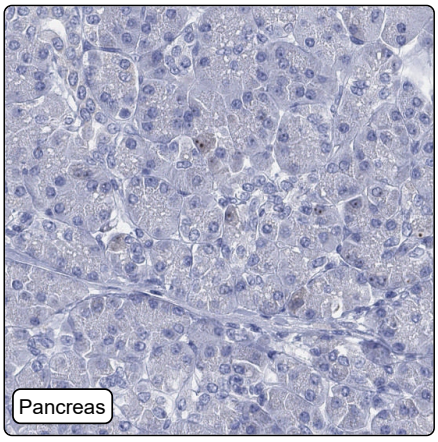
CPTC-STING1-1 (CAB080401)

Uniprot ID: Q86WV6
Protein name: STING_HUMAN
Full name: Stimulator of interferon genes protein
Tissue specificity: Ubiquitously expressed. Expressed in skin endothelial cells, alveolar type 2 pneumocytes, bronchial epithelium and alveolar macrophages.
Function: Facilitator of innate immune signaling that acts as a sensor of cytosolic DNA from bacteria and viruses and promotes the production of type I interferon (IFN-alpha and IFN-beta) (PubMed:18724357, PubMed:18818105, PubMed:19433799, PubMed:19776740, PubMed:23027953, PubMed:23910378, PubMed:23747010, PubMed:29973723, PubMed:30842659, PubMed:35045565). Innate immune response is triggered in response to non-CpG double-stranded DNA from viruses and bacteria delivered to the cytoplasm (PubMed:26300263). Acts by binding cyclic dinucleotides: recognizes and binds cyclic di-GMP (c-di-GMP), a second messenger produced by bacteria, and cyclic GMP-AMP (cGAMP), a messenger produced by CGAS in response to DNA virus in the cytosol (PubMed:21947006, PubMed:23258412, PubMed:23707065, PubMed:23722158, PubMed:26229117, PubMed:23910378, PubMed:23747010, PubMed:30842659). Upon binding of c-di-GMP or cGAMP, STING1 oligomerizes, translocates from the endoplasmic reticulum and is phosphorylated by TBK1 on the pLxIS motif, leading to recruitment and subsequent activation of the transcription factor IRF3 to induce expression of type I interferon and exert a potent anti-viral state (PubMed:22394562, PubMed:25636800, PubMed:29973723, PubMed:30842653, PubMed:35045565). In addition to promote the production of type I interferons, plays a direct role in autophagy (PubMed:30568238, PubMed:30842662). Following cGAMP-binding, STING1 buds from the endoplasmic reticulum into COPII vesicles, which then form the endoplasmic reticulum-Golgi intermediate compartment (ERGIC) (PubMed:30842662). The ERGIC serves as the membrane source for WIPI2 recruitment and LC3 lipidation, leading to formation of autophagosomes that target cytosolic DNA or DNA viruses for degradation by the lysosome (PubMed:30842662). The autophagy- and interferon-inducing activities can be uncoupled and autophagy induction is independent of TBK1 phosphorylation (PubMed:30568238, PubMed:30842662). Autophagy is also triggered upon infection by bacteria: following c-di-GMP-binding, which is produced by live Gram-positive bacteria, promotes reticulophagy (By similarity). Exhibits 2',3' phosphodiester linkage-specific ligand recognition: can bind both 2'-3' linked cGAMP (2'-3'- cGAMP) and 3'-3' linked cGAMP but is preferentially activated by 2'-3' linked cGAMP (PubMed:26300263, PubMed:23910378, PubMed:23747010). The preference for 2'-3'-cGAMP, compared to other linkage isomers is probably due to the ligand itself, whichs adopts an organized free-ligand conformation that resembles the STING1-bound conformation and pays low energy costs in changing into the active conformation (PubMed:26150511). May be involved in translocon function, the translocon possibly being able to influence the induction of type I interferons (PubMed:18724357). May be involved in transduction of apoptotic signals via its association with the major histocompatibility complex class II (MHC-II) (By similarity). (Microbial infection) Antiviral activity is antagonized by oncoproteins, such as papillomavirus (HPV) protein E7 and adenovirus early E1A protein (PubMed:26405230). Such oncoproteins prevent the ability to sense cytosolic DNA (PubMed:26405230).
Subcellular location:
Endoplasmic reticulum membrane (*experimental evidence*) (Topo: Multi-pass membrane protein (*match to sequence model, experimental evidence*))
Cytoplasm > Perinuclear region (*experimental evidence*)
Endoplasmic reticulum-Golgi intermediate compartment membrane (*experimental evidence*) (Topo: Multi-pass membrane protein (*match to sequence model, experimental evidence*))
Golgi apparatus membrane (*experimental evidence*) (Topo: Multi-pass membrane protein (*match to sequence model*))
Cytoplasmic vesicle > Autophagosome membrane (*experimental evidence*) (Topo: Multi-pass membrane protein (*match to sequence model*))
Mitochondrion outer membrane (*experimental evidence*) (Topo: Multi-pass membrane protein (*match to sequence model*))
Cell membrane (*by similarity*) (Topo: Multi-pass membrane protein (*match to sequence model*))
NOTE: In response to double-stranded DNA stimulation, translocates from the endoplasmic reticulum through the endoplasmic reticulum-Golgi intermediate compartment and Golgi to post-Golgi vesicles, where the kinase TBK1 is recruited (PubMed:19433799, PubMed:30842659, PubMed:30842653, PubMed:29694889). Upon cGAMP-binding, translocates to the endoplasmic reticulum-Golgi intermediate compartment (ERGIC) in a process that is dependent on COPII vesicles; STING1-containing ERGIC serves as a membrane source for LC3 lipidation, which is a key step in autophagosome biogenesis (PubMed:30842662).
Protein existence: Experimental evidence at protein level

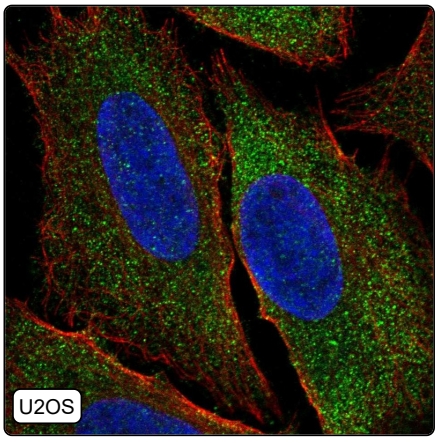
Comment: IF: cytosol localization OK but not very convincing staining and negative in the other cell line/Charlotte

Immunohistochemistry



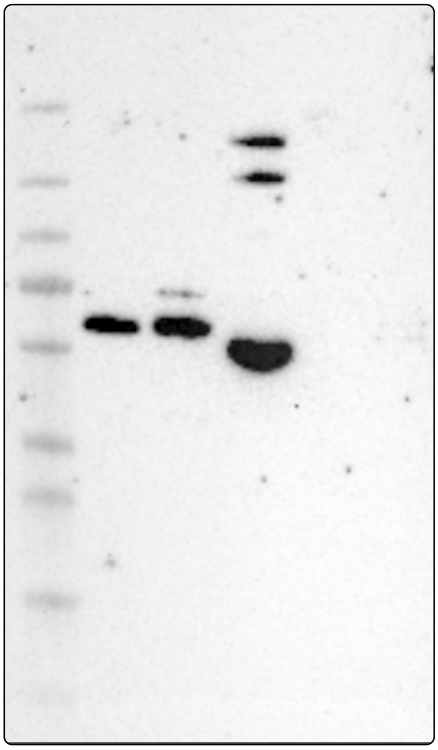
IHC protocol:	HIER pH6, Dilution 1:600
IHC test staining:	Nucleoli staining in Cerebral cortex. Additional plasma positivty.
Literature conformance:	Not consistent with gene/protein characterization data
Literature significance:	
RNA similarity:	Very low consistency between antibody staining and RNA expression data
RNA tissue specificity:	Low tissue specificity
RNA tissue distribution:	Detected in many
IHC Sibling similarity:	Other antibody shows dissimilar IHC staining pattern

Immunofluorescence



IF Overlay:	antibody (green), anti-tubulin (red) and DAPI (blue)
IF main location:	Cytosol - 3: **Supportive** (auto)
IF additional location:	
IF approved for publication on HPA:	Yes
IF in THP-1:	Negative
IF in U2OS:	Cytosol

Western blot



WB Size markers (kDa):	250, 130, 100, 70, 55, 35, 25, 15, 10
WB Lanes:	Marker (1), RT-4 (2), U-251MG (3), Plasma (4), Liver (5), Tonsil (6)
WB Target weight (kDa):	18, 29, 32, 32, 42, 42, 42
WB Validation:	Supported (Band of predicted size in kDa (+/-20%) with additional bands present.)