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MB21D1 Antibody

Purified Mouse Monoclonal Antibody (Mab)
Catalog # AM8562b

Product Information

Application	WB, E
Primary Accession	Q8N884
Reactivity	Human
Host	Mouse
Clonality	monoclonal
Isotype	IgG1,k
Clone Names	1697CT136.65.30
Calculated MW	58814

Additional Information

Gene ID	115004
Other Names	Cyclic GMP-AMP synthase, cGAMP synthase, cGAS, h-cGAS, 2.7.7.86, Mab-21 domain-containing protein 1, MB21D1, C6orf150
Target/Specificity	This MB21D1 antibody is generated from a mouse immunized with a KLH conjugated synthetic peptide between 1-185 amino acids from human MB21D1.
Dilution	WB~~1:4000 E~~Use at an assay dependent concentration.
Format	Purified monoclonal antibody supplied in PBS with 0.09% (W/V) sodium azide. This antibody is purified through a protein G column, followed by dialysis against PBS.
Storage	Maintain refrigerated at 2-8°C for up to 2 weeks. For long term storage store at -20°C in small aliquots to prevent freeze-thaw cycles.
Precautions	MB21D1 Antibody is for research use only and not for use in diagnostic or therapeutic procedures.

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.

Background

Nucleotidyltransferase that catalyzes the formation of cyclic GMP-AMP (cGAMP) from ATP and GTP. 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]. Has antiviral activity by acting as a key cytosolic DNA sensor, the presence of double- stranded DNA (dsDNA) in the cytoplasm being a danger signal that triggers the immune responses. Binds cytosolic DNA directly, leading to activation and synthesis of cGAMP, a second messenger that binds to and activates TMEM173/STING, thereby triggering type-I interferon production.

References

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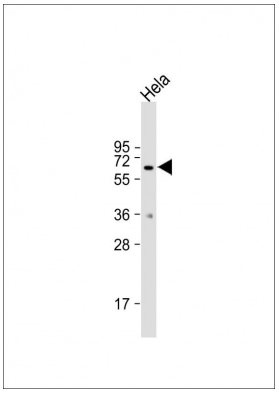
Olsen J.V.,et al.Sci. Signal. 3:RA3-RA3(2010).

Images



All lanes : Anti-MB21D1 Antibody at 1:1000 dilution Lane 1: Hela whole cell lysate Lysates/proteins at 20 µg per lane. Secondary Goat Anti-Mouse IgG/A/M(H/L), Peroxidase conjugated at 1/2000 dilution. Observed band size : 62kDa Blocking/Dilution buffer: 5% NFDM/TBST.

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