



INVIVOGEN'S PRODUCTS FOCUS

STING LIGANDS

InvivoGen 社は、天然・合成環状ジヌクレオチド (CDN) やキサンテノン誘導体を含む幅広い STING リガンドのコレクションを提供しています。これらのアゴニストは、STING に直接結合して TBK1 を介した IRF3 を活性化し、I 型インターフェロンを産生させます。炎症誘発性サイトカインも、下流の STING 活性化で産生されます。



www.invivogen.com/cyclic-dinucleotide

PRODUCTS SUMMARY

NATURAL STING AGONIST

Mammalian CDN

- 2'3'-cGAMP **BEST #1**
- 2'3'-cGAMP VacciGrade™

Bacterial CDN

- 3'3'-cGAMP **BEST #2**
- c-di-AMP
- c-di-AMP VacciGrade™
- c-di-GMP
- c-di-GMP VacciGrade™

SYNTHETIC STING AGONIST

cGAMP-derived CDN

- 2'3'-cGAM(PS)2 (Rp/Sp)
- 3'3'-cGAMP Fluorinated

cAIMP-derived CDN

- cAIMP (CL592)
- cAIMP Difluor (CL614)
- cAIM(PS)2 Difluor (Rp/Sp) (CL656) **RECOMMENDED!**

c-di-AMP-derived CDN

- c-di-AMP Fluorinated
- 2'3'-c-di-AM(PS)2 (Rp,Rp) (Identical to ADU-S100) **HOT!**
- 2'3'-c-di-AM(PS)2 (Rp,Rp) VacciGrade™

c-di-GMP-derived CDN

- c-di-GMP Fluorinated

Xanthene analog (non-CDN)

- DMXAA **HOT!**

PRODUCT FEATURES

CDN

2'3'-cGAMP **BEST #1**

- InvivoGen 社の STING アゴニストでは売り上げ No.1
- 文献で最も多く引用されている STING アゴニスト
- 哺乳類細胞から産生された天然 CDN で、(3',5')(3',5') ホスホジエステル結合を保有
- 細菌の CDN とは構造的に異なるので、「非カノニカル」
- STING への高い結合親和性を持つ強力なインターフェロン誘導因子
- さまざまな STING 変異体を幅広く活性化¹
- VacchiGrade™ は *in vivo* で使用可能

2'3'-cGAM(PS)2 (Rp/Sp)

- 2'3'-cGAMP の合成ビス - ホスホリチオエート類似体 (Rp, Sp 異性体)
- 2'3'-cGAM(PS)2 (Rp/Sp) を提供できるのは InvivoGen 社だけ
- ホスホリチオエート修飾により、2'3'-cGAMP2 よりも高い安定性と効力を実現
- 細菌や哺乳類の他の CDN に対する応答が弱い STING H232 変異体を活性化 (図 1)

3'3'-cGAMP **BEST #2**

- 細菌により産生された天然 CDN で、「カノニカル」な (3',5')(3',5') 結合を保有
- 2'3'-cGAMP と比較して、STING 結合親和性は低いが、インターフェロン誘導応答は同等

3'3'-cGAMP Fluorinated

- 3'3'-cGAMP Fluorinated を提供できるのは InvivoGen 社だけ
- 3'3'-cGAMP よりもインターフェロン - β 誘導を大幅に増強 (THP-1 Dual 細胞を使用) (図 2)
- 細菌や哺乳類の他の CDN に対する応答が弱い STING H232 変異体の活性化が可能 (図 1)

cAIMP (CL592)

- 3'3'-cGAMP の合成類似体 ; アデニン / イノシンで構成されたヌクレオチド
- InvivoGen 社が特許所有
- 2'3'-cGAMP と同等の効力 (THP-1 Dual 細胞を使用) (図 3)

cAIMP Difluor (CL614)

- 3'3'-cGAMP の合成類似体 ; cAIMP のジフルオロ化誘導体
- InvivoGen 社が特許所有
- ジフルオロ化修飾により効力が増強 (THP-1 Dual 細胞を使用) (図 3)

cAIM(PS)2 Difluor (Rp/Sp) (CL656) **RECOMMENDED!**

- 3'3'-cGAMP の合成類似体、cAIMP のビス - ホスホロチオエートおよびジフルオロ化誘導体
- InvivoGen 社が特許所有
- ホスホロチオエート修飾により、酵素的切断に対する抵抗性が向上
- ジフルオロ化修飾により安定性が向上
- 2'3'-cGAMP と比較して有意に高い効力 (THP-1 Dual 細胞を使用) (図 3)

c-di-AMP

- 細菌により産生された天然 CDN で、「カノニカル」な (3',5')(3',5') 結合を保有
- 細菌の生理機能の調節に重要
- VacciGrade™ は *in vivo* で使用可能

c-di-AMP Fluorinated

- c-di-AMP Fluorinated を提供できるのは InvivoGen 社だけ
- c-di-AMP よりもインターフェロン- β 誘導を大幅に増強 (THP-1 Dual 細胞を使用) (図 2)

2'3'-c-di-AM(PS)2 (Rp,Rp) (Identical to ADU-S100) **HOT!**

- 2'3'-c-di-AMP のビス - ホスホロチオエート類似体 (Rp,Rp 異性体)
- ヒトおよびマウスの既知の STING 対立遺伝子全てに対する強力な活性化因子
- 臨床的に重要な ADU-S100/MIW815 (開発元: Aduro/Novartis) と構造的に同一
- VacciGrade™ は *in vivo* で使用可能

c-di-GMP

- 細菌により産生された天然 CDN で、「カノニカル」な (3',5')(3',5') 結合を保有
- 細菌において最も優勢な細胞内シグナル伝達中間体; 細菌の生理機能の調節に重要
- c-di-AMP と比較して高い STING 結合親和性
- VacciGrade™ は *in vivo* で使用可能

c-di-GMP Fluorinated

- c-di-GMP Fluorinated を提供できるのは InvivoGen 社だけ
- c-di-GMP よりもインターフェロン- β 誘導を大幅に増強 (図 2)

XANTHENONE ANALOG

DMXAA (also known as Vadimezan or ASA404)

- マウス特異的な合成 STING アゴニスト
- インターフェロン- β の強力な誘導因子
- もとは腫瘍血管破壊剤として同定され、マウスで有望な抗腫瘍活性を示したが、第 III 相臨床試験で不合格^{3,4}
- ヒト (h)STING 変異体 A162 の CDN 結合部位の S162A 点突然変異により、DMXAA に感受性化⁵

STING variants differentially respond to CDN

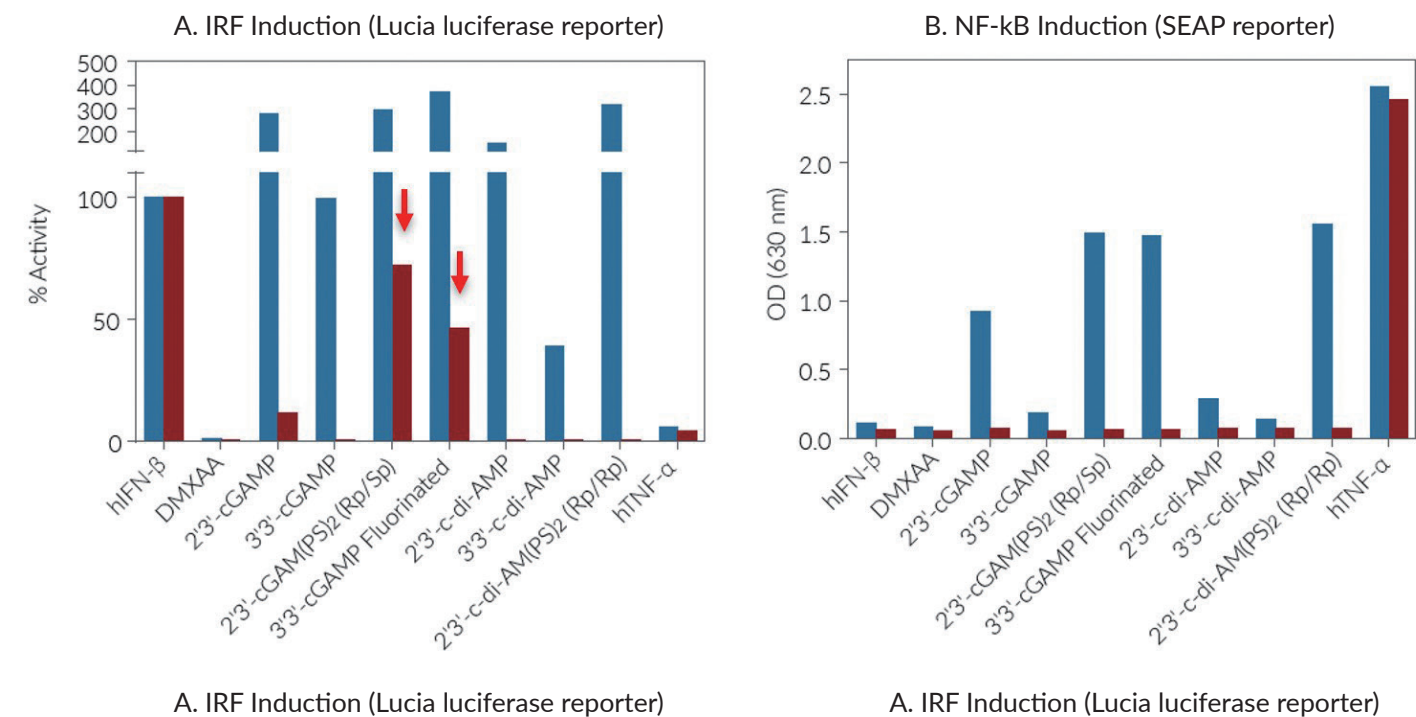


Fig 1: The IRF pathway (A) and NF- κ B pathway (B) induction in THP1-Dual™ KI-hSTING-H232 cells in response to the STING ligands CDNs has been assessed after 24h incubation. In contrast to THP1-Dual™ KI-hSTING-R232 cells expressing the “wild-type” R232 human STING variant, THP1-Dual™ KI-hSTING-H232 cells do not respond to bacterial CDNs such as 3'3'-cGAMP and display only a weak IRF induction in response to mammalian CDNs such as 2'3'-cGAMP, while 3'3'-cGAMP Fluorinated or 2'3'-cGAMP(PS)₂ (Rp/Sp) induce a moderate IRF induction (red arrows). In THP1-Dual™ KI-hSTING-H232 cells, no NF- κ B induction was observed following a 24-hour incubation with various CDNs.

IFN induction improved by fluorinated modification

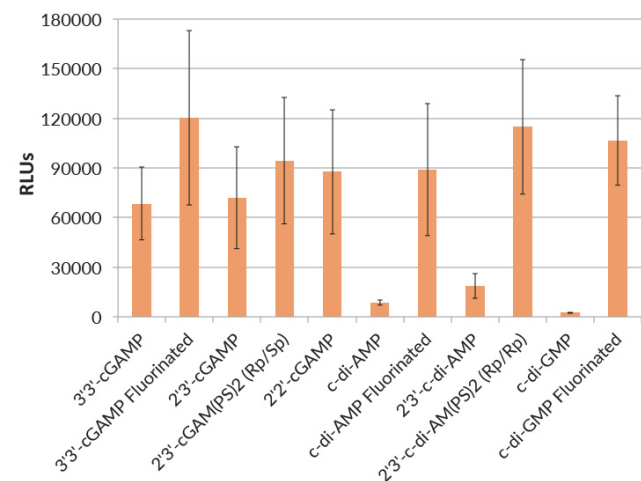


Fig 2: Induction of the interferon regulatory factor (IRF) pathway by various STING ligands in THP1-Dual™ cells. Cells were stimulated for 24 hours with the STING ligands as shown (all at 10 μ g/ml) and assessed IRF induction by measuring the relative light units (RLUs) in a luminometer using QUANTI-Luc™.

IFN induction improved by modification with cAIMPs

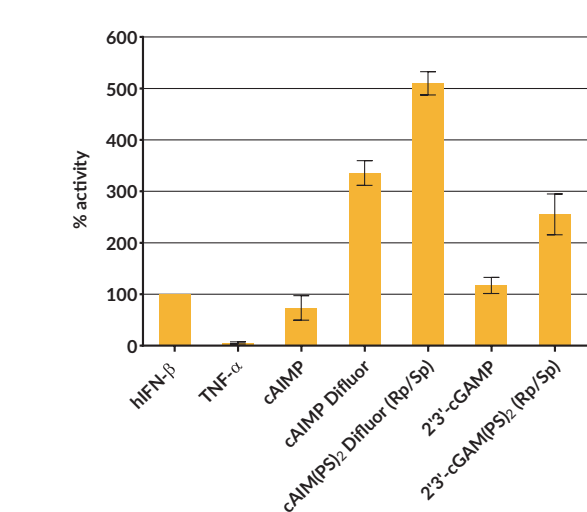


Fig 3: Induction of the interferon regulatory factor (IRF) pathway by various STING ligands in THP1-Dual™ cells. Cells were stimulated for 24 hours with CDN at 10 μ g/ml. IRF induction was determined by measuring the relative light units (RLUs) in a luminometer using QUANTI-Luc™.

EXAMPLES OF APPLICATION

STING アゴニストは、さまざまな意味合いを持つ研究試薬として利用されてきました。自然免疫応答の誘導に加えて、その他の DNA センサーや RNA センサー、オートファジー、ER ストレス、アポトーシスなどのシグナル伝達経路に関与しています。STING アゴニストは、抗腫瘍性と免疫原性を備えているため、新規のクラス免疫療法剤やアジュバントにもなっています。ここでは、細菌感染やウイルス感染、自己免疫、がん、ワクチン接種の各研究に関連する応用例をいくつか紹介します。

Microbial infection

- 2'3'-cGAMP を使用して、*in vitro* で STING 媒介性抗ウイルス応答を抑制する SARS-CoV-2 の薬剤候補をスクリーニング^{6,7}
- 2'3'-cGAMP、3'3'-cGAMP、および c-di-GMP を使用して、STING 媒介性 I 型インターフェロン応答を阻害する結核菌 (*M. tuberculosis*) の酵素作用を研究⁸
- 3'3'-cGAMP、c-di-AMP、および c-di-GMP を使用して、肺炎レンサ球菌 (*S. pneumoniae*) 感染させた老齢マウスにおける STING 媒介性インターフェロン- β 産生のための BMDM を刺激⁹
- 2'3'-cGAM(PS)2 (Rp/Sp) を使用して、マウスモデルでの HSV-2 を治療¹⁰

Autoimmunity

- 2'3'-cGAMP、c-di-AMP を使用して、全身性エリテマトーデス (SLE) 血清によって駆動される I 型インターフェロン産生カスケードにおける STING 経路の役割を研究¹¹
- PBMC および線維芽細胞の刺激に 3'3'-cGAMP を使用して、乳児発症 STING 関連血管炎 (SAVI) 症候群患者の遺伝子発現の研究を実施¹²
- マウス B 細胞の刺激に DMXAA を使用して、コラーゲン誘発関節炎モデルでの STING 媒介性 B 細胞死を検討¹³
- BMDM の刺激に 2'3'-cGAMP および DMXAA を使用して、Tollip 欠損による STING 媒介性インターフェロンシグナル伝達障害を研究¹⁴

Cancer

- *in vivo* および *in vitro* で PD-1 遮断とともに 2'3'-c-di-AM (PS) 2 (Rp, Rp) (ADU-S100) を使用して、卵巣がんに対するカルボプラチン化学療法の改善効果を評価¹⁵
- マウスモデルで cAIMP (CL592) を使用して、STING 経路を標的とした肝細胞がん治療の可能性を探索¹⁶
- BMDM および T 細胞の刺激に 2'3'-cGAMP、3'3'-cGAMP、2'3'-c-di-AM(PS)2 (Rp,Rp) (ADU-S100)、DMXAA を使用して、STING のインターフェロン非依存的な活性の探索と、STING 媒介性の T 細胞死の研究を実施¹⁷
- ATP とともに BMDM の刺激に 2'3'-cGAMP および DMXAA を使用して、STING 活性化における腫瘍由来 cGAMP の促進における細胞外 ATP の役割を検討¹⁸
- 2'2'-cGAMP、2'3'-cGAMP、3'3'-cGAMP を使用して、悪性 B 細胞のアポトーシス誘導に対する STING 活性化の影響を検討¹⁹
- 3'3'-cGAMP の腹腔内注射により、マウスにおける悪性 B 細胞を標的とした直接効果を検討¹⁹
- 2'3'-cGAMP と DMXAA は、CAR-T 細胞の持続性を促進し、腫瘍抑制を増強するとの報告あり²⁰
- DMXAA を抗 CD47 抗体と併用することにより、腫瘍免疫療法を促進²¹

Vaccination

- 2'3'-cGAMP を使用して、ヘリコバクターピロリ (*H. pylori*) ワクチンの鼻腔内、皮下、および筋肉内経路でのマウス接種におけるアジュバント効果を評価²²
- OVA とともに 2'3'-cGAMP を筋肉内注射することにより、抗原特異的 T 細胞を活性化、および抗体産生を促進²³
- 粘膜アジュバントとして 2'3'-cGAMP を使用して、マウスにおける全粒子不活化 H7N9 ワクチンの液性、細胞性、および粘膜性免疫応答を増強²⁴
- 2'3'-cGAMP を使用して、大腸がん治療および肝転移の抑制を目的としたがんワクチンにおけるアジュバント効果を評価²⁵
- 3'3'-cGAMP は、炭疽毒素に対する Th1/Th2/Th17 舌下免疫応答を促進²⁶
- 組換えタンパク質とともに粘膜アジュバントとして c-di-AMP を使用して、ブルセラ症(呼吸器感染症)に対する免疫をマウスに付与²⁷
- c-di-GMP を使用して、マウス B16 黒色腫に対するペプチドワクチンの免疫原性および抗腫瘍効果を増強²⁸
- OVA とともに c-di-GMP を使用して、マウスにおける Th1/Th2/Th17 応答を促進²⁹
- 2'3'-cGAM(PS)2 (Rp/Sp) は、HSV-21010 予防のアジュバント候補であるとする報告あり
- 2'3'-c-di-AM(PS)2 (Rp,Rp) (ADU-S100 と同一) を使用して、B16 黒色腫担持マウスにおける免疫原性および抗腫瘍効果を増強³⁰

Check out InvivoGen's Infocus Newsletter to learn more about STING

InvivoGen
infocus

TABLE OF CONTENTS

- Introduction
- STING activity
- STING-specific inhibitors
- STING regulation
- Genetic variation in STING
- Therapeutic targeting of STING
- Conclusion

InvivoGen
2015-2016
The InvivoGen Infocus Newsletter
is available at www.invivogen.com/infocus

Use STING, the InvivoGen Center
for Research and Development
at www.invivogen.com/sting

Follow the path to STING

STING (Stimulator of Interferon Genes) has become a focal point in immunology research as well as a target in drug discovery. As a signaling hub in innate immunity, STING is a pattern recognition receptor (PRR) of pericellular lipopeptides in endoplasmic reticulum (ER) and cytoplasm. InvivoGen offers a growing variety of products to help you explore STING, its signaling partners, cytokine induction activity and therapeutic potential.

Introduction

Entry of self or foreign nucleic acids into the cytoplasm can signal various problems, including pathogen infection or tissue damage, mitochondrial or nuclear damage, and the presence of tumors. Until the discovery of STING in 2006, detection of nucleic acids in the cytoplasm was thought to be the domain of the innate immune system. However, STING has been largely ignored by the immune system. In 2013, a study of STING activity in the nucleus and its role in the regulation of type I interferon (IFN) responses and the control of cancer via iNOS/IFN- γ was presented to be an essential molecule which integrates signaling between signaling of both the ER and cytoplasmic STING (cSTING) and its downstream signaling pathway. STING is a novel sensor of cytosolic nucleic acids, which is involved in the regulation of innate immunity. In this review, we discuss the role of STING in the regulation of innate immunity and its potential as a therapeutic target.

InvivoGen STING

InvivoGen offers a growing variety of products to help you explore STING, its signaling partners, cytokine induction activity and therapeutic potential.

STING activity

STING is a pattern recognition receptor (PRR) of pericellular lipopeptides in endoplasmic reticulum (ER) and cytoplasm. InvivoGen offers a growing variety of products to help you explore STING, its signaling partners, cytokine induction activity and therapeutic potential.

STING-specific inhibitors

STING is a pattern recognition receptor (PRR) of pericellular lipopeptides in endoplasmic reticulum (ER) and cytoplasm. InvivoGen offers a growing variety of products to help you explore STING, its signaling partners, cytokine induction activity and therapeutic potential.

STING regulation

STING is a pattern recognition receptor (PRR) of pericellular lipopeptides in endoplasmic reticulum (ER) and cytoplasm. InvivoGen offers a growing variety of products to help you explore STING, its signaling partners, cytokine induction activity and therapeutic potential.

Genetic variation in STING

STING is a pattern recognition receptor (PRR) of pericellular lipopeptides in endoplasmic reticulum (ER) and cytoplasm. InvivoGen offers a growing variety of products to help you explore STING, its signaling partners, cytokine induction activity and therapeutic potential.

Therapeutic targeting of STING

STING is a pattern recognition receptor (PRR) of pericellular lipopeptides in endoplasmic reticulum (ER) and cytoplasm. InvivoGen offers a growing variety of products to help you explore STING, its signaling partners, cytokine induction activity and therapeutic potential.

Conclusion

STING is a pattern recognition receptor (PRR) of pericellular lipopeptides in endoplasmic reticulum (ER) and cytoplasm. InvivoGen offers a growing variety of products to help you explore STING, its signaling partners, cytokine induction activity and therapeutic potential.

Figure 1: The STING signaling pathway

Visit

<https://www.invivogen.com/sting-products>
for product details



PRODUCTS

STING Ligands

PRODUCT	DESCRIPTION	QTY	CAT. CODE
Natural CDNs			
2'3'-cGAMP	Cyclic [G(2',5')pA(3',5')p]	200 µg 500 µg 1 mg 5 mg	tlrl-nacga23-02 tlrl-nacga23 tlrl-nacga23-1 tlrl-nacga23-5
2'3'-cGAMP VacciGrade™	Preclinical grade of 2'3'-cGAMP	1 mg	vac-nacga23
3'3'-cGAMP	Cyclic [G(3',5')pA(3',5')p]	500 µg 1 mg 5x 0.5 mg	tlrl-nacga tlrl-nacga-1 tlrl-nacga-2.5
c-di-AMP	Cyclic diadenylate monophosphate	1 mg 5 x 1 mg	tlrl-nacda tlrl-nacda-5
c-di-AMP VacciGrade™	Preclinical grade of c-di-AMP	1 mg	vac-nacda
c-di-GMP	Cyclic diguanylate monophosphate	1 mg 5 x 1 mg	tlrl-nacdg tlrl-nacdg-5
c-di-GMP VacciGrade™	Preclinical grade of c-di-GMP	1 mg	vac-nacdg
cGAMP-derived CDNs			
2'3'-cGAM(PS)2 (Rp/Sp)	Bisphosphorothioate analog of 2'3'-cGAMP, Rp,Sp-isomers	250 µg	tlrl-nacga2srs
3'3'-cGAMP Fluorinated	Difluoro 3'3'-cGAMP	2 x 100 µg	tlrl-nacgaf-2
c-di-AMP-derived CDNs			
c-di-AMP Fluorinated	Difluoro 3'3'-c-di-AMP	2 x 100 µg	tlrl-nacdaf-2
2'3'-c-di-AM(PS)2 (Rp,Rp) (Identical to ADU-S100)	Bisphosphorothioate analog of 2'3'-c-di-AMP, Rp isomers	100 µg 500 µg	tlrl-nacda2r-01 tlrl-nacda2r
2'3'-c-di-AM(PS)2 (Rp,Rp) VacciGrade™	Preclinical grade of 2'3'-c-di-AM(PS)2 (Rp,Rp)	500 µg	vac-nacda2r
c-di-GMP-derived CDNs			
c-di-GMP Fluorinated	Difluoro 3'3'-c-di-GMP	2 x 100 µg	tlrl-nacdgf-2
cAIM-derived CDNs			
cAIMP (CL592)	Cyclic (adenine monophosphate- inosine monophosphate)	500 µg	tlrl-nacai
cAIMP Difluor (CL614)	cAIMP difluorinated	250 µg	tlrl-nacaidf
cAIM(PS)2 Difluor (Rp/Sp) (CL656)	cAIMP bisphosphorothioate and difluorinated, Rp,Sp-isomers	2 x 100 µg	tlrl-nacairs-2
Non-CDN			
DMXAA	Murine STING ligand - Xanthenone Analog	5 mg	tlrl-dmx

Reporter cell lines related to cGAS/STING signaling

PRODUCT	DESCRIPTION	QTY	CAT. CODE
THP-1 monocytes			
THP1-Dual™ Cells	NF-κB-SEAP and IRF-Lucia reporter cells	3-7 x 10 ⁶ cells	thpd-nfis
THP1-Dual™ KO-STING Cells	STING knockout NF-κB-SEAP and IRF-Lucia reporter cells	3-7 x 10 ⁶ cells	thpd-kostg
THP1-Dual™ KO-cGAS Cells	cGAS knockout NF-κB-SEAP and IRF-Lucia reporter cells	3-7 x 10 ⁶ cells	thpd-kocgas
THP1-Dual™ KO-IFI16 cells	IFI16 knockout NF-κB-SEAP and IRF-Lucia reporter cells	3-7 x 10 ⁶ cells	thpd-koif16
THP1-Dual™ KO-IRF3 Cells	IRF3 knockout NF-κB-SEAP and IRF-Lucia reporter cells	3-7 x 10 ⁶ cells	thpd-koirf3
THP1-Dual™ KO-TBK1 Cells	TBK1 knockout NF-κB-SEAP and IRF-Lucia reporter cells	3-7 x 10 ⁶ cells	thpd-kotbk
THP1-Dual™ KO-TREX1 Cells	TREX1 knockout NF-κB-SEAP and IRF-Lucia reporter cells	3-7 x 10 ⁶ cells	thpd-kotrex
THP1-Dual™ KI-hSTING-S154 Cells	NF-κB-SEAP and IRF-Lucia reporter S154 human STING knockin cells	3-7 x 10 ⁶ cells	thpd-s154
THP1-Dual™ KI-hSTING-M155 Cells	NF-κB-SEAP and IRF-Lucia reporter M155 human STING knockin cells	3-7 x 10 ⁶ cells	thpd-m155
THP1-Dual™ KI-hSTING-A162 Cells	NF-κB-SEAP and IRF-Lucia reporter A162 human STING knockin cells	3-7 x 10 ⁶ cells	thpd-a162
THP1-Dual™ KI-hSTING-H232 Cells	STING (H232 isoform) knockin NF-κB-SEAP and IRF-Lucia Reporter Cells	3-7 x 10 ⁶ cells	thpd-h232
THP1-Dual™ KI-hSTING-R232 Cells	STING (R232 isoform) knockin NF-κB-SEAP and IRF-Lucia reporter cells	3-7 x 10 ⁶ cells	thpd-r232
THP1-Dual™ KI-mSTING Cells	Murine STING knockin NF-κB-SEAP and IRF-Lucia reporter cells	3-7 x 10 ⁶ cells	thpd-mstg
293T			
293-Dual™ hSTING-A162 Cells	Dual IRF and IFN-β reporter 293 cells expressing A162 isoform of human STING (S162A)	3-7 x 10 ⁶ cells	293d-a162
293-Dual™ hSTING-H232 Cells	Dual IRF and IFN-β reporter 293 cells expressing H232 isoform of human STING (R232H)	3-7 x 10 ⁶ cells	293d-h232
293-Dual™ hSTING-R232 Cells	Dual IRF and IFN-β reporter 293 cells expressing R232 isoform of human STING	3-7 x 10 ⁶ cells	293d-r232
293-Dual™ mSTING Cells	Dual IRF and IFN-β reporter 293 cells expressing murine STING	3-7 x 10 ⁶ cells	293d-mstg
293-Dual™ Null Cells	Dual IRF and IFN-β reporter 293 cells	3-7 x 10 ⁶ cells	293d-null
HEK 293			
HEK-Blue™ ISG Cells	IRF-inducible SEAP reporter cells	3-7 x 10 ⁶ cells	hkb-isg
HEK-Blue™ ISG-KO-STING Cells	STING knockout IRF-SEAP reporter cells	3-7 x 10 ⁶ cells	hkb-kostg
HEK-Blue™ STAT6-hSTING-R232 Cells	Human STING (R232 variant)-dependent STAT6 HEK293 reporter cells	3-7 x 10 ⁶ cells	hkb-st6r232
Murine B16 melanocytes			
B16-Blue™ ISG Cells	IRF-inducible SEAP reporter cells	3-7 x 10 ⁶ cells	bb-ifnabg
B16-Blue™ ISG-KO-STING Cells	STING knockout IRF-SEAP reporter cells	3-7 x 10 ⁶ cells	bb-kostg
Murine RAW 264.7 macrophages			
RAW-Lucia™ ISG Cells	IRF-Lucia reporter cells	3-7 x 10 ⁶ cells	rawl-isg
RAW-Lucia™ ISG-KO-STING Cells	STING knockout IRF-Lucia reporter cells	3-7 x 10 ⁶ cells	rawl-kostg
RAW-Lucia™ ISG-KO-cGAS Cells	cGAS knockout IRF-Lucia reporter cells	3-7 x 10 ⁶ cells	rawl-kocgas
RAW-Lucia™ ISG-KO-IFI16 Cells	IFI16 knockout IRF-Lucia reporter cells	3-7 x 10 ⁶ cells	rawl-koif16
RAW-Lucia™ ISG-KO-IRF3 Cells	IRF3 knockout IRF-Lucia reporter cells	3-7 x 10 ⁶ cells	rawl-koirf3
RAW-Lucia™ ISG-KO-TBK1 Cells	TBK1 knockout IRF-Lucia reporter cells	3-7 x 10 ⁶ cells	rawl-kotbk
RAW-Lucia™ ISG-KO-TREX1 Cells	TREX1 knockout IRF-Lucia reporter cells	3-7 x 10 ⁶ cells	rawl-kotrex

Other ligands related to cGAS/STING signaling

PRODUCT	DESCRIPTION	QTY	CAT. CODE
dsDNA-EC	CDS & TLR9 Agonist - Double-stranded genomic DNA from E. coli K12	200 µg	tlrl-ecdna
G3-YSD	Y-form DNA - cGAS Agonist	200 µg	tlrl-ydna
HSV-60	CDS Agonist	200 µg	tlrl-hsv60n
HSV-60/LyoVec™	Complexed with LyoVec™	100 µg	tlrl-hsv60c
ISD	Interferon stimulatory DNA - CDS Agonist	200 µg	tlrl-isdn
ISD/LyoVec™	Complexed with LyoVec™	100 µg	tlrl-isdc
ODN TTAGGG (A151)	Suppressive oligonucleotide - human preferred cGAS, TLR9 and AIM2 Antagonist	200 µg 1 mg	tlrl-ttag151 tlrl-ttag151-1
Poly(dA:dT)	dsDNA naked - CDS, RIG-I Agonist and AIM2 Inducer	200 µg 1 mg	tlrl-patn tlrl-patn-1
Poly(dA:dT)/LyoVec™	Complexed with LyoVec™	100 µg	tlrl-patc
Poly(dA:dT) Rhodamine	Rhodamine labeled	10 µg	tlrl-patrh
Poly(dG:dC)	dsDNA naked - CDS Agonist	200 µg	tlrl-pgcn
Poly(dG:dC)/LyoVec™	Complexed with LyoVec™	100 µg	tlrl-pgcc
VACV-70	CDS Agonist	200 µg	tlrl-vav70n
VACV-70/LyoVec™	Complexed with LyoVec™	100 µg	tlrl-vav70c

Synthetic inhibitors of cGAS/STING pathway

PRODUCT	DESCRIPTION	QTY	CAT. CODE
BX795	TBK1/IKKε inhibitor	5 mg	tlrl-bx7
G140	Human cGAS inhibitor	2 mg	inh-g140
H-151	Synthetic Indole Derivative - STING Inhibitor	10 mg	inh-h151
RU.521	Murine cGAS inhibitor	2 mg	inh-ru521

Selective antibiotics

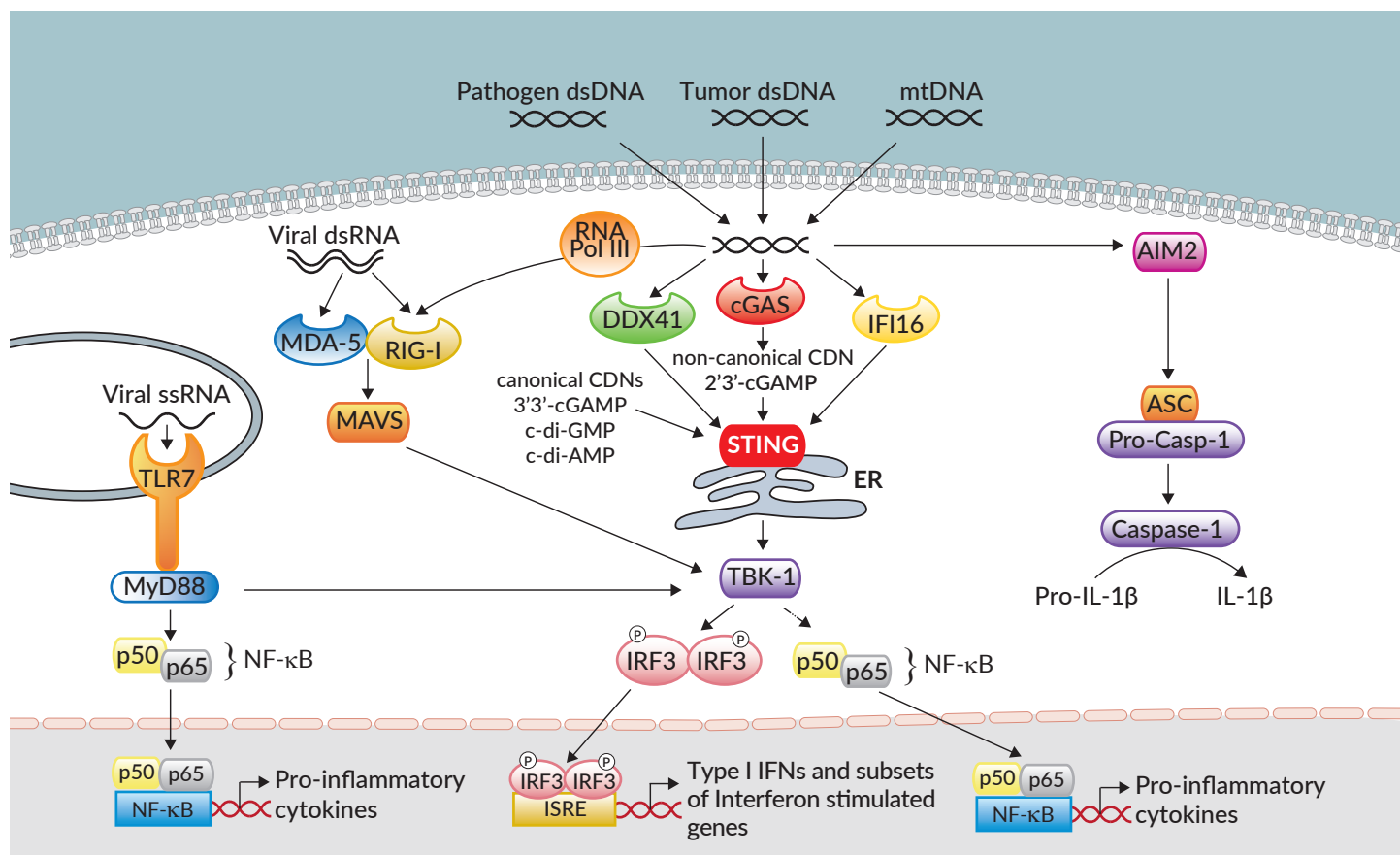
PRODUCT	DESCRIPTION	QTY	CAT. CODE
Blasticidin	Selective antibiotic for the bsr, bls, or BSD genes	100 mg (10 x 1 ml)	ant-bl-1
G418 (Geneticin)	Selective antibiotic for the neo gene	1 g (10 x 1 ml)	ant-gn-1
Hygromycin B Gold™	Selective antibiotic for the hph gene	1 g (10 x 1 ml)	ant-hg-1
Puromycin	Selective antibiotic for the pac gene	100 mg (10 x 1 ml)	ant-pr-1
Zeocin™	Selective antibiotic for the Sh ble gene	1 g (10 x 1 ml)	ant-zn-1

REFERENCES

1. Kranzusch, P.J. et al., 2015. Ancient origin of cGAS-STING reveals mechanism of universal 2', 3' cGAMP signaling. *Molecular cell*, 59(6), 891-903.
2. Li L. et al., 2014. Hydrolysis of 2'3'-cGAMP by ENPP1 and design of nonhydrolyzable analogs. *Nat Chem Biol*. 10(12):1043-8.
3. Conlon J. et al., 2013. Mouse, but not human STING, binds and signals in response to the vascular disrupting agent 5,6-dimethylxanthenone-4-acetic acid. *J Immunol*. 190(10):5216-25.
4. Kim S. et al., 2013. Anticancer Flavonoids Are Mouse-Selective STING Agonists. *ACS Chem Biol*. 8(7): 1396-1401.
5. Che X. et al., 2017. Single Mutations Reshape the Structural Correlation Network of the DMXAA-Human STING Complex. *J Phys Chem B*. 2017 Mar 9;121(9):2073-2082.
6. Olagnier, D.P. et al., 2020. Identification of SARS-CoV2-mediated suppression of NRF2 signaling reveals a potent antiviral and anti-inflammatory activity of 4-octyl-itaconate and dimethyl fumarate. [Pre-print]
7. Han, L. et al. 2020. SARS-CoV-2 ORF9b antagonizes type I and III interferons by targeting multiple components of RIG-I/MDA-5-MAVS, TLR3-TRIF, and cGAS-STING signaling pathways. *bioRxiv*.
8. Dey, R. et al., 2017. Inhibition of innate immune cytosolic surveillance by an M. tuberculosis phosphodiesterase. *Nat Chem Biol* 13, 210-217.
9. Mitzel, D.N. et al., 2014. Age-enhanced endoplasmic reticulum stress contributes to increased Atg9A inhibition of STING-mediated IFN- β production during *Streptococcus pneumoniae* infection. *The Journal of Immunology*, 192(9), 4273-4283.
10. Koubou, M.K. et al., 2018. STING agonists enable antiviral cross-talk between human cells and confer protection against genital herpes in mice. *PLoS pathogens*, 14(4), e1006976.
11. Kato, Y. et al., 2018. Apoptosis-derived membrane vesicles drive the cGAS-STING pathway and enhance type I IFN production in systemic lupus erythematosus. *Annals of the rheumatic diseases*, 77(10), 1507-1515.
12. Liu, Y. et al., 2014. Activated STING in a vascular and pulmonary syndrome. *New England Journal of Medicine*, 371(6), 507-518.
13. Tansakul, M. et al., 2020. Deficiency of STING Promotes Collagen-Specific Antibody Production and B Cell Survival in Collagen-Induced Arthritis. *Frontiers in Immunology*, 11, 1101.
14. Pokatayev, V. et al., 2020. Homeostatic regulation of STING protein at the resting state by stabilizer TOLLIP. *Nature immunology*, 21(2), 158-167.
15. Ghaffari, A. et al., 2018. STING agonist therapy in combination with PD-1 immune checkpoint blockade enhances response to carboplatin chemotherapy in high-grade serous ovarian cancer. *British journal of cancer*, 119(4), 440-449.
16. Thomsen, M.K. et al., 2020. The cGAS-STING pathway is a therapeutic target in a preclinical model of hepatocellular carcinoma. *Oncogene*, 39(8), 1652-1664.
17. Wu, J. et al., 2020. Interferon-independent activities of mammalian STING mediate antiviral response and tumor immune evasion. *Immunity*, 53(1), 115-126.
18. Zhou, Y. et al., 2020. Blockade of the phagocytic receptor MerTK on tumor-associated macrophages enhances P2X7R-dependent STING activation by tumor-derived cGAMP. *Immunity*, 52(2), 357-373.
19. Tang, C.H.A. et al., 2016. Agonist-mediated activation of STING induces apoptosis in malignant B cells. *Cancer research*, 76(8), 2137-2152.
20. Xu, N. et al., 2021. STING agonist promotes CAR T cell trafficking and persistence in breast cancer. *Journal of Experimental Medicine*, 218(2).
21. Shi, Y. et al., 2020. Intratumoral accumulation of gut microbiota facilitates CD47-based immunotherapy via STING signaling. *The Journal of experimental medicine*, 217(5), e20192282.
22. Chen, J. et al., 2020. Parenteral immunization with a cyclic guanosine monophosphate-adenosine monophosphate (cGAMP) adjuvanted *Helicobacter pylori* vaccine induces protective immunity against *H. pylori* infection in mice. *Human Vaccines & Immunotherapeutics*, 1-6.
23. Li, X.D. et al., 2013. Pivotal roles of cGAS-cGAMP signaling in antiviral defense and immune adjuvant effects. *Science*, 341(6152), 1390-1394.
24. Luo, J. et al., 2019. Enhancing immune response and heterosubtypic protection ability of inactivated H7N9 vaccine by using STING agonist as a mucosal adjuvant. *Frontiers in immunology*, 10, 2274.
25. Goodwin, T.J. & Huang, L., 2017. Investigation of phosphorylated adjuvants co-encapsulated with a model cancer peptide antigen for the treatment of colorectal cancer and liver metastasis. *Vaccine*, 35(19), 2550-2557.
26. Martin, T.L. et al., 2017. Sublingual targeting of STING with 3' 3'-cGAMP promotes systemic and mucosal immunity against anthrax toxins. *Vaccine*, 35(18), 2511-2519.
27. Muñoz González, F. et al., 2019. The BtaF adhesin is necessary for full virulence during respiratory infection by *Brucella suis* and is a novel immunogen for nasal vaccination against *Brucella* infection. *Frontiers in Immunology*, 10, 1775.
28. Wang, Z. & Celis, E., 2015. STING activator c-di-GMP enhances the anti-tumor effects of peptide vaccines in melanoma-bearing mice. *Cancer Immunology, Immunotherapy*, 64(8), 1057-1066.
29. Ebensen, T. et al., 2011. Bis-(3' 5')-cyclic dimeric adenosine monophosphate: strong Th1/Th2/Th17 promoting mucosal adjuvant. *Vaccine*, 29(32), 5210-5220.
30. Fu, J., et al., 2015. STING agonist formulated cancer vaccines can cure established tumors resistant to PD-1 blockade. *Sci Transl Med*. 7(283), 283ra52.

STING LIGANDS

INVIVOGEN'S PRODUCTS FOCUS



www.invivogen.com

ナカライテスク株式会社



URL

<https://www.nacalai.co.jp/>

価格・納期のご照会

0120-489-552

製品に関する技術的なご照会

<https://www.e-nacalai.jp/URL/?P=Contact>

※ 試験・研究用以外には使用しないでください。
※ 掲載内容は予告なく変更になる場合があります。