PRODUCT INFORMATION

STING AQ variant (human, recombinant)

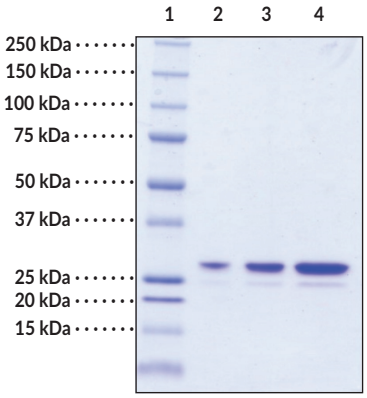
Item No. 23592

Overview and Properties

Synonyms:	Endoplasmic Reticulum Interferon Stimulator, Stimulator of Interferon Genes, TMEM173
Source:	N-terminal histidine-tagged human recombinant STING R232, G230A, R293Q mutant purified from *E. coli*
Amino acids:	138-379 (N-terminal truncation)
Molecular Weight:	28.8 kDa
Storage:	-80°C (as supplied)
Stability:	≥2 years
Purity:	***batch specific*** (≥80% estimated by SDS-PAGE)
Supplied in:	50 mM HEPES, pH 8.0, 150 mM sodium chloride, and 10% glycerol
Protein Concentration:	***batch specific***
Activity:	Serial dilutions of canonical 3'3'-cGAMP were incubated with 5 µg recombinant human STING AQ variant in 50 mM HEPES, pH 7.5, 150 mM NaCl, 10% glycerol, and SYPRO® Orange dye at 4°C.[1] The reaction was read on a BioRad CFX96 Touch™ Real-Time PCR Detection System at 4-100°C.[2] The binding of the ligand stabilizes the protein structure, increasing the melting temperature (T_m), which is detected *via* a thermal shift assay (TSA), also known as a differential scanning fluorimetry (DSF) assay.[2]

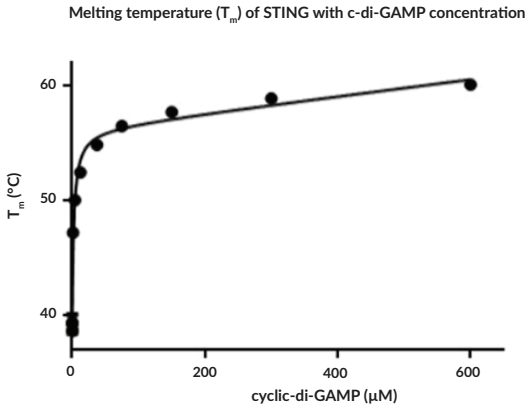
Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Images



Lane 1: MW Markers
Lane 2: STING AQ variant (1 µg)
Lane 3: STING AQ variant (2 µg)
Lane 4: STING AQ variant (4 µg)

Representative gel image shown; actual purity may vary between each batch.



Binding Activity of STING AQ variant (Item No. 23592). STING AQ variant (5 µg) was incubated with serial dilutions of 3'3'-cGAMP (Item No. 17966) and SYPRO® Orange dye. The detected increase in T_m indicates binding.

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Description

STING AQ variant (human recombinant) contains amino acids 138-379 of the wild-type STING variant (R232) with an alanine substituted for glycine at position 230 and a glutamine substituted for arginine at position 293. Stimulator of interferon genes (STING) is a component of the innate immune response that binds to cyclic dinucleotides, which are bacterial second messengers.[3] Recognition of cyclic-di-GMP (c-di-GMP), c-di-AMP, or c-GMP-AMP leads to activation of NF-κB and transcription of immunomodulatory genes, including type I interferons (IFN).[4-6] The R232 variant of STING is the most common variant in the human population, found at a frequency of 57.9% in the 1000 Genome Project.[7] The SNP variant H232 is found at a 13.7% frequency. The G230A, R293Q double mutation occurs in 5.2% of the human population and when expressed in HEK293T cells, this mutation reduces the IFN response to bacterial ligands by 30-40% compared to wild-type STING. Whereas the R293Q substitution alone is severely defective in response to bacterial cyclic dinucleotides, the G230A substitution is thought to help maintain some ability of this variant to respond to bacterial cyclic dinucleotides. Based on crystal structure of STING, the G230A mutation alters the conformation of the lid region that clamps onto the c-di-GMP, however, the R293 residue does not directly bind to c-di-GMP.[7] The R293Q mutation may instead disrupt STING activity indirectly by altering the function of a nearby cysteine residue required for IFN-β expression.[8]

References

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4. Sun, L., Wu, J., Du, F., *et al.* Cyclic GMP-AMP synthase is a cytosolic DNA sensor that activates the type I interferon pathway. *Science* **339(6121)**, 786-791 (2013).
5. Wu, J., Sun, L., Chen, X., *et al.* Cyclic GMP-AMP is an endogenous second messenger in innate immune signaling by cytosolic DNA. *Science* **339(6121)**, 826-830 (2013).
6. Konno, H., Konno, K., and Barber, G.N. Cyclic dinucleotides trigger ULK1 (ATG1) phosphorylation of STING to prevent sustained innate immune signaling. *Cell* **155(3)**, 688-698 (2013).
7. Yi, G., Brendel, V.P., Shu, C., *et al.* Single nucleotide polymorphisms of human STING can affect innate immune response to cyclic dinucleotides. *PLoS One* **8(10)**, e77846 (2013).
8. Jin, L., Xu, L.-G., Yang, I.V., *et al.* Identification and characterization of a loss-of-function human MPYS variant. *Genes Immun.* **12(4)**, 263-269 (2011).

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