{140}N_{14}O_{18}S$
MW: 1666.2
CAS: 322455-70-9 (R/S)



Potent stimulator of TLR2/TLR6. The naturally occurring R-stereoisomer is biologically more active than the S-stereoisomer.

FSL-1
AG-CP3-0009 — 100 µg

TLR1/2 Complex Agonist

Pam_3Cys-Ser-$(Lys)_4$. 3HCl
AG-CP3-0003 — 2 mg

TLR3/MDA5 Agonist

Poly(I:C) (Endotoxin-free) (sterile)
IAX-200-021 — 2 mg | 5 mg | 10 mg

TLR4 Agonists (synthetic)

Kdo2-Lipid A (ready-to-use)
AG-CU1-0001 — 1 mg

MPLA (synthetic) Sterile Solution
AG-CU1-0002 — 100 µg

TLR11/TLR12 Agonist

Profilin (*Toxoplasma gondii*) (rec.)
AG-40B-0121 — 10 µg | 3 x 10 µg

Mincle Agonist – Cord Factor [TDM]

Trehalose 6,6'-dimycolate Endotoxin-free (sterile)
IAX-200-101 — 1 mg

LATEST INSIGHT

New PAMP discovered

R.G. Gaudet, et al. (2015) recently demonstrated that mammalian cells can detect and respond to the Gram-negative bacteria-derived monosaccharide heptose-1,7-bisphosphate (HBP). Detection of HBP within the host cytosol activated the NF-κB pathway *in vitro* and induced innate and adaptive immune responses *in vivo*. The activation triggered by HBP was mediated by phosphorylation-dependent oligomerization of the TRAF-interacting protein with forkhead-associated domain (TIFA).

LIT: Cytosolic detection of the bacterial metabolite HBP activates TIFA-dependent innate immunity: R.G. Gaudet, et al.; Science **348,** 1251 (2015)

AdipoGen® LIFE SCIENCES

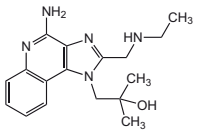
APPLICATIONS: FACS: Flow Cytometry; **FUNC:** Functional Application; **ICC:** Immunocytochemistry; **IHC:** Immunohistochemistry **IP:** Immunoprecipitation; **WB:** Western blot

FORMULATION: PF = Preservative free
SPECIES: Hu = Human; **Ms** = Mouse; **Rt** = Rat; **Rb** = Rabbit; **Prm** = Primate

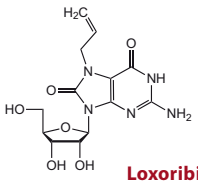
TLR7/TLR8 Agonists & NLRP3 Activator

Toll-like receptor 7 (TLR7) and TLR8 play an important role in the immune response to viral infection. They recognize single stranded RNAs as their natural ligand and also small synthetic molecules such as imidazoquinolines* and nucleoside** analogs.

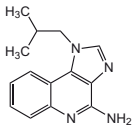
PRODUCT NAME	PID	SIZE
TLR7 Agonists		
Gardiquimod *	AG-CR1-3583	5 mg | 25 mg
Imiquimod *	AG-CR1-3569	100 mg | 250 mg
Loxoribine **	AG-CR1-3584	5 mg | 25 mg
TLR7/8 Agonist & NLRP3 Activator		
R-848 *	AG-CR1-3582	5 mg | 25 mg



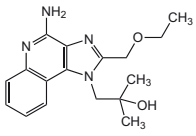
Gardiquimod



Loxoribine



Imiquimod



R-848

THE SOURCE

TLR5/TLR11/NLRC4 Agonist – Flagellin

Toll-like receptor 5 (TLR5) recognizes **flagellin** from both Gram-positive and Gram-negative bacteria. Activation of the receptor stimulates the production of proinflammatory cytokines, such as TNF-α, through signaling via the adapter proteins MyD88, TIRAP and TRIF. Flagellin is the subunit protein which polymerizes to form the filaments of bacterial flagella. It activates the innate immune system not only through the TLR5, but also through the intracellular NAIP5/NLRC4 (IPAF) inflammasome protein.

AdipoGen Life Sciences offers different types of **low endotoxin** and **high purity flagellins,** including pathway specific mutants. The Flagellin (NLRC4 Mutant) (rec.) (Prod. No. AG-40B-0126) is only detected by TLR5 not by NLRC4, whereas the Flagellin (TLR5 Mutant) (rec.) (Prod. No. AG-40B-0127) is only detectd by NLRC4.

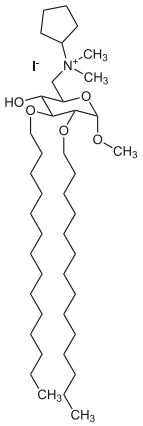
PRODUCT NAME	PID	SIZE
Flagellin	AG-40B-0095	100 µg
Flagellin (high purity)	AG-40B-0025	10 µg | 3 x 10 µg
Flagellin (rec.)	AG-40B-0125	10 µg | 3 x 10 µg
NEW **Flagellin (NLRC4 Mutant) (rec.)**	AG-40B-0126	10 µg | 3 x 10 µg
NEW **Flagellin (TLR5 Mutant) (rec.)**	AG-40B-0127	10 µg | 3 x 10 µg

UNIQUE

IAXO Compounds – Inhibitors of Sterile Inflammation

The novel IAXO compounds are synthetic TLR4/CD14 ligands with TLR4 modulating activities *in vitro* and conferring protection against TLR4/CD14-mediated tissue damage and inflammation *in vivo* [1-3]. IAXOs are useful to explore CD14- dependent and TLR4-independent pathways and TLR4 activation by endogenous ligands (e.g. hyaluronic acid oligosaccharides, oxLDL, HMGB1) in sterile inflammation. IAXO compounds have been shown to inhibit neuropathic pain [1], secondary necrosis of acute drug-induced liver failure [2] and vascular inflammation and abdominal aortic aneurysm [3] by blocking non-hematopoietic TLR4 signaling. They are useful tools, where inhibition of sterile (auto-) inflammation is desired, without compromising TLR4's key role in the defense of pathogens.

LIT: [1] I. Bettoni, et al.; Glia **56,** 1312 (2008) • **[2]** N. Shah, et al.; Gut **61,** A28 (2012) • **[3]** C. Huggins, et al.; Atherosclerosis **241,** e53 (2015)



PRODUCT NAME	PID	SIZE
IAXO-101 (CD14/TLR4 Antagonist) (synthetic)	IAX-600-001	1 mg | 5 mg
IAXO-102 (CD14/TLR4 Antagonist) (synthetic)	IAX-600-002	1 mg | 5 mg
IAXO-103 (CD14/TLR4 Antagonist) (synthetic)	IAX-600-003	1 mg | 5 mg
IAXO-201 (Control for IAXO-102)	IAX-600-004	1 mg
IAXO-202 (Control for IAXO-101/IAXO-103)	IAX-600-005	1 mg

TLR4 Agonists

Innate Immunity to Life

LPS, Lipid A, MPLA & IAXO Compounds

Bacterial lipopolysaccharide (LPS) is the major structural component of the outer wall of all Gram-negative bacteria and a potent activator of the immune system. Activation of cells by LPS is mediated via extracellular receptor Toll-like receptor 4 (TLR4) followed by intracellular recognition and activation of caspase-11 (caspase-4/5 in humans). For optimal interaction with LPS, TLR4 requires association with myeloid differentiation protein 2 (MD2). According to current consensus activation of TLR4 is preceded by the transfer of LPS to membrane-bound (m) or soluble (s) CD14 by LPS-binding protein (LBP). R-form LPS and lipid A, but not S-form LPS, are capable of inducing TNF-α responses also in the absence of CD14. LPS, synthesized by most wild-type (WT) Gram-negative bacteria (S-form LPS), consists of three regions, the O-polysaccharide chain, which is made up of repeating oligosaccharide units, the core oligosaccharide and the lipid A, which harbors the endotoxic activity of the entire molecule. R-form LPS synthesized by the so-called rough (R) mutants of Gram-negative bacteria lacks the O-specific chain. The core-oligosaccharide may be present in different degrees of completion, depending on the class (Ra to Re) to which the mutant belongs. LPS are amphipathic molecules whose hydrophobicity decreases with increasing length of the sugar part. Based upon these differences, S- and R-form LPS show marked differences in the kinetics of their blood clearance and cellular uptake as well as in the ability to induce oxidative burst in human granulocytes and to activate the host complement system. **S-form LPS is the prefered *in vivo* TLR4 agonist, whereas R-form LPS can activate TLR4 on a variety of cells *in vitro*, which do not express CD14 or where the cell culture medium does not contain sufficient quantities of soluble CD14 or LBP.**

LIT: CD14 is required for MyD88-independent LPS signaling: Z. Jiang, et al.; Nat. Immunol. **6**, 565 (2005) • R-form LPS, the master key to the activation ofTLR4/MD-2-positive cells: M. Huber, et al.; Eur. J. Immunol. **36**, 701 (2006)

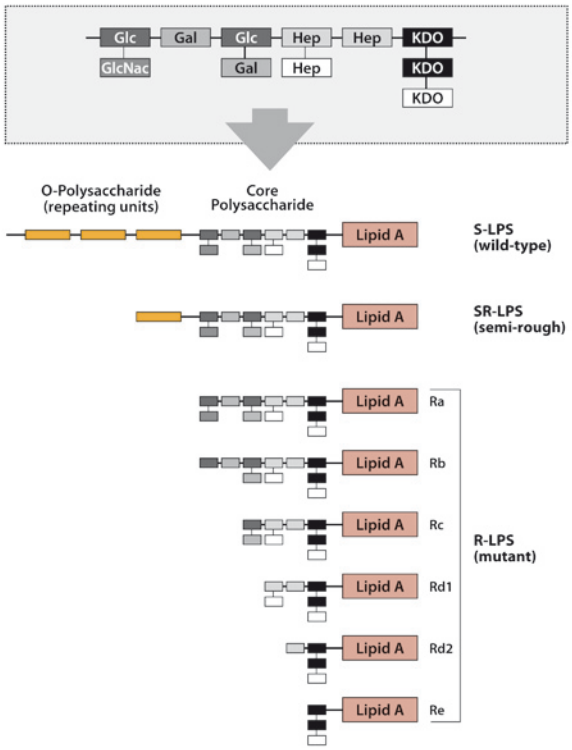


FIGURE: Schematic representation of the different LPS chemotypes: GlcNAc = N-Acetylglucosamine; Glc = Glucose; Gal = Galactose; Hep = Heptose; KDO = 2-Keto-3-desoxyoctonate. Adapted from M. Huber, et al.; Eur. J. Immunol. **36**, 701 (2006).

TLR*pure*™ LPS from Innaxon

The TLR4/LPS Experts – Highest Quality

- **TLR*pure*™: Qualified Purity & Activity**
- **High potency TLR4-specific ligands**
- **Ultrapure (no detectable protein, RNA & DNA)**
- **Tested on TLR4 KO murine macrophages**
- **Standardized aqueous sterile solutions or powder form**
- **BULK available for *in vivo* studies**
- **Excellent lot-to-lot reproducibility**
- **Broadest LPS chemotype and serotype selection**

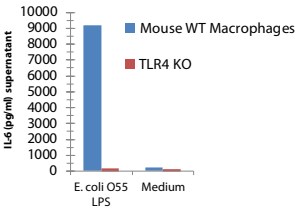


FIGURE: Macrophages from wild-type (WT) TLR4 expressing or TLR4 deficient (TLR4 KO) mice were stimulated ith 1µg/ml TLR*pure*™ E. coli O55:B5 S-(smooth) LPS (Prod. No. IAX-100-013). Cell culture supernatants were analysed by ELISA for IL-6 after 24h.

TLR4 Agonist Explorer Sets™

UNIQUE

PRODUCT NAME	PID	SIZE
TLR4 Agonist (Salmonella) Explorer Set™ I TLR*pure*™ (S-LPS, R-LPS, MPLA)	IAX-300-001	1 Set
TLR4 Agonist (Salmonella) Explorer Set™ II TLR*pure*™ (S-LPS, R-LPS, Lipid A, MPLA)	IAX-300-002	1 Set
TLR4 Agonist (E. coli) Explorer Set™ I TLR*pure*™ (S-LPS, R-LPS, MPLA)	IAX-300-003	1 Set
TLR4 Agonist (E. coli) Explorer Set™ II TLR*pure*™ (S-LPS, R-LPS, Lipid A, MPLA)	IAX-300-004	1 Set

AdipoGen® LIFE SCIENCES

APPLICATIONS: FACS: Flow Cytometry; **FUNC:** Functional Application; **ICC:** Immunocytochemistry; **IHC:** Immunohistochemistry **IP:** Immunoprecipitation; **WB:** Western blot

FORMULATION: PF = Preservative free
SPECIES: Hu = Human; **Ms** = Mouse; **Rt** = Rat; **Rb** = Rabbit; **Prm** = Primate

Natural & Biosynthetic TLR4 Agonists

PRODUCT NAME	PID	SIZE
S-form LPS		
LPS from E. coli O8:K27 (S-form) TLR*pure*™ Sterile Solution	IAX-100-006	500 µg | 1 mg | 5 x 1 mg
LPS from E. coli O111:B4 (S-form) TLR*pure*™ Sterile Solution	IAX-100-012	500 µg | 1 mg | 5 x 1 mg
LPS from E. coli O55:B5 (S-form) TLR*pure*™ Sterile Solution	IAX-100-013	500 µg | 1 mg | 5 x 1 mg
LPS (Universal) from S. abortus equi (S-form) TLR*pure*™ Sterile Solution	IAX-100-009	500 µg | 1 mg | 5 x 1 mg
LPS from S. enteritidis (S-form) TLR*pure*™ Sterile Solution	IAX-100-019	500 µg | 1 mg | 5 x 1 mg
LPS from S. minnesota (S-form) TLR*pure*™ Sterile Solution	IAX-100-020	500 µg | 1 mg | 5 x 1 mg
LPS from S. typhimurium (S-form) TLR*pure*™ Sterile Solution	IAX-100-011	500 µg | 1 mg | 5 x 1 mg
R-form LPS		
LPS from E. coli EH100 (Ra) TLR*pure*™ Sterile Solution	IAX-100-010	500 µg | 1 mg | 5 x 1 mg
LPS from E. coli J5 (Rc) TLR*pure*™ Sterile Solution	IAX-100-014	500 µg | 1 mg | 5 x 1 mg
THE STANDARD LPS from E. coli R515 (Re) TLR*pure*™ Sterile Solution	IAX-100-007	500 µg | 1 mg | 5 x 1 mg
THE STANDARD LPS from S. minnesota R595 (Re) TLR*pure*™ Sterile Solution	IAX-100-008	500 µg | 1 mg | 5 x 1 mg
LPS from S. minnesota R345 (Rb) TLR*pure*™ Sterile Solution	IAX-100-015	500 µg | 1 mg | 5 x 1 mg
LPS from S. minnesota R60 (Ra) TLR*pure*™ Sterile Solution	IAX-100-016	500 µg | 1 mg
LPS from S. minnesota R5 (Rc) TLR*pure*™ Sterile Solution	IAX-100-017	500 µg | 1 mg | 5 x 1 mg
LPS from S. minnesota R7 (Rd1) TLR*pure*™ Sterile Solution	IAX-100-018	500 µg | 1 mg | 5 x 1 mg
LPS from S. minnesota R3 (Rd2) TLR*pure*™ Sterile Solution	IAX-100-021	500 µg | 1 mg | 5 x 1 mg
Lipid A und MPLA		
Lipid A from E. coli R515 (Re) TLR*pure*™ Sterile Solution	IAX-100-004	250 µg | 500 µg | 1 mg
NEW Lipid A from E. coli R515 (Re) TLR*pure*™ Powder	IAX-100-004DF	1 mg | 5 mg
Lipid A from S. minnesota R595 (Re) TLR*pure*™ Sterile Solution	IAX-100-001	250 µg | 500 µg | 1 mg
NEW Lipid A from S. minnesota R595 (Re) TLR*pure*™ Powder	IAX-100-001DF	1 mg | 5 mg
MPLA from E. coli R515 (Re) TLR*pure*™ Sterile Solution	IAX-100-003	250 µg | 500 µg | 1 mg
NEW MPLA from E. coli R515 (Re) TLR*pure*™ Powder	IAX-100-003DF	1 mg | 5 mg
MPLA from S. minnesota R595 (Re) TLR*pure*™ Sterile Solution	IAX-100-002	250 µg | 500 µg | 1 mg
NEW MPLA from S. minnesota R595 (Re) TLR*pure*™ Powder	IAX-100-002DF	1 mg | 5 mg

TECHNICAL NOTE

Contaminations in TLR Ligands

Specific recognition of different PAMPs by TLRs revealed that only the purest ligands, free of any other immuno-stimulatory contamination, allow to successfully elucidate the role of each TLR. While LPS was thought to not only activate TLR4 but also TLR2, repurification of commercial preparations of both *E. coli* and *Salmonella minnesota* LPS showed that this LPS no longer induces cellular activation through TLR2 [1]. Furthermore it has been shown that purified peptidoglycans activate Nod1 and do not involve TLR2 or TLR4 [2]. Synthetic CpG ODNs (contaminated with LPS) show different activation of certain immune cell subsets even when highly purified.

LIT : [1] Repurification of lipopolysaccharide eliminates signalling through both human and murine toll-like receptor 2: M. Hirschfeld, et al.; J. Immunol. **165,** 618 (2000) • **[2]** Toll-like receptor 2-dependent bacterial sensing does not occur via peptidoglycan recognition: L. H. Travassos, et al.; EMBO Rep. **5,** 1000 (2004)

innaxon

offers endotoxin-free and sterile buffers to avoid contaminations upon solubilization of powder form ligands!

PRODUCT NAME	PID	SIZE
PBS Endotoxin-free (sterile)	IAX-900-001	1.5 ml | 10 ml | 3 x 10 ml
ddWater Endotoxin-free (sterile)	IAX-900-002	1.5 ml | 10 ml | 3 x 10 ml
Physiological Saline [Sodium Chloride 0.9%] Sterile Solution	IAX-900-003	1.5 ml | 10 ml | 3 x 10 ml

TLR9 Agonists – Unmethylated CpG Dinucleotides [ODNs]

Unmethylated CpG dinucleotides within particular sequence contexts are responsible for the immunostimulatory activity of bacterial DNA. Synthetic oligonucleotides (ODN), that contain such CpG motifs (CpG ODNs), mimic microbial DNA and are detected by Toll-like receptor 9 (TLR9).

Endotoxin-free & Sterile ODNs from Innaxon

- **TLR*pure*™: Qualified Purity & Activity**
- **Endotoxin-free and sterile**
- **Potent TLR9 ligands**
- **Tested on TLR9 KO murine macrophages**
- **BULK available for *in vivo* studies (pre-clinical grade)**
- **ddWater Endotoxin-free (sterile) included**

Stimulatory ODNs (CpG ODNs)

Different types of CpG ODNs were identified based on their biological effects on different cell types: **ODN Type A** is a potent inducer of IFN-α in human PDC, leading to antigen presenting cell (APC) maturation, whereas **ODN Type B** is a weak inducer of IFN-α but rather stimulates IL-8 production and increasing costimulatory and Ag-presenting molecules and triggers proliferation of B cells and IL-6 production. A third type of CpG ODN, termed **ODN Type C**, shows high induction of INF-α in PDC and activation of B cells.

PRODUCT NAME	PID	SIZE
THE STANDARD **ODN 1668 (Type B) Endotoxin-free (sterile)**	IAX-200-001	100 µg | 1 mg | 3 x 1 mg
THE STANDARD **ODN 1826 (Type B) Endotoxin-free (sterile)**	IAX-200-002	100 µg | 1 mg | 3 x 1 mg
THE STANDARD **ODN 2216 (Type A) Endotoxin-free (sterile)**	IAX-200-005	100 µg | 1 mg | 3 x 1 mg
ODN 1585 (Type A) Endotoxin-free (sterile)	IAX-200-003	100 µg | 1 mg | 3 x 1 mg
ODN M362 (Type C) Endotoxin-free (sterile)	IAX-200-004	100 µg | 1 mg
ODN 2006 (Type B) Endotoxin-free (sterile)	IAX-200-006	100 µg | 1 mg | 3 x 1 mg
ODN 2395 (Type C) Endotoxin-free (sterile)	IAX-200-007	100 µg | 1 mg | 3 x 1 mg

TLR9 Agonist Explorer Sets™

UNIQUE

PRODUCT NAME	PID	SIZE
TLR9 Agonist (human) Explorer Set™ Endotoxin-free (CpG ODN Type A, B and C)	IAX-300-007	1 Set
TLR9 Agonist (mouse) Explorer Set™ Endotoxin-free (CpG ODN Type A, B and C)	IAX-300-008	1 Set

Control ODNs (GpC ODNs)

Inactive control compounds for CpG ODNs do not stimulate TLR9. They are composed of same sequence as their stimulatory counterparts, but instead of CpG they contain GpC dinucleotides.

PRODUCT NAME	PID	SIZE
ODN 1720 (Control for ODN 1668) Endotoxin-free (sterile)	IAX-200-200	100 µg
ODN 1982 (Control for ODN 1826) Endotoxin-free (sterile)	IAX-200-201	100 µg
Neutral-ODN (Control for iODNs) Endotoxin-free (sterile)	IAX-200-202	100 µg | 1 mg | 3 x 1 mg
ODN 2118 (Control for ODN 1585) Endotoxin-free (sterile)	IAX-200-203	100 µg
ODN M383 (Control for ODN M362) Endotoxin-free (sterile)	IAX-200-204	100 µg
ODN 2243 (Control for ODN 2216) Endotoxin-free (sterile)	IAX-200-205	100 µg
ODN 2137 (Control for ODN 2006) Endotoxin-free (sterile)	IAX-200-206	100 µg

APPLICATIONS: FACS: Flow Cytometry; **FUNC:** Functional Application; **ICC:** Immunocytochemistry; **IHC:** Immunohistochemistry **IP:** Immunoprecipitation; **WB:** Western blot

FORMULATION: PF = Preservative free

SPECIES: Hu = Human; **Ms** = Mouse; **Rt** = Rat; **Rb** = Rabbit; **Prm** = Primate

TLR9 Antagonists — Inhibitory ODNs (iODNs)

In recent years several groups have studied the sequence requirements, specificity, signaling pathways and kinetics of the Toll-like receptor 9 (TLR9) suppression by inhibitory oligonucleotide motifs, which led to a class of novel inhibitory oligonucleotides (iODNs). Subsequently it has been discovered that telomeric DNA repeats $(TTAGGG)_n$, can block immune activation by CpG-ODNs. Consequently, a classification for iODNs has been proposed.

Class I: G-stretch ODNs: TLR9-specific competitors, some iODNs may also affect TLR7 and TLR8 signaling.
Class II: ODNs with telomeric repeats: TLR-independent inhibitors of STAT signaling (cellular uptake via an "ODN receptor"?)
Class III: Inhibitors of DNA uptake in a sequence independent manner.
Class IV: Long phosphorothioate ODNs as direct competitors of TLR9 signaling in a sequence independent manner.

LIT: Immunotherapeutic utility of stimulatory and suppressive oligodeoxynucleotides: K.J. Ishii, et al.; Curr. Opin. Mol. Ther. **6,** 166 (2004) • Inhibitory oligodeoxynucleotides - therapeutic promise for systemic autoimmune diseases?: P. Lenert; Clin. Exp. Immunol. **140,** 1 (2005) • DNA motifs suppressing TLR9 responses: A. Trieu, et al.; Crit. Rev. Immunol. **26,** 527 (2006)

iODNs — Potent Inhibitors of TLR9 Signaling

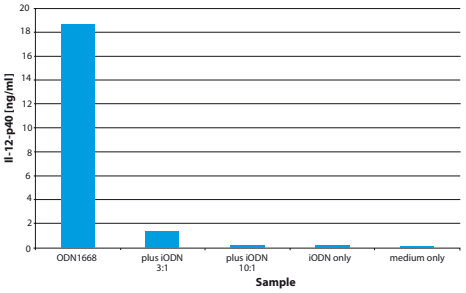


FIGURE: ODN 1668 (Prod. No. IAX-200-001) was added at 50pM/ml to macrophages in a 96-well plate simultaneously together with iODN 2088 (Prod. No. IAX-200-050) at the indicated molar excess, cell supernatants harvested after 24 hours and IL-12-p40 analyzed by cytokine ELISA.

PRODUCT NAME	PID	SIZE
iODN (inhibitory ODN) 2088 Endotoxin-free (sterile)	IAX-200-050	100 µg | 1 mg | 3 x 1 mg
iODN (inhibitory ODN) $(ttaggg)_4$ Endotoxin-free (sterile)	IAX-200-051	100 µg | 1 mg | 3 x 1 mg
G-type iODN (inhibitory ODN) Endotoxin-free (sterile)	IAX-200-052	100 µg | 1 mg
***Mini*-iODN (inhibitory ODN) Endotoxin-free (sterile)**	IAX-200-053	100 µg | 1 mg
***Mega*-iODN (inhibitory ODN) Endotoxin-free (sterile)**	IAX-200-054	100 µg | 1 mg
***Duo*-iODN (inhibitory ODN) Endotoxin-free (sterile)**	IAX-200-055	100 µg | 1 mg

▸ All ODNs include 1 vial of ddWater Endotoxin-free (sterile) (IAX-900-002).

innaxon iODN Explorer Sets™

UNIQUE

PRODUCT NAME	PID	SIZE
iODN (inhibitory ODN) Explorer Set™ I Endotoxin-free (4 class I iODNs + Control ODN)	IAX-300-005	1 Set
iODN (inhibitory ODN) Explorer Set™ II Endotoxin-free (6 class I / II iODNs + Control ODN)	IAX-300-006	1 Set

NEW

cGAMP & NLRC3 STING-dependent Innate Immune Activation

cGAMP synthase (cGAS) is the latest candidate for the cytosolic DNA sensor that induces interferons by producing **the second messenger cGAMP,** which may activate STING and IRF3.

LIT: STING and the innate immune response to nucleic acids in the cytosol: D.L. Burdette & R.E. Vance; Nat. Immunol. **14,** 19 (2013)

PRODUCT NAME	PID	SIZE
cGAMP . 2Na (STING Ligand)	AG-CR1-3588	100 µg | 500 µg

NLRC3 belongs to the NLR family of cytosolic pathogen recognition receptors. NLRC3 is expressed in T lymphocytes and may be involved in suppression of T cell activation. NLRC3 is a cytoplasmic protein that negatively regulates pro-IL-1β expression and inhibits toll-like receptor (TLR)-dependent activation of the transcription factor NF-κB. NLRC3 also reduces STING-dependent innate immune activation in response to cytosolic DNA, cyclic di-GMP (c-di-GMP) and DNA viruses.

PRODUCT NAME	PID	SIZE	ISOTYPE	SPECIES	APPLICATIION
anti-NLRC3 (mouse), mAb (Eowyn-1)	AG-20B-0067	100 µg	Mouse IgG1	Ms	WB

NEW

*Mega*Vax™ BULK TLR4 Agonists for *In Vivo* Studies

PRODUCT NAME	PID	SIZE
***Mega*VAX™ Lipid A from Salmonella Powder**	IAX-550-001	5 mg | 10 mg | 20 mg
***Mega*VAX™ MPLA from Salmonella Powder**	IAX-550-002	5 mg | 10 mg | 20 mg
***Mega*VAX™ MPLA from E. coli Powder**	IAX-550-003	5 mg | 10 mg | 20 mg
***Mega*VAX™ Lipid A from E. coli Powder**	IAX-550-004	5 mg | 10 mg | 20 mg
***Mega*VAX™ LPS from Salmonella Powder**	IAX-550-005	5 mg | 10 mg | 25 mg | 50 mg
***Mega*VAX™ LPS from E. coli Powder**	IAX-550-006	5 mg | 10 mg | 25 mg | 50 mg

TLR4 Agonist Arrays

PRODUCT NAME	PID	SIZE
LPS On-The-Plate™ (Sterile)	IAX-500-001	1 Plate (12 x 8 Tests)
Lipid A On-The-Plate™ (Sterile)	IAX-500-002	1 Plate (12 x 8 Tests)
MPLA On-The-Plate™ (Sterile)	IAX-500-003	1 Plate (12 x 8 Tests)
MPLA (synthetic) 96-well Plate (Sterile)	AG-44T-0001	1 Plate (12 x 8 Tests)
Kdo2-Lipid A 96-well Plate (Sterile)	AG-44T-0002	1 Plate (12 x 8 Tests)

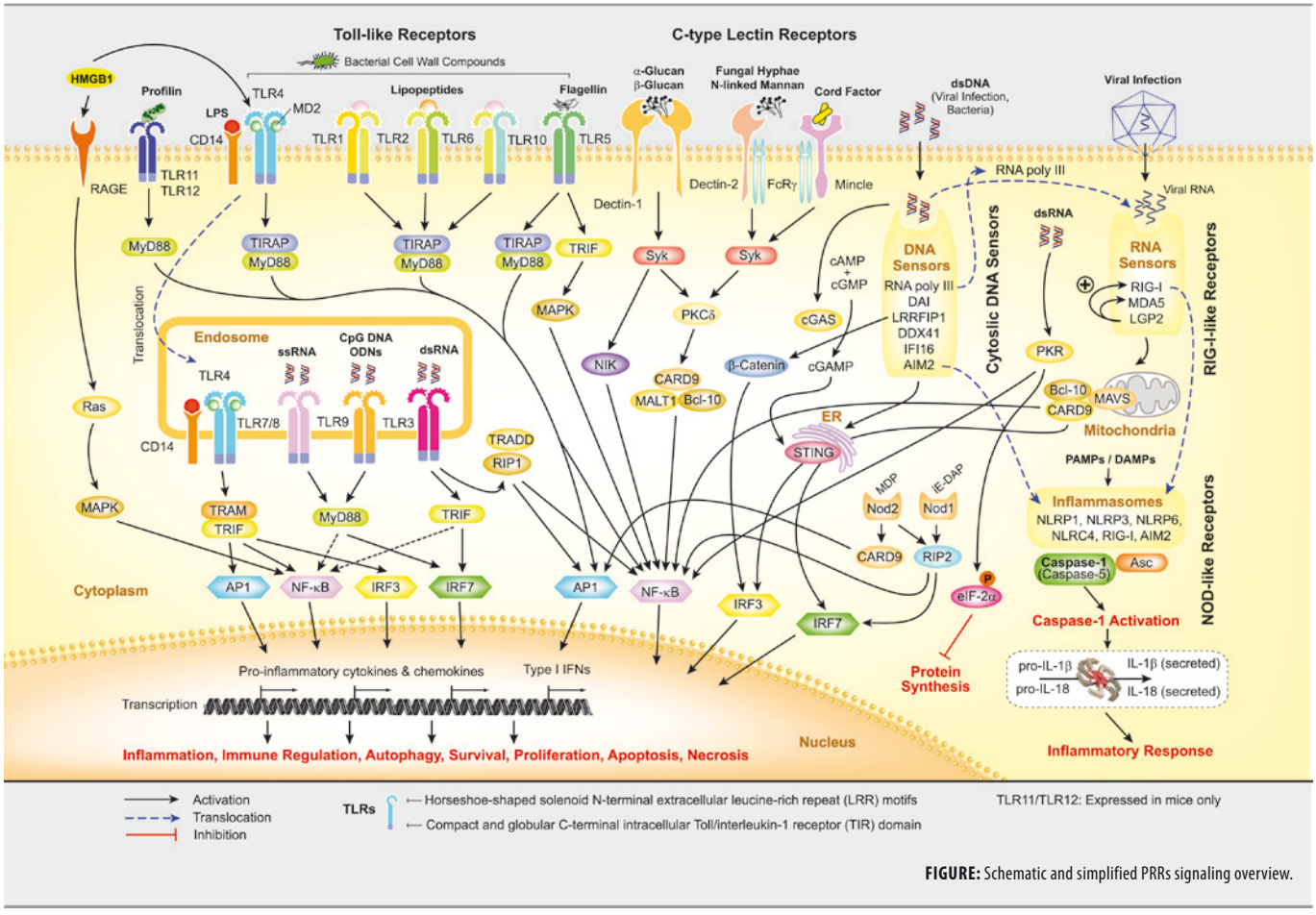


FIGURE: Schematic and simplified PRRs signaling overview.

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