

Recombinant Human CGAS Protein

For Research Use Only

1. Basic Product Information

Catalog No.: REP50174

Size: 10ug, 100ug

Protein Name: Cyclic GMP-AMP synthase (cGAMP synthase) (cGAS) (h-cGAS) (EC 2.7.7.86) (2'3'-cGAMP synthase) (Mab-21 domain-containing protein 1)

Synonym: CGAS, C6orf150, MB21D1

UniProt ID: Q8N884

UniProt Link: www.uniprot.org/uniprotkb/Q8N884/entry

Species Source: Human

Expression System: HEK293T eukaryotic cell expression system Sequence

Length: 522 AA

Molecular Weight: 59 KD

Protein Tag: C-terminal His6

2. Amino Acid Sequence

MQPWHGKAMQRASEAGATAPKASARNARGAPMDPTESPAAPEAALPKAGKFGPARKSGSRQKKS
APDTQERPPVRATGARAKKAPQRAQDTQPSDATSAPGAEGLEPPAAREPALS RAGSCRQRGARCS
TKPRPPPGPVDVPSPLPVSA PILVRRDAAPGASKLRVLEK LKLSRDDISTAAGMVKG VVDHLLLR
LKCD S AFRGVGLLNTGSYYEHVKISAPNEFDVMFKLEV PRIQLEEYSNTRAYYFVKFKRNPKENPLS
QFLEGEILSASKMLSKFRKIIKEEINDIKD TDVIMKRKRGGSPAVTLLISEKISVDITLALESKSSWPAST
QEGLRIQNWLSAKVRKQLRLKPFYLV PKHAKENG FQEETWRLSFSHIEKEILNNHGKSKTCCENKE
EKCCRKDKLKM KYLLEQLKERFKDKKHLDFSSYHVKT AFFHVCTQNPQDSQWDRKDLGLCFDN
CVTYFLQCL RTEKLENYFIPEFNL FSSNLIDKRSKEFLTKQIEYERNNEFPVFDEF

3. Buffer Composition

Liquid format: PBS-based buffer containing 50% glycerol. Glycerol concentration can be customized upon customer request; please state special requirements when placing your order.

Lyophilized format: Buffer before lyophilization is PBS supplemented with 6% trehalose.

4. Storage Conditions

Upon receipt, store the product at -20 °C or -80 °C. Aliquot the product for on-demand use to preserve protein activity and prevent denaturation and inactivation caused by repeated freeze-thaw cycles.

5. Product Description

This product is recombinant Cyclic GMP-AMP synthase (cGAMP synthase) (cGAS) (h-cGAS) (EC 2.7.7.86) (2',3'-cGAMP synthase) (Mab-21 domain-containing protein 1) produced using the HEK293T eukaryotic cell expression system. It is suitable for in-vitro functional assays, protein-protein interaction studies, antibody preparation and other biomedical research applications.

Protein Function: Nucleotidyltransferase that catalyzes the formation of cyclic GMP-AMP (2',3'-cGAMP) from ATP and GTP and plays a key role in innate immunity (PubMed:21478870, PubMed:23258413, PubMed:23707061, PubMed:23707065, PubMed:23722159, PubMed:24077100, PubMed:24116191, PubMed:24462292, PubMed:25131990, PubMed:26300263, PubMed:29976794, PubMed:30799039, PubMed:31142647, PubMed:32814054, PubMed:33273464, PubMed:33542149, PubMed:33762328, PubMed:37217469, PubMed:37802025, PubMed:39694035, PubMed:38740774). Catalysis involves both the formation of a 2',5' phosphodiester linkage at the GpA step and the formation of a 3',5' phosphodiester linkage at the ApG step, producing c[G(2',5')pA(3',5')p] (PubMed:28214358, PubMed:28363908). Acts as a key DNA sensor: directly binds double-stranded DNA (dsDNA), inducing the formation of liquid-like droplets in which CGAS is activated, leading to synthesis of 2',3'-cGAMP, a second messenger that binds to and activates STING1, thereby triggering type-I interferon production (PubMed:28314590, PubMed:28363908, PubMed:29976794, PubMed:32817552, PubMed:33230297, PubMed:33606975, PubMed:33762328, PubMed:35322803, PubMed:35438208, PubMed:35460603, PubMed:35503863, PubMed:38740774, PubMed:40461475). Preferentially recognizes and binds curved long dsDNAs of a minimal length of 40 bp (PubMed:30007416). Acts as a key foreign DNA sensor, the presence of double-stranded DNA (dsDNA) in the cytoplasm being a danger signal that triggers the immune responses (PubMed:28363908). Has antiviral activity by sensing the presence of dsDNA from DNA viruses in the cytoplasm (PubMed:28363908, PubMed:35613581). Also acts as an innate immune sensor of infection by retroviruses, such as HIV-2, by detecting the presence of reverse-transcribed DNA in the cytosol (PubMed:23929945, PubMed:24269171, PubMed:30270045, PubMed:32852081). In contrast, HIV-1 is poorly sensed by CGAS, due to its capsid that cloaks viral DNA from CGAS detection (PubMed:24269171, PubMed:30270045, PubMed:32852081). Detection of retroviral reverse-transcribed DNA in the cytosol may be indirect and be mediated via interaction with PQBP1, which directly binds reverse-transcribed retroviral DNA (PubMed:26046437). Also detects the presence of DNA from bacteria, such as M.tuberculosis (PubMed:26048138). 2',3'-cGAMP can be transferred from producing cells to neighboring cells through gap junctions, leading to promote STING1 activation and convey immune response to connecting cells (PubMed:24077100, PubMed:31992625). 2',3'-cGAMP can also be transferred between cells by virtue of packaging within viral particles contributing to IFN-induction in newly infected cells in a cGAS-independent but STING1-dependent manner (PubMed:26229115). Also senses the presence of neutrophil extracellular traps (NETs) that are translocated to the cytosol following phagocytosis, leading to synthesis of 2',3'-cGAMP (PubMed:33688080). In addition to foreign DNA, can also be activated by endogenous nuclear or mitochondrial DNA (PubMed:28738408, PubMed:28759889, PubMed:31299200, PubMed:33031745, PubMed:33230297, PubMed:34648591). When self-DNA leaks into the cytosol during cellular stress (such as mitochondrial stress, SARS-CoV-2 infection causing severe COVID-19 disease, DNA damage, mitotic arrest or senescence), or is present in form of cytosolic micronuclei, CGAS is activated leading to a state of sterile inflammation (PubMed:28738408, PubMed:28759889, PubMed:31299200, PubMed:33031745, PubMed:33230297, PubMed:34648591, PubMed:35045565, PubMed:41610251). Acts as a regulator of cellular senescence by binding to cytosolic chromatin fragments that are present in senescent cells, leading to trigger type-I interferon production via STING1 and promote cellular senescence (By similarity). Also involved in the inflammatory response



to genome instability and double-stranded DNA breaks: acts by localizing to micronuclei arising from genome instability (PubMed:28738408, PubMed:28759889, PubMed:41610251). Micronuclei, which are frequently found in cancer cells, consist of chromatin surrounded by their own nuclear membrane: following breakdown of the micronuclear envelope, a process associated with chromothripsis, CGAS binds self-DNA exposed to the cytosol, leading to 2',3'-cGAMP synthesis and subsequent activation of STING1 and type-I interferon production (PubMed:28738408, PubMed:28759889, PubMed:41610251). Activated in response to prolonged mitotic arrest, promoting mitotic cell death (PubMed:31299200). In a healthy cell, CGAS is however kept inactive even in cellular events that directly expose it to self-DNA, such as mitosis, when cGAS associates with chromatin directly after nuclear envelope breakdown or remains in the form of postmitotic persistent nuclear cGAS pools bound to chromatin (PubMed:31299200, PubMed:33542149). Nuclear CGAS is inactivated by chromatin via direct interaction with nucleosomes, which block CGAS from DNA binding and thus prevent CGAS-induced autoimmunity (PubMed:31299200, PubMed:32911482, PubMed:32912999, PubMed:33051594, PubMed:33542149). Also acts as a suppressor of DNA repair in response to DNA damage: inhibits homologous recombination repair by interacting with PARP1, the CGAS-PARP1 interaction leading to impede the formation of the PARP1-TIMELESS complex (PubMed:30356214, PubMed:31544964). In addition to DNA, also sense translation stress: in response to translation stress, translocates to the cytosol and associates with collided ribosomes, promoting its activation and triggering type-I interferon production (PubMed:34111399). In contrast to other mammals, human CGAS displays species-specific mechanisms of DNA recognition and produces less 2',3'-cGAMP, allowing a more fine-tuned response to pathogens (PubMed:30007416).

Subcellular Localization: Nucleus . Chromosome . Cell membrane ; Peripheral membrane protein . Cytoplasm, cytosol . Note=Mainly localizes in the nucleus, and at low level in the cytosol (PubMed:31544964, PubMed:31808743). On chromosomes, enriched on centromeric satellite and LINE DNA repeat elements (PubMed:30811988). Exported from the nucleus to the cytosol in a XPO1/CRM1 via the nuclear export signal in response to DNA stimulation (PubMed:33406424). Outside the nucleus, localizes at the cell membrane as a peripheral membrane protein in resting conditions: association to the cell membrane is mediated via binding to phosphatidylinositol 4,5-bisphosphate (PtdIns(4,5)P2) (PubMed:30827685). Localization at the cell membrane is required to limit the recognition of self-DNA (PubMed:30827685). Following detection of double-stranded DNA (dsDNA), released from the cell membrane into the cytosol in order to signal (PubMed:30827685). Upon transfection with dsDNA forms punctate structures that co-localize with DNA and Beclin-1 (BECN1) (PubMed:26048138). Phosphorylation at Tyr-215 promotes cytosolic retention (PubMed:30356214). In response to translation stress, translocates to the cytosol and associates with collided ribosomes (PubMed:34111399).; Note=(Microbial infection) Upon infection with virulent M.tuberculosis forms aggregates with dsDNA, non-virulent bacteria (without the ESX-1 locus) do not form these aggregates (PubMed:26048138).

6. Notes

- Avoid repeated freeze-thaw cycles to maintain protein stability and biological activity.
- Please specify special buffer-composition requirements at the time of order placement.
- For research use only. Not intended for clinical diagnosis, therapeutic use or commercial manufacturing.