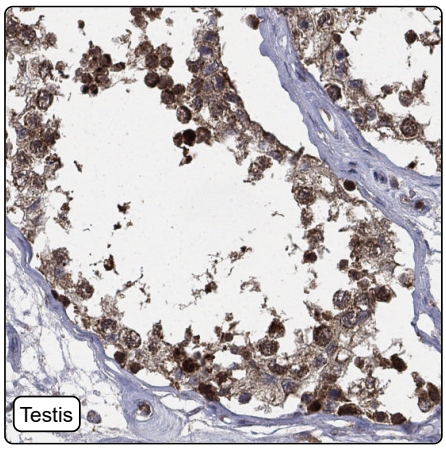
CPTC-MTOR-8 (CAB080097)

Uniprot ID: P42345
Protein name: MTOR_HUMAN
Full name: Serine/threonine-protein kinase mTOR
Tissue specificity: Expressed in numerous tissues, with highest levels in testis.
Function: Serine/threonine protein kinase which is a central regulator of cellular metabolism, growth and survival in response to hormones, growth factors, nutrients, energy and stress signals (PubMed:12087098, PubMed:12150925, PubMed:12150926, PubMed:12231510, PubMed:12718876, PubMed:14651849, PubMed:15268862, PubMed:15467718, PubMed:15545625, PubMed:15718470, PubMed:18497260, PubMed:18762023, PubMed:18925875, PubMed:20516213, PubMed:20537536, PubMed:21659604, PubMed:23429703, PubMed:23429704, PubMed:25799227, PubMed:26018084). MTOR directly or indirectly regulates the phosphorylation of at least 800 proteins. Functions as part of 2 structurally and functionally distinct signaling complexes mTORC1 and mTORC2 (mTOR complex 1 and 2) (PubMed:15268862, PubMed:15467718, PubMed:18925875, PubMed:18497260, PubMed:20516213, PubMed:21576368, PubMed:21659604, PubMed:23429704). Activated mTORC1 up-regulates protein synthesis by phosphorylating key regulators of mRNA translation and ribosome synthesis (PubMed:12087098, PubMed:12150925, PubMed:12150926, PubMed:12231510, PubMed:12718876, PubMed:14651849, PubMed:15268862, PubMed:15467718, PubMed:15545625, PubMed:15718470, PubMed:18497260, PubMed:18762023, PubMed:18925875, PubMed:20516213, PubMed:20537536, PubMed:21659604, PubMed:23429703, PubMed:23429704, PubMed:25799227, PubMed:26018084). This includes phosphorylation of EIF4EBP1 and release of its inhibition toward the elongation initiation factor 4E (eiF4E) (By similarity). Moreover, phosphorylates and activates RPS6KB1 and RPS6KB2 that promote protein synthesis by modulating the activity of their downstream targets including ribosomal protein S6, eukaryotic translation initiation factor EIF4B, and the inhibitor of translation initiation PDCD4 (PubMed:12150925, PubMed:12087098, PubMed:18925875). This also includes mTORC1 signaling cascade controlling the MiT/TFE factors TFEB and TFE3: in the presence of nutrients, mediates phosphorylation of TFEB and TFE3, promoting their cytosolic retention and inactivation (PubMed:22576015, PubMed:22343943, PubMed:22692423). Upon starvation or lysosomal stress, inhibition of mTORC1 induces dephosphorylation and nuclear translocation of TFEB and TFE3, promoting their transcription factor activity (PubMed:22576015, PubMed:22343943, PubMed:22692423). Stimulates the pyrimidine biosynthesis pathway, both by acute regulation through RPS6KB1-mediated phosphorylation of the biosynthetic enzyme CAD, and delayed regulation, through transcriptional enhancement of the pentose phosphate pathway which produces 5-phosphoribosyl-1-pyrophosphate (PRPP), an allosteric activator of CAD at a later step in synthesis, this function is dependent on the mTORC1 complex (PubMed:23429704, PubMed:23429703). Regulates ribosome synthesis by activating RNA polymerase III-dependent transcription through phosphorylation and inhibition of MAF1 an RNA polymerase III-repressor (PubMed:20516213). In parallel to protein synthesis, also regulates lipid synthesis through SREBF1/SREBP1 and LPIN1 (By similarity). To maintain energy homeostasis mTORC1 may also regulate mitochondrial biogenesis through regulation of PPARGC1A (By similarity). mTORC1 also negatively regulates autophagy through phosphorylation of ULK1 (By similarity). Under nutrient sufficiency, phosphorylates ULK1 at 'Ser-758', disrupting the interaction with AMPK and preventing activation of ULK1 (By similarity). Also prevents autophagy through phosphorylation of the autophagy inhibitor DAP (PubMed:20537536). Also prevents autophagy by phosphorylating RUBCNL/Pacer under nutrient-rich conditions (PubMed:30704899). Prevents autophagy by mediating phosphorylation of AMBRA1, thereby inhibiting AMBRA1 ability to mediate ubiquitination of ULK1 and interaction between AMBRA1 and PPP2CA (PubMed:23524951, PubMed:25438055). mTORC1 exerts a feedback control on upstream growth factor signaling that includes phosphorylation and activation of GRB10 a INSR-dependent signaling suppressor (PubMed:21659604). Among other potential targets mTORC1 may phosphorylate CLIP1 and regulate microtubules (PubMed:12231510). As part of the mTORC2 complex MTOR may regulate other cellular processes including survival and organization of the cytoskeleton (PubMed:15268862, PubMed:15467718). Plays a critical role in the phosphorylation at 'Ser-473' of AKT1, a pro-survival effector of phosphoinositide 3-kinase, facilitating its activation by PDK1 (PubMed:15718470). mTORC2 may regulate the actin cytoskeleton, through phosphorylation of PRKCA, PXN and activation of the Rho-type guanine nucleotide exchange factors RHOA and RAC1A or RAC1B (PubMed:15268862). mTORC2 also regulates the phosphorylation of SGK1 at 'Ser-422' (PubMed:18925875). Regulates osteoclastogenesis by adjusting the expression of CEBPB isoforms (By similarity). Plays an important regulatory role in the circadian clock function; regulates period length and rhythm amplitude of the suprachiasmatic nucleus (SCN) and liver clocks (By similarity). Phosphorylates SQSTM1, promoting interaction between SQSTM1 and KEAP1 and subsequent inactivation of the BCR(KEAP1) complex (By similarity).
Subcellular location:
Endoplasmic reticulum membrane (*experimental evidence*) (Topo: Peripheral membrane protein (*experimental evidence*) ; Orientation: Cytoplasmic side (*experimental evidence*))
Golgi apparatus membrane (*experimental evidence*) (Topo: Peripheral membrane protein (*experimental evidence*) ; Orientation: Cytoplasmic side (*experimental evidence*))
Mitochondrion outer membrane (*experimental evidence*) (Topo: Peripheral membrane protein (*experimental evidence*) ; Orientation: Cytoplasmic side (*experimental evidence*))
Lysosome (*experimental evidence*)
Cytoplasm (*experimental evidence*)
Nucleus > PML body (*by similarity*)
Microsome membrane (*experimental evidence*)
Lysosome membrane (*experimental evidence*)
Cytoplasmic vesicle > Phagosome (*experimental evidence*)
NOTE: Shuttles between cytoplasm and nucleus. Accumulates in the nucleus in response to hypoxia (By similarity). Targeting to lysosomes depends on amino acid availability and RRAGA and RRAGB (PubMed:18497260, PubMed:20381137). Lysosome targeting also depends on interaction with MEAK7. Translocates to the lysosome membrane in the presence of TM4SF5 (PubMed:30956113).
Protein existence: Experimental evidence at protein level

Comment:

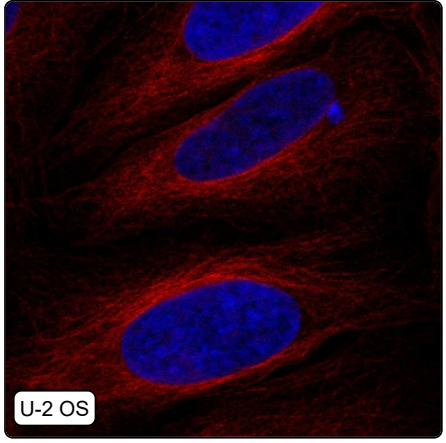
Immunohistochemistry



IHC protocol:	HIER pH6, Dilution 1:750
IHC test staining:	Granular cytoplasmic positivity in most tissues.
Literature conformance:	Consistent with extensive gene/protein characterization data
Literature significance:	
RNA similarity:	High consistency between antibody staining and RNA expression data
RNA tissue specificity:	Low tissue specificity
RNA tissue distribution:	Detected in all
IHC Sibling similarity:	Other antibody shows similar IHC staining pattern

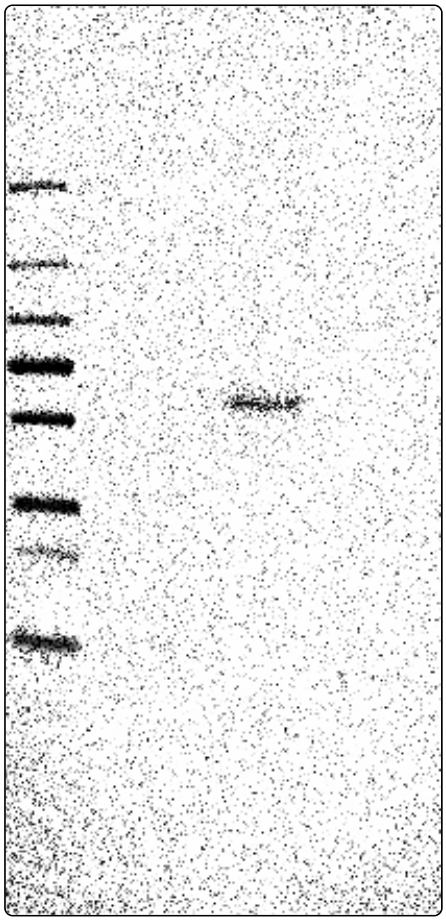
Immunofluorescence

IF Overlay:	antibody (green), anti-tubulin (red) and DAPI (blue)
IF main location:	



IF additional location:	
IF approved for publication on HPA:	No
IF in SiHa:	Negative
IF in SK-MEL-30:	Negative
IF in U-2 OS:	Negative

Western blot



WB Size markers (kDa):	250, 130, 100, 70, 55, 35, 25, 15, 10
WB Lanes:	Marker (1), RT4 (2), U-251 MG (3), Plasma (4), Liver (5), Tonsil (6)
WB Target weight (kDa):	18, 86, 289
WB Validation:	Uncertain (Single band differing more than +/-20% from predicted size in kDa and not supported by experimental and/or bioinformatic data.)