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INNATE IMMUNE SIGNALING: *cGAS/STING*

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cGAS and STING Nucleic Acid Sensors: Potential Therapeutic Targets in Innate Immunity and Oncology

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Innate immunity is a key pathway activated in response to bacterial and viral infections. The invasion of foreign nucleic acids results in the production of interferons and cytokines that comprise the host defense. More recently, roles for innate immunity in tumorigenesis, autoimmune disease, and senescence also have been elucidated. In these diseases, it is 'self' nucleic acids, RNA and DNA (including mitochondrial DNA), which escape into the cytosol and trigger immune responses. Two proteins, cyclic GMP-AMP synthase (cGAS) and stimulator of interferon genes (STING), are the key sensors of nucleic acids in the immunity pathway. Emerging data for the regulation of cGAS and STING suggests that under some conditions, such as autoimmune disease, inhibition of the pathway is desirable, while in the case of tumor immunity, stimulation of cytokine production is beneficial. This suggests cGAS and STING are potential therapeutic targets, though the details of activation or inhibition remain to be elucidated.[1-4]

Nucleic acids activate a number of cytosolic sensors, including retinoic acid-inducible gene I (RIG-I) and melanoma differentiation-associated protein 5 (MDA5) for RNA and absent in melanoma 2 (AIM2), DNA-dependent activator of interferon-regulatory factors (DAI), and interferon-γ-inducible protein 16 (IFI16) for DNA.[5] An unresolved issue in the immunity field, however, was that none of the DNA sensors completely accounted for interferon (IFN) production. This conundrum was solved in 2013 with the discovery of a new cytosolic DNA sensor, cGAS, and accumulating evidence now suggests cGAS is the primary sensor in innate immune activation.[6,7]

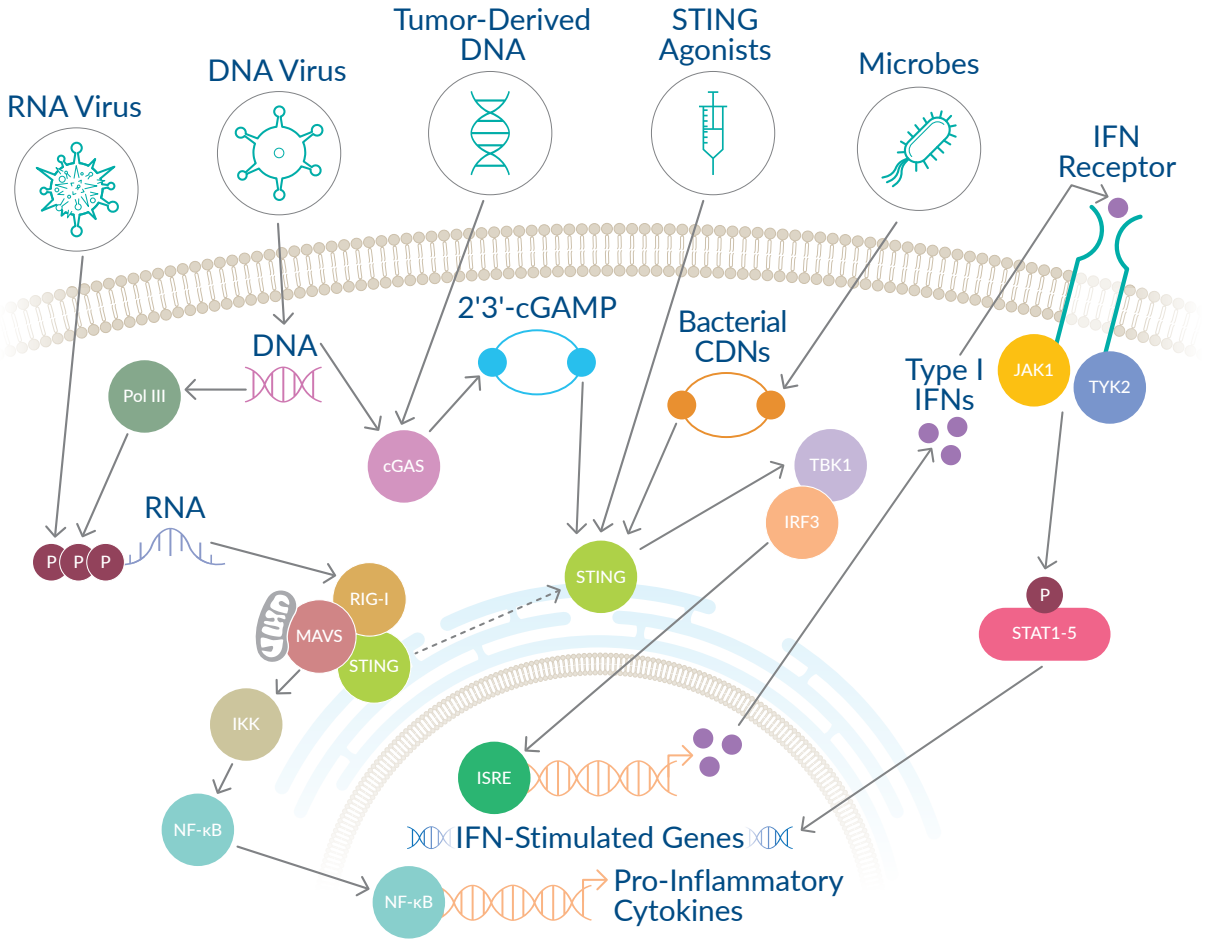

Figure 1. Cytosolic DNA and cyclic dinucleotides trigger the innate immune system through IFN production. Double-stranded DNA-bound cGAS produces the secondary messenger cGAMP that binds and activates STING resulting in the production of interferon (IFN).

Cytosolic cGAS binds double-stranded DNA and catalyzes the production of the novel second messenger 2′-3′-cyclic AMP-GMP (2′3′-cGAMP) from ATP and GTP. cGAMP binds to the ER-resident protein STING. The resulting conformational change in STING leads to the recruitment of the kinase TANK-binding kinase 1, IFN-inducible gene activation, and IFN production *via* IRF3 phosphorylation and nuclear translocation (**Figure 1**).

Studies comparing cyclic dinucleotide binding and STING activation identified genetic variants of human STING and important differences between human and mouse STING. The five human haplotypes are denoted WT (R232), REF (R232H), HAQ (R71H, G230A, R293Q), AQ (G230A, R293Q), and Q (R293Q).[8,9] Metazoan 2′3′-cGAMP contains G(2′5′)-pA(3′5′) phosphodiester linkages in contrast to bacterial cGAMP (3′3′-cGAMP), which contains G(3′5′)pA(3′5′) linkages. The R232H allele, which occurs in 14% of the population, responds to 2′3′-cGAMP, but responds weakly to bacterial cyclic dinucleotides. In contrast, STING-HAQ responds to both metazoan and bacterial cGAMPs and is found in 20% of the population. DMXAA (5,6-dimethylxanthenone-4-acetic acid, Vadimezan) is a small molecule that exhibits immune modulatory activities *via* induction of cytokines and shows efficacy in mouse tumor models.[10] This compound was taken into clinical trials in combination with paclitaxel and carboplatin but failed in the phase III trials.[11] Although mouse and human STING share high sequence identity, it was shown subsequently that DMXAA activates mouse but not human STING. Mutation at a single cyclic-dinucleotide binding site of human STING (S162A) allows DMXAA binding and restores sensitivity.[12]

> It will be important to develop sensitive tools suitable to measure cGAMP levels in human biological samples as well as potent inhibitors that can be used to clinically test whether modulation of cGAS activity affects disease outcomes.

Activation of cGAS and STING is important in host defense against pathogens, but uncontrolled activation of this pathway has been implicated in autoinflammatory disease including type I interferonopathies such as Aicardi-Goutières syndrome (AGS), a severe inflammatory disease, and systemic lupus erythematosus (SLE). Self-DNA that escapes into the cytosol is normally degraded by the primary mammalian exonuclease TREX1. TREX1 is one of seven human genes whose mutation causes AGS, and a small percentage of SLE patients have TREX1 mutations.[13,14] TREX1 knockout mice have elevated levels of dsDNA, elevated levels of cGAMP, and display multi-organ inflammation (especially myocarditis) leading to morbidity.[15,16] The double TREX1/cGAS knockout rescues the TREX1 phenotype, demonstrating a key role for cGAS stimulation in autoinflammation.[17] Elevated levels of cGAMP have been reported in a subset of SLE patients with a more severe disease phenotype (as shown by higher SLEDAI scores) compared to SLE patients in whom no cGAMP was detected.[18] In the case of STING, gain-of-function mutations result in the autoinflammatory disease SAVI (STING-associated vasculopathy with onset in infancy), characterized by interferonopathy, which causes skin lesions, interstitial lung disease, and systemic inflammation.[19]

In contrast to autoimmunity, in tumorigenesis the cGAS/STING pathway can be both stimulatory as well as inhibitory. Tumor-derived DNA is taken up by dendritic cells (DC) and activates cGAS/STING, resulting in type 1 IFN production and DC maturation. This innate immunity activation induces an adaptive immune response by stimulating $CD8^+$ T cell priming, resulting in a tumor antigen-specific T cell response to kill cancer cells. In a mouse melanoma model, PD-L1 antibody treatment resulted in increased levels of tumor-specific $CD8^+$ T cells in wild-type (WT) mice but not in cGAS knockout or mice which do not express STING ("golden ticket mice"). Likewise, tumor volume was decreased and survival was increased only in the WT mice, demonstrating the dependence on cGAS/STING. Direct intramuscular injection of cGAMP reduced tumor size in this and other mouse tumor models. The efficacy of DMXAA treatment in mouse tumor models has led to the discovery of stable cyclic dinucleotide STING agonists that activate human STING and show antitumor efficacy in colon, breast, and melanoma models.[20-22] The cancer vaccine STINGVAX that combines stable cyclic dinucleotide STING agonists with granulocyte-macrophage colony-stimulating factor (GM-CSF) is effective in multiple tumor models.[23] Clinical trials are ongoing to test the effect of STING agonists in patients with advanced/metastatic solid tumors or lymphomas (NCT02675439).

The complexity of the role of the cGAS/STING pathway in tumor immunity is increased by the observation that under some circumstances activation of this pathway promotes tumorigenesis. Mutagens such as 7,12-dimethylbenz(a) anthracene (DMBA) as well as cisplatin and etoposide induce nuclear DNA leakage, activation of cGAS and STING,

and the production of proinflammatory cytokines such as IL-1 and TNF-α. These cytokines stimulate phagocyte infiltration, resulting in an increased inflammatory response and tumor development. STING-deficient mice are resistant to DMBA-induced skin cancer, demonstrating the requirement for cGAS/STING activation.[24] In contrast, STING-deficient mice developed colonic tumors at an enhanced frequency compared to WT mice.[25] STING agonists induced indoleamine 2,3-dioxygenase (IDO) activity, an immune checkpoint that activates regulatory T cells and suppresses immunity, and promoted tumor growth in a Lewis lung carcinoma model.[26,27] These examples illustrate that there are many details yet to be uncovered in how cGAS/STING are controlled in the context of DNA sensing. It appears that the ability of innate immune pathways to modify tumorigenesis depends on multiple factors including acute or chronic DNA exposure, level of STING activation, tumor cell types and location, and the tumor microenvironment.

As the biological roles of cGAS and STING unfold, assessing their potential as therapeutic targets is a critical next step. The identification of activators and inhibitors is key to that process. As outlined above, considerable progress has been made in identifying STING agonists, including testing them clinically. In the case of cGAS, we at Pfizer and others have established cGAS assays utilizing purified cGAS suitable for high-throughput screening.[28,29] Riboswitch aptamers have been used to measure bacterial dinucleotides, and Bose, *et al.* engineered an aptamer to measure 2′3′-cGAMP with high specificity.[28] This aptamer was used to measure cGAMP in a biochemical assay as well as cGAMP levels in DNA-stimulated L929 cells overexpressing cGAS.[28] Our group at Pfizer developed a specific monoclonal antibody that recognizes cGAMP and used it to establish a fluorescence polarization assay. Using this assay as well as structural and biophysical studies, we identified a low affinity fragment hit that was chemically optimized to bind cGAS with high affinity (PF-06928215, K_d = 200 nM) and inhibit enzymatic activity (**Figure 2**). This compound did not inhibit DNA-stimulated IFN-β production in THP-1 cells, which could be a result of poor cell permeability or lack of potency. It will be important to develop sensitive tools suitable to measure cGAMP levels in human biological samples as well as potent inhibitors that can be used to clinically test whether modulation of cGAS activity affects disease outcomes.

Flip through the pages of this Currents to learn more about the cGAMP ligands, 2'3'-cGAMP ELISA Kit, recombinant STING variants, and additional key proteins and antibodies Cayman Chemical offers to help in this endeavor.

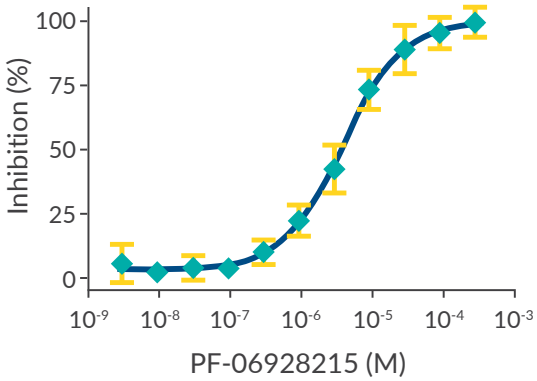

Figure 2. The small molecule inhibitor PF-06928215 causes a concentration-dependent inhibition of cGAS activity. Activity was monitored through displacement of a Cy5-cGAMP probe from the anti-cGAMP mAb 80-2, as described in Hall, *et al.* Image used under CC BY 4.0.

READ MORE

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How do you envision future cGAS and STING discoveries will impact cancer therapies or other healthcare outcomes related to host defense against pathogens?

Identification of the cGAS-STING pathway has opened novel opportunities for cancer and autoimmune therapies. They have provided a new understanding of mechanisms resulting in type 1 IFN production, and regulatory targets within that signaling network. In the case of cGAS, therapies targeting cGAS inhibition may ameliorate autoimmune diseases such as SLE. In oncology the story appears to be more complex, with innate immunity activation driving an adaptive immunity response. There is considerably more to be learned about the disease triggers and cellular responses, but reports of the efficacy of STING agonists exemplify the promise of new targeted therapies for oncology.

about how the authors discovered PF-06928215 as a high affinity inhibitor of cGAS.

About the Authors

KL

Karen L. Leach, Ph.D.

Dr. Leach is a molecular pharmacologist with over 30 years' experience in the pharmaceutical industry. Her research has focused heavily on pathways of signal transduction, which afforded her the opportunity to contribute across multiple therapeutic areas. She has led drug discovery project teams in Oncology, Alzheimer's, and Innate Immunology and successfully advanced two compounds to clinical candidacy. As a director of Academic Research Collaborations at Pfizer's Centers for Therapeutic Innovation, she led outreach efforts to identify academic partners and established joint pharma-academic project teams that were focused on advancing novel targets, including cGAS, through the drug discovery process. She is currently an independent consultant for emerging biotech.

JH

Justin D. Hall, Ph.D.

Dr. Hall is a scientist at Pfizer, where he works in the structural biology and biophysics technology group in support of the pre-clinical research portfolio. His work brings him in contact with all of Pfizer's therapeutic units, where he makes contributions from the leadership and bench-top levels. Justin is currently working on several therapeutic projects, such as cGAS, and as the biophysics lead for technology development platforms. Justin has an MBA and a Ph.D., and has consistently contributed on Pfizer's behalf to research collaborations with academic, profit, government, and non-profit organizations. He is particularly interested in collaborations targeting diseases that disproportionately affect disadvantaged populations.

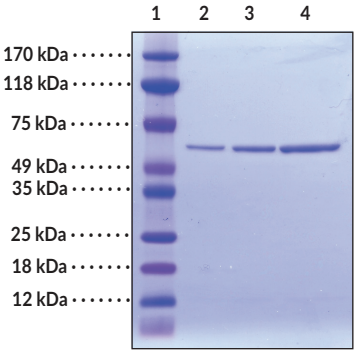
Cytosolic DNA Sensing

Specific families of pattern recognition receptors are responsible for detecting DNA from invading microbes or host cells and generating innate immune responses. Cayman has developed a protein, antibody, and assay tool set along with key chemical modulators to study cytosolic DNA sensing that leads to activation of the type I interferon pathway.

cGAS (human recombinant)

Item No. 22810

- Human recombinant enzyme
- **Amino Acids:** 2-543 (full length)
- **Purity:** ≥90%

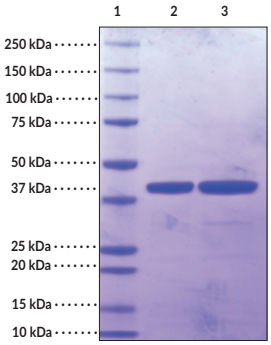


Lane 1: MW Markers
Lane 2: cGAS (1 µg)
Lane 3: cGAS (2 µg)
Lane 4: cGAS (4 µg)

cGAS (161-522) (human recombinant)

Item No. 25001

- Human recombinant protein
- **Amino Acids:** 161-522 (truncated)
- **Purity:** ≥90%

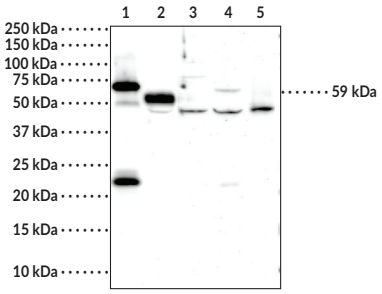


Lane 1: MW Marker
Lane 2: cGAS (161-522) (2 µg)
Lane 3: cGAS (161-522) (4 µg)

cGAS Monoclonal Antibody (Clone 5G10)

Item No. 23853

- Recognizes the full length human cGAS protein at ~59 kDa
- **Host:** Mouse
- **Applications:** IF, IP, WB



Lane 1: cGAS Recombinant Protein (0.01 µg)
Lane 2: Raji Cell Lysate (50 µg)
Lane 3: Jurkat Cell Lysate (50 µg)
Lane 4: THP-1 Cell Lysate (50 µg)
Lane 5: HepG2 Cell Lysate (50 µg)

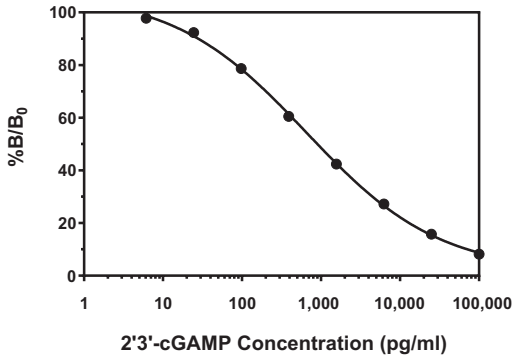
NEW! ASSAY TO MONITOR cGAS-PRODUCED cGAMP

Directly measure 2'3'-cGAMP levels with unrivaled sensitivity

2'3'-cGAMP ELISA Kit

Item No. 501700

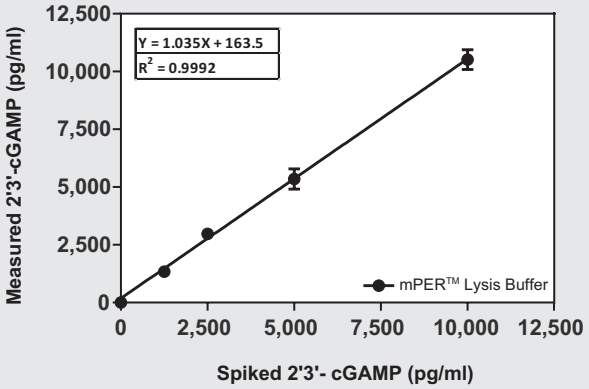
- Measure 2'3'-cGAMP in cell lysates
- Assay 24 samples in triplicate or 36 samples in duplicate
- Lower limit of detection (LLOD) is 9.6 pg/ml (0.01 pmol/ml)
- Run with overnight or 2-hour incubation protocols without compromising sensitivity



Assay Range = 100 ng/ml - 6.1 pg/ml
Sensitivity (defined as 80% B/B_0) = 85.3 pg/ml
Mid-point (defined as 50% B/B_0) = 907.7 pg/ml
Lower Limit of Detection (LLOD) = 9.6 pg/ml

Proven Accuracy and Precision

Cell lysis buffer (mPER™) was spiked with 2'3'-cGAMP and analyzed using Cayman's 2'3'-cGAMP ELISA. 2'3'-cGAMP recovery showed excellent linearity and remained within the assay range.



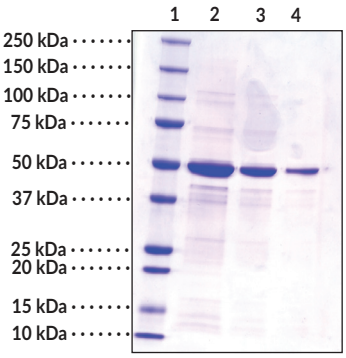
Cyclic Dinucleotides (CDNs), cGAMPs, and Other STING Activators

Item No.	Product Name	Summary
17753	Cyclic di-AMP	A bacteria-derived CDN; binds and activates mammalian STING
17144	Cyclic di-GMP	A bacteria-derived CDN; binds and activates mammalian STING (K_d = 1.21 µM)
22485	Cyclic di-IMP (sodium salt)	A synthetic analog of cyclic di-AMP and cyclic di-GMP with adjuvant properties
22419	2'2'-cGAMP	A synthetic CDN with non-canonical 2'5'-phosphodiester bonds; binds STING (K_d = 287 nM)
19887	2'3'-cGAMP (sodium salt)	A mammalian cell-derived CDN with non-canonical 2'5'- and canonical 3'5'-phosphodiester bonds; binds STING (K_d = 3.79 nM)
17966	3'3'-cGAMP (sodium salt)	A bacteria-derived CDN with canonical 3'5'-phosphodiester bonds; binds and activates mammalian STING (K_d = 1.04 µM)
14617	DMXAA	A mouse-specific STING activator; triggers the TBK1/IRF3 signaling pathway in leukocytes, inducing IFN production
22353	G10	An indirect activator of STING signaling; induces IRF3- and IFN-dependent transcription
24106	ML RR-S2 CDA (ammonium salt)	A synthetic CDN with non-canonical 2'5'-phosphodiester bonds; demonstrates enhanced action at human STING relative to unmodified cyclic di-AMP

CdnP (*Mycobacterium tuberculosis* strain ATCC 25618/H37Rv recombinant)

Item No. 22809

- Human recombinant enzyme
- **Amino Acids:** 1-336 (full length)
- **Purity:** ≥70%



Lane 1: MW Markers
Lane 2: CdnP (5 µg)
Lane 3: CdnP (2 µg)
Lane 4: CdnP (1 µg)

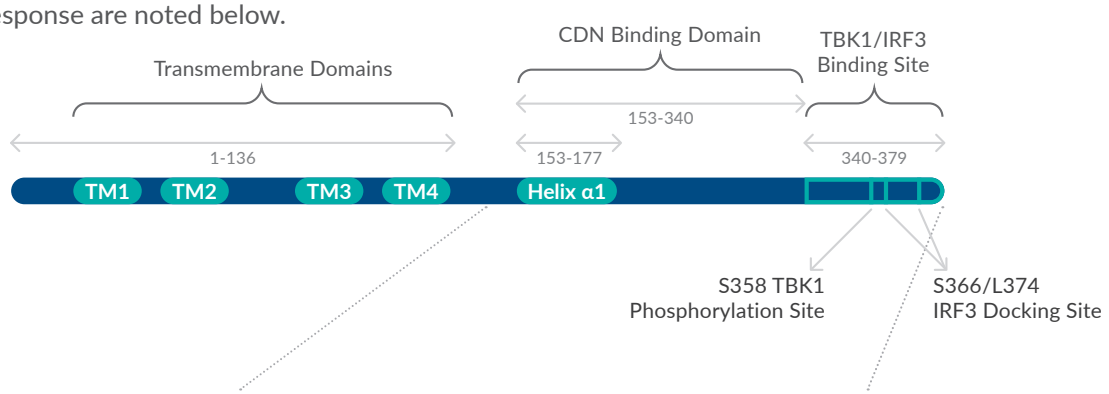
Cyclic di-nucleotide phosphodiesterase (CdnP) is a soluble, stand-alone phosphodiesterase that regulates cyclic dinucleotide signaling during intracellular infections of *M. tuberculosis*.

CdnP hydrolyzes c-di-AMP as a strategy to avoid activation of the innate immune response in the host.

M. tuberculosis infection leads to cytosolic release of c-di-AMP, which is recognized by STING and subsequently triggers type I interferon response.

Interferon Gene Stimulation

STING (Stimulator of Interferon Genes) is an ER resident protein that binds to CDNs through its C-terminal, cytoplasmic domain. Two STING molecules bind one c-di-GMP, implying that a STING dimer shares one CDN binding site. Residues 153-177 form part of helix α1 and are involved in the dimerization of STING and the binding of c-di-GMP (**Figure 1**). Studies comparing CDN binding and STING activation identified several significant single nucleotide polymorphisms of human STING. Each has evolved differently to distinguish conventional bacterial CDNs (*i.e.*, 3′3′-cGAMP containing G(3′5′) pA(3′5′) linkages, c-di-GMP, and c-di-AMP) from noncanonical metazoan CDNs (*i.e.*, 2′3′-cGAMP containing G(2′5′)-pA(3′5′) phosphodiester linkages). Cayman offers human recombinant variants of the STING protein expressed in *E. coli*. Some of these variants occur as natural haplotypes and others introduce point mutations within the CDN binding domain to further understand the amino acids important for CDN binding and/or IFN induction. Because N-terminal, transmembrane domain deletion truncations can be expressed as highly soluble proteins, Cayman's STING variants include the key, soluble residues of the C-terminal domain. Known differences in how these variants respond to CDNs and/or affect the downstream IFN response are noted below.



Item No.	*Human Variants*	*138*	*155*	*162*	*200*	*224*	*230*	*232*	*284*	*293*	*341*	*379*	*Key Features*
22816	R232		V	S	I	K	G	R	R	R	V		wild-type
22815	H232		V	S	I	K	G	H	R	R	V		less dominant allele
15139	H232; SUMO-tagged	SUMO		S	I	K	G	H	R	R			SUMOpro-tagged
23592	AQ		V	S	I	K	A	R	R	Q	V		reduced IFN response
23594	M284		V	S	I	K	G	R	M	R	V		constitutively active
23593	R224		V	S	I	R	G	R	R	R	V		reduced ubiquitination
25306	A162		V	A	I	K	G	R	R	R	V		binds DMXAA

Figure 1. Domain structure of the human STING protein with amino acid substitutions noted for the STING variants available from Cayman.

STING Variants

STING R232 variant (human recombinant)
(Item No. 22816)

- contains amino acids 138-379 with an arginine at position 232
- considered "wild type" since it occurs in 60% of human population
- binds both 2'3'- and 3'3'-cGAMPs with preferential activation *via* metazoan cGAMPs

STING H232 variant (human recombinant)
(Item No. 22815)

- contains amino acids 138-379 with a histidine at position 232
- variation found in 13.7% of the human population
- binds metazoan 2'3'-cGAMP but demonstrates a reduced IFN response to bacterial c-di-GMP and a complete loss of IFN response to c-di-AMP and 3'3'-cGAMP

STING H232 variant; SUMO-tagged (human recombinant) *(Item No. 15139)*

- contains amino acids 155-341 of the H232 variant and a removable N-terminal SUMOpro™tag
- contains only the central CDN binding domain
- N- and C-terminal truncations eliminate the four transmembrane domains and the tail-end TBK1/IRF3 binding sites

STING M284 variant (human recombinant) *(Item No. 23594)*

- contains amino acids 138-379 of the wild-type variant with a methionine at position 284
- associated with constitutive activation of downstream signaling
- increases the propensity of STING to dimerize and associate with the TBK1, which can lead to a type I IFN response

STING A162 variant (human recombinant) *(Item No. 25306)*

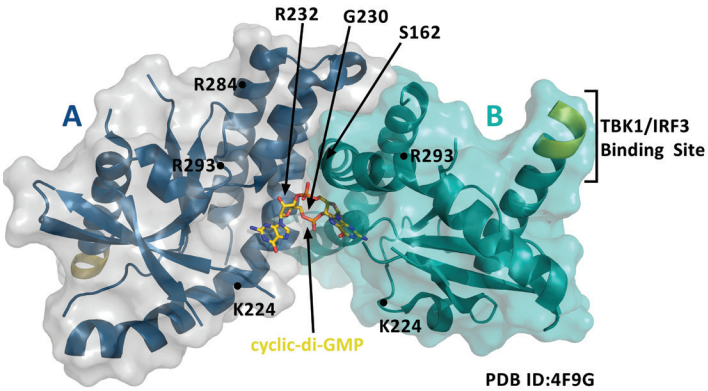
- contains amino acids 138-379 of the wild-type variant with an alanine at position 162
- allows human STING to bind to DMXAA, a compound previously known to bind mouse, but not human, STING
- when bound to DMXAA, activates the IFN pathway similarly to mouse STING

STING AQ variant (human recombinant) *(Item No. 23592)*

- contains amino acids 138-379 of the wild-type variant with an alanine at position 230 and a glutamine at position 293
- occurs in 5.2% of the human population
- demonstrates a partially reduced IFN response to bacterial ligands (30-40% reduction compared to wild type)

STING R224 variant (human recombinant) *(Item No. 23593)*

- contains amino acids 138-379 of the wild-type variant with an arginine at position 224
- reduces the ubiquitination of STING, which interrupts optimal STING trafficking
- inhibits TBK1-mediated IRF3 activation but not NF-κB activation



STING dimer (A and B are both aa 139-379) bound to cyclic-di-GMP and notated with key amino acid modifications of Cayman's STING variants.

Immunotherapeutic Potential

The importance of STING in facilitating innate immune responses following infection with DNA viruses makes this pathway a key target for immunotherapeutics. The STING variants that Cayman offers can be used to better understand the key amino acids involved in recognizing non-canonical *versus* bacterial CDNs and triggering a specific IFN response.

Read more about how amino acid variations affect innate immune response to foreign DNA at www.caymanchem.com/STINGvariants

STING Antibodies

Item No.	Product Name	Immunogen	Host	Species Reactivity	Application(s)
17857	STING Polyclonal Antibody	STING (human recombinant), aa 155-341	Rabbit	(+) Human STING	ELISA, IP, WB
24791	STING Constitutively Active Mutant (R284M) Polyclonal Antibody	Synthetic peptide from internal region of the human protein	Rabbit	(+) Human STING	WB

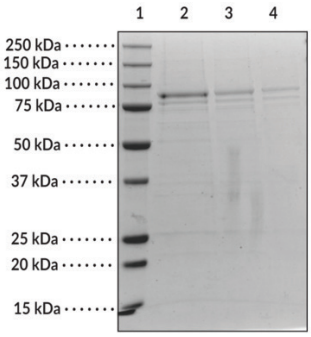
Type I Interferon Activation

Phosphorylation of the transcription factor IRF3 by the IKK-related kinase TBK1 leads to production of type I interferon. Cayman has developed key proteins, antibodies, and chemical modulators to study the important players in this process.

TBK1 (human recombinant)

Item No. 22817

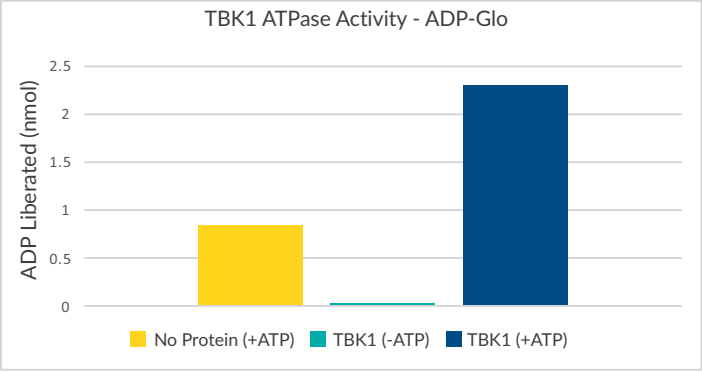
- Active human recombinant enzyme
- **Amino Acids:** 1-729 (full length)
- **Purity:** ≥50%



Lane 1: MW Markers
Lane 2: TBK1 (4 µg)
Lane 3: TBK1 (2 µg)
Lane 4: TBK1 (1 µg)

Proven Enzyme Activity

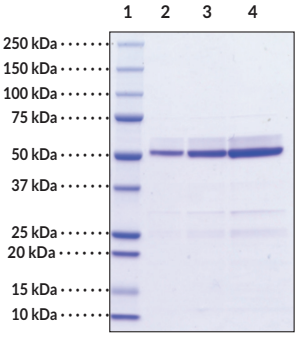
Activity of Cayman's TBK1 enzyme was monitored using ADP-Glo. TBK1 produces a significantly higher concentration of ADP in the presence of ATP.



IRF3 (human recombinant)

Item No. 22811

- Human recombinant enzyme
- **Amino Acids:** 1-427 (full length)
- **Purity:** ≥85%

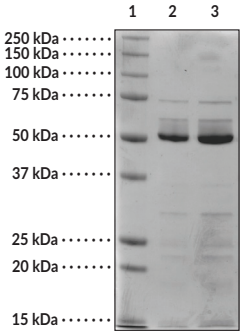


Lane 1: MW Markers
Lane 2: IRF3 (1 µg)
Lane 3: IRF3 (2 µg)
Lane 4: IRF3 (4 µg)

IFR3 (S386A, S396A mutant; human recombinant)

Item No. 23590

- IRF3 Negative Control
- **Amino Acids:** 1-427 (full length)
- **Purity:** ≥75%

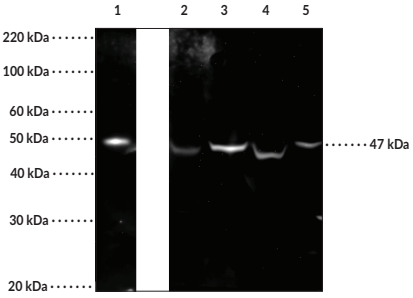


Lane 1: MW Markers
Lane 2: IRF3 (S386A, S396A mutant) (2 µg)
Lane 3: IRF3 (S386A, S396A mutant) (4 µg)

IRF3 Polyclonal Antibody

Item No. 24937

- **Immunogen:** IRF3 (human recombinant)
- **Host:** Rabbit
- **Species Reactivity:** (+) Human IRF3
- **Applications:** ELISA, WB



Lane 1: IRF3 (human recombinant) (1 ng)
Lane 2: Jurkat Cell Lysate (50 µg)
Lane 3: MCF-7 Cell Lysate (50 µg)
Lane 4: COS-1 Cell Lysate (50 µg)
Lane 5: A549 Cell Lysate (50 µg)

IFN Pathway Modulators

Item No.	Product Name	Summary
17869	Dimethyl biphenyl-4,4'-dicarboxylate	A stimulator of JAK/STAT signaling and induces the expression of IFN-α-stimulated genes
16881	Polyinosinic-polycytidylic Acid (potassium salt)	A synthetic dsRNA that activates NF-κB, induces IFN-α, promotes dendritic cell maturation, and stimulates both innate and adaptive immunity
20449	RO8191	An agonist of IFN-α receptor type 2 with antiviral activity
22402	StA-IFN-1	An inhibitor of the IFN induction pathway (IC_{50} = 4.1 µM)

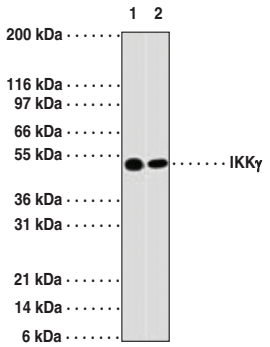
NF-κB Activation

Activation of NF-κB triggered by IκB kinases (IKK) controls the expression of an array of cytokine genes. Cayman offers antibodies, assays, and chemical modulators to study this major pathway of the innate immune response.

IKKγ Monoclonal Antibody (Clone 72C627)

Item No. 13931

- **Immunogen:** His-tagged full length human IKKγ
- **Host:** Mouse
- **Application:** WB

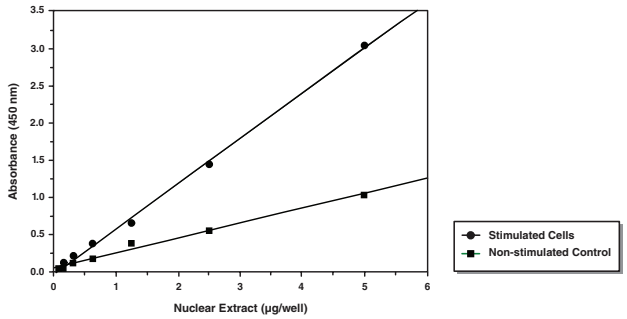


Lane 1: Jurkat Cell Lysate
Lane 2: NIH 3T3 Cells

Also available: *IκBα (Phospho-Ser$^{32/36}$) Monoclonal Antibody (Clone 39A1413) Item No. 13923*

NF-κB Transcription Factor Assays

- Sensitive, non-radioactive method to detect human p50 or p65 NF-κB from whole cell lysates
- 96-well plate format replaces EMSAs
- Capture the transcription factor using a specific dsDNA sequence bound to the plate
- Detect the dsDNA-bound transcription factor with specific antibodies in an ELISA format
- Nuclear Extraction Kit available to aid in the isolation of nuclear and cytoplasmic fractions from cell lysates or tissue homogenates



Assay of cell lysates isolated from stimulated and non-stimulated HeLa cells demonstrating NF-κB (p65) activity.

Item No.	Product Name
10006912	NF-κB (human p50) Transcription Factor Assay Kit
10007889	NF-κB (p65) Transcription Factor Assay Kit
10009277	Nuclear Extraction Kit

IKK Inhibitors

Item No.	Product Name
19184	BI-605906
16667	BMS 345541 (trifluoroacetate salt)
10011248	CAY10575
10011249	CAY10576
11140	CAY10657
17276	IKK2 Inhibitor VI
13313	IKK-16 (hydrochloride)
17290	IMD 0354
18774	LY2409881
14862	PS-1145
10010267	SC-514
15115	TPCA-1

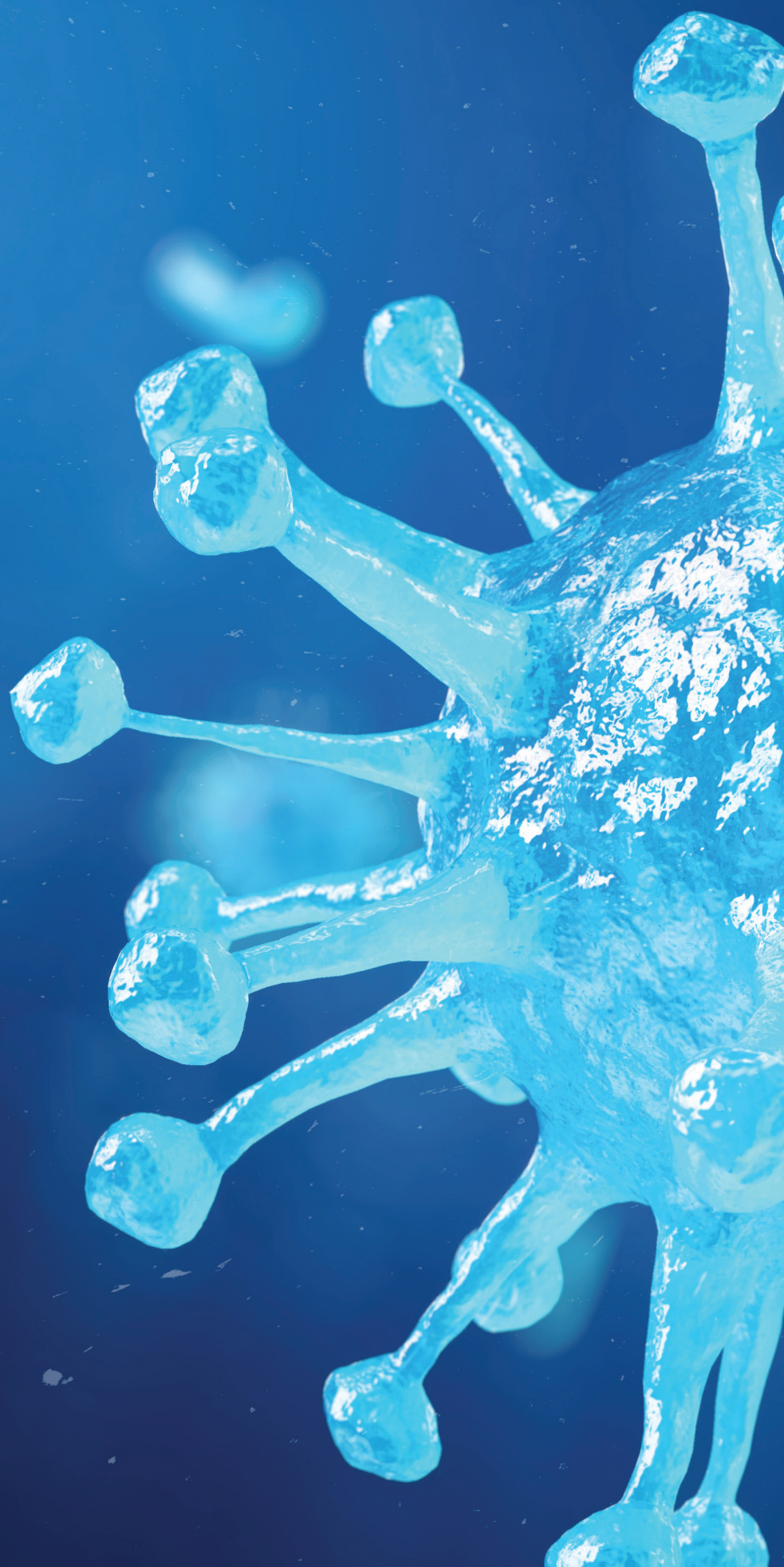
NF-κB Inhibitors

Item No.	Product Name
10011336	Avenanthramide-C methyl ester
10010266	BAY 11-7082
70750	Caffeic Acid phenylethyl ester
19110	CBL0137
14122	CID-2858522
15036	JSH-23
19083	NF-κB Activation Inhibitor III
17493	NF-κB Inhibitor
13327	PPM-18
10006734	QNZ
11796	Wedelolactone

Cytokine ELISAs

Item No.	Product Name
583301	Interleukin-1α (human) ELISA Kit
583311	Interleukin-1β (human) ELISA Kit
501030	Interleukin-6 (human) ELISA Kit
583371	Interleukin-6 (mouse) ELISA Kit

Additional cytokine ELISAs for use in pig models available online



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