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CGAS Rabbit pAb

Catalog # AP98817

Product Information

Application	IHC-P, IHC-F, IF, E
Primary Accession	Q8N884
Other Accession	Q8N884
Reactivity	Human
Predicted	Rat, Mouse
Host	Rabbit
Clonality	Polyclonal
Calculated MW	58814
Physical State	Liquid
Immunogen	KLH conjugated synthetic peptide derived from human C6orf150
Epitope Specificity	251-350/522
Isotype	IgG
Purity	affinity purified by Protein A
Buffer	0.01M TBS (pH7.4) with 1% BSA, 0.02% Proclin300 and 50% Glycerol.
SIMILARITY	Belongs to the mab-21 family.
Important Note	This product as supplied is intended for research use only, not for use in human, therapeutic or diagnostic applications.
Background Descriptions	Making up nearly 6% of the human genome, chromosome 6 contains around 1,200 genes within 170 million base pairs of sequence. Deletion of a portion of the q arm of chromosome 6 is associated with early onset intestinal cancer suggesting the presence of a cancer susceptibility locus. Porphyria cutanea tarda is associated with chromosome 6 through the HFE gene which, when mutated, predisposes an individual to developing this porphyria. Notably, the PARK2 gene, which is associated with Parkinson's disease, and the genes encoding the major histocompatiblity complex proteins, which are key molecular components of the immune system and determine predisposition to rheumatic diseases, are also located on chromosome 6. Stickler syndrome, 21-hydroxylase deficiency and maple syrup urine disease are also associated with genes on chromosome 6. A bipolar disorder susceptibility locus has been identified on the q arm of chromosome 6. The C6orf150 gene product has been provisionally designated C6orf150 pending further characterization.

Additional Information

Gene ID	115004
Other Names	C6orf150; D4; MB21D1; h-cGAS; CGAS_HUMAN; CGAS; cGAMP synthase; 2'3'-cGAMP synthase; Mab-21 domain-containing protein 1; 2.7.7.86; cyclic GMP-AMP synthase; chromosome 6 open reading frame 150; Mab-21 domain containing 1; DANGER family member 4
Dilution	IHC-P=1:100-500,IHC-F=1:400-800,IF=1:100-500,ELISA=1:5000-10000

Storage	Store at -20 °C for one year. Avoid repeated freeze/thaw cycles. When reconstituted in sterile pH 7.4 0.01M PBS or diluent of antibody the antibody is stable for at least two weeks at 2-4 °C.

Protein Information

Name	CGAS {ECO:0000303|PubMed:23258413, ECO:0000312|HGNC:HGNC:21367}
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).

Cellular Location

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).

Tissue Location

Expressed in the monocytic cell line THP1.

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