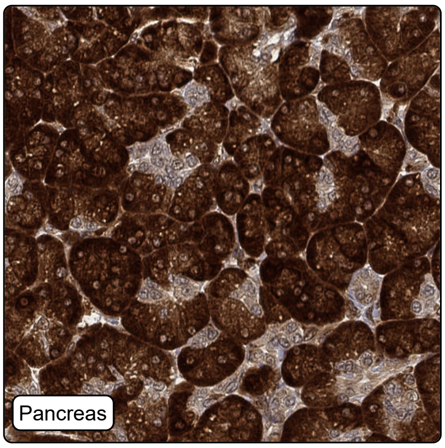
CPTC-OTUB2-1 (CAB080075)

Uniprot ID: Q96FW1
Protein name: OTUB1_HUMAN
Full name: Ubiquitin thioesterase OTUB1
Tissue specificity: Isoform 1 is ubiquitous. Isoform 2 is expressed only in lymphoid tissues such as tonsils, lymph nodes and spleen, as well as peripheral blood mononuclear cells.
Function: Hydrolase that can specifically remove 'Lys-48'-linked conjugated ubiquitin from proteins and plays an important regulatory role at the level of protein turnover by preventing degradation. Regulator of T-cell anergy, a phenomenon that occurs when T-cells are rendered unresponsive to antigen rechallenge and no longer respond to their cognate antigen. Acts via its interaction with RNF128/GRAIL, a crucial inductor of CD4 T-cell anergy. Isoform 1 destabilizes RNF128, leading to prevent anergy. In contrast, isoform 2 stabilizes RNF128 and promotes anergy. Surprisingly, it regulates RNF128-mediated ubiquitination, but does not deubiquitinate polyubiquitinated RNF128. Deubiquitinates estrogen receptor alpha (ESR1). Mediates deubiquitination of 'Lys-48'-linked polyubiquitin chains, but not 'Lys-63'-linked polyubiquitin chains. Not able to cleave di-ubiquitin. Also capable of removing NEDD8 from NEDD8 conjugates, but with a much lower preference compared to 'Lys-48'-linked ubiquitin. Plays a key non-catalytic role in DNA repair regulation by inhibiting activity of RNF168, an E3 ubiquitin-protein ligase that promotes accumulation of 'Lys-63'-linked histone H2A and H2AX at DNA damage sites. Inhibits RNF168 independently of ubiquitin thioesterase activity by binding and inhibiting UBE2N/UBC13, the E2 partner of RNF168, thereby limiting spreading of 'Lys-63'-linked histone H2A and H2AX marks. Inhibition occurs by binding to free ubiquitin: free ubiquitin acts as an allosteric regulator that increases affinity for UBE2N/UBC13 and disrupts interaction with UBE2V1. The OTUB1-UBE2N/UBC13-free ubiquitin complex adopts a configuration that mimics a cleaved 'Lys48'-linked di-ubiquitin chain.
Subcellular location:
Cytoplasm (*by similarity*)
Protein existence: Experimental evidence at protein level

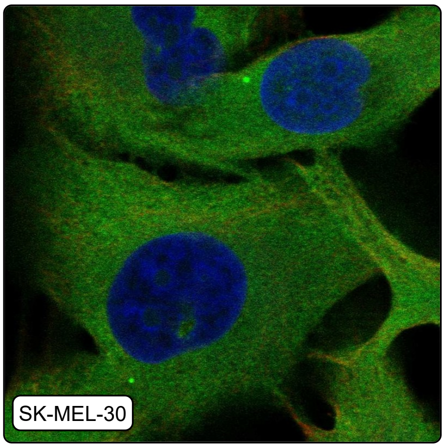
Comment:

Immunohistochemistry



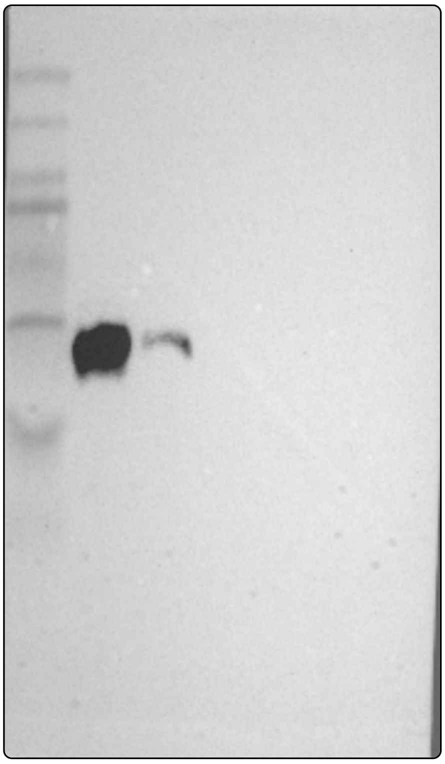
IHC protocol:	HIER pH6, Dilution 1:900
IHC test staining:	Cytoplasmic positivity in most tissues.
Literature conformance:	Consistent with extensive gene/protein characterization data
Literature significance:	
RNA similarity:	Low consistency between antibody staining and RNA expression data
RNA tissue specificity:	Low tissue specificity
RNA tissue distribution:	Detected in all
IHC Sibling similarity:	Other antibody shows partly similar IHC staining pattern

Immunofluorescence



IF Overlay:	antibody (green), anti-tubulin (red) and DAPI (blue)
IF main location:	Cytosol - 7: **Approved** (auto) Cytoplasmic bodies - 7: **Approved** (auto)
IF additional location:	
IF approved for publication on HPA:	Yes
IF in SiHa:	Cytoplasmic bodies
IF in SK-MEL-30:	Cytosol Cytoplasmic bodies
IF in U-2 OS:	Cytosol Cytoplasmic bodies

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):	19, 28, 31, 31, 31, 32, 32
WB Validation:	Supported (Single band corresponding to the predicted size in kDa (+/-20%).)