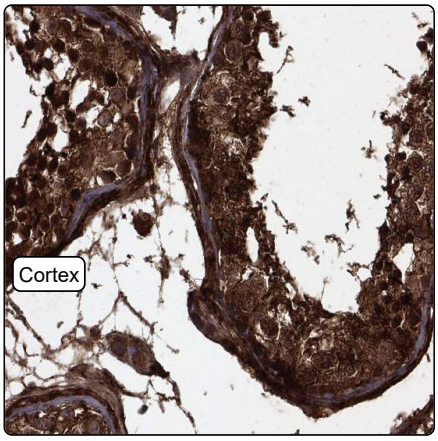
CPTC-CLU-1 (CAB080180)

Uniprot ID: P10909
Protein name: CLUS_HUMAN
Full name: Clusterin
Tissue specificity: Detected in blood plasma, cerebrospinal fluid, milk, seminal plasma and colon mucosa. Detected in the germinal center of colon lymphoid nodules and in colon parasympathetic ganglia of the Auerbach plexus (at protein level). Ubiquitous. Detected in brain, testis, ovary, liver and pancreas, and at lower levels in kidney, heart, spleen and lung.
Function: [Isoform 1]: Functions as extracellular chaperone that prevents aggregation of non native proteins (PubMed:11123922, PubMed:19535339). Prevents stress-induced aggregation of blood plasma proteins (PubMed:11123922, PubMed:12176985, PubMed:17260971, PubMed:19996109). Inhibits formation of amyloid fibrils by APP, APOC2, B2M, CALCA, CSN3, SNCA and aggregation-prone LYZ variants (in vitro) (PubMed:12047389, PubMed:17412999, PubMed:17407782). Does not require ATP (PubMed:11123922). Maintains partially unfolded proteins in a state appropriate for subsequent refolding by other chaperones, such as HSPA8/HSC70 (PubMed:11123922). Does not refold proteins by itself (PubMed:11123922). Binding to cell surface receptors triggers internalization of the chaperone-client complex and subsequent lysosomal or proteasomal degradation (PubMed:21505792). Protects cells against apoptosis and against cytolysis by complement (PubMed:2780565). Intracellular forms interact with ubiquitin and SCF (SKP1-CUL1-F-box protein) E3 ubiquitin-protein ligase complexes and promote the ubiquitination and subsequent proteasomal degradation of target proteins (PubMed:20068069). Promotes proteasomal degradation of COMMD1 and IKBKB (PubMed:20068069). Modulates NF-kappa-B transcriptional activity (PubMed:12882985). A mitochondrial form suppresses BAX-dependent release of cytochrome c into the cytoplasm and inhibit apoptosis (PubMed:16113678, PubMed:17689225). Plays a role in the regulation of cell proliferation (PubMed:19137541). An intracellular form suppresses stress-induced apoptosis by stabilizing mitochondrial membrane integrity through interaction with HSPA5 (PubMed:22689054). Secreted form does not affect caspase or BAX-mediated intrinsic apoptosis and TNF-induced NF-kappa-B-activity (PubMed:24073260). Secreted form act as an important modulator during neuronal differentiation through interaction with STMN3 (By similarity). Plays a role in the clearance of immune complexes that arise during cell injury (By similarity). [Isoform 6]: Does not affect caspase or BAX-mediated intrinsic apoptosis and TNF-induced NF-kappa-B-activity. [Isoform 4]: Does not affect caspase or BAX-mediated intrinsic apoptosis and TNF-induced NF-kappa-B-activity (PubMed:24073260). Promotes cell death through interaction with BCL2L1 that releases and activates BAX (PubMed:21567405).
Subcellular location:
Unnamed:
Nucleus (*experimental evidence*)
Cytoplasm (*experimental evidence*)
Mitochondrion membrane (Topo: Peripheral membrane protein ; Orientation: Cytoplasmic side (*experimental evidence*))
Cytoplasm > Cytosol (*experimental evidence*)
Microsome (*experimental evidence*)
Endoplasmic reticulum (*experimental evidence*)
Mitochondrion (*experimental evidence*)
Mitochondrion membrane (*experimental evidence*)
Cytoplasm > Perinuclear region (*by similarity*)
Cytoplasmic vesicle > Secretory vesicle > Chromaffin granule (*by similarity*)
NOTE: Secreted isoforms can retrotranslocate from the secretory compartments to the cytosol upon cellular stress (PubMed:17451556). Detected in perinuclear foci that may be aggresomes containing misfolded, ubiquitinated proteins (PubMed:20068069). Detected at the mitochondrion membrane upon induction of apoptosis (PubMed:17689225). Under ER stress, a immaturely glycosylated pre-secreted form retrotranslocates from the endoplasmic reticulum (ER)-Golgi network to the cytoplasm to localize in the mitochondria through HSPA5 interaction (PubMed:22689054). ER stress reduces secretion (PubMed:22689054). Under the stress, minor amounts of non-secreted forms accumulate in cytoplasm (PubMed:24073260, PubMed:22689054, PubMed:17451556). Non-secreted forms emerge mainly from failed translocation, alternative splicing or non-canonical initiation start codon (PubMed:24073260, PubMed:12551933).
Isoform 1:
Secreted (*experimental evidence*)
NOTE: Can retrotranslocate from the secretory compartments to the cytosol upon cellular stress.
Isoform 4:
Cytoplasm (*experimental evidence*)
NOTE: Keeps cytoplasmic localization in stressed and unstressed cell.
Isoform 6:
Cytoplasm (*experimental evidence*)
NOTE: Keeps cytoplasmic localization in stressed and unstressed cell.
Protein existence: Experimental evidence at protein level

Comment:

Immunohistochemistry



IHC protocol:	HIER pH6, Dilution 1:800
IHC test staining:	Cytoplasmic positivity in most tissues. Additional plasma positivity.
Literature conformance:	Consistent with extensive gene/protein characterization data
Literature significance:	
RNA similarity:	Medium consistency between antibody staining and RNA expression data
RNA tissue specificity:	Tissue enhanced (brain,liver)
RNA tissue distribution:	Detected in all
IHC Sibling similarity:	Other antibody shows partly similar IHC staining pattern
Reliability score:	Supported
APE summary:	General cytoplasmic protein expression most tissues.
APE explanatory sentences:	At least one protein variant secreted, tissue location of RNA and protein might differ and correlation is complex.
Orthogonal validation:	No
Independent validation:	No
IHC Annotation summary:	Moderate to strong cytoplasmic staining was observed in essentially all normal tissues. Smooth muscle tissue was negative. Moderate to strong cytoplasmic staining was observed in a majority of cases of all cancer types.