

Uniprot ID: P46934

Protein name: NEDD4\_HUMAN

Full name: E3 ubiquitin-protein ligase NEDD4

Protein existence: evidence at protein level

**Function:** E3 ubiquitin-protein ligase which accepts ubiquitin from an E2 ubiquitin-conjugating enzyme in the form of a thioester and then directly transfers the ubiquitin to targeted substrates. Involved in the pathway leading to the degradation of VEGFR-2/ KDFR, independently of its ubiquitin-ligase activity. Monoubiquitinates IGF1R at multiple sites, thus leading to receptor internalization and degradation in lysosomes. Ubiquitinates FGFR1, leading to receptor internalization and degradation in lysosomes. Promotes ubiquitination of RAPGEF2. According to PubMed:18562292 the direct link between NEDD4 and PTEN regulation through polyubiquitination described in PubMed:17218260 is questionable. Involved in ubiquitination of ERBB4 intracellular domain E4ICD. Involved in the budding of many viruses. Part of a signaling complex composed of NEDD4, RAP2A and TNIK which regulates neuronal dendrite extension and arborization during development. Ubiquitinates TNK2 and regulates EGF-induced degradation of EGFR and TNF2. Involved in the ubiquitination of ebola virus VP40 protein and this ubiquitination plays a role in facilitating viral budding.

Subcellular location: Cytoplasm (by similarity)

Cell membrane > Peripheral membrane protein (by similarity)

NOTE: Recruited to the plasma membrane by GRB10. Once complexed with GRB10 and IGF1R, follows IGF1R internalization, remaining associated with early endosomes. Uncouples from IGF1R-containing endosomes before the sorting of the receptor to the lysosomal compartment (By similarity). May be recruited to exosomes by NDFIP1.

**Three antibodies: NEED4-1, NEED4-2 and NEED4-3 were tested. NEED4-2 was selected for full protein profiling.**

## NEDD4-2 (CAB072833)

OK



Colon



U-2 OS

### Immunohistochemistry

**IHC protocol:** HIER pH 6, Dilution 1:135

**IHC test staining:** General cytoplasmic and nuclear staining.

### HC Annotators comments

Normal tissues showed weak to moderate cytoplasmic and nuclear staining. Gastrointestinal tract, respiratory epithelium of bronchus and endometrial glands exhibited additional membranous immunoreactivity.

Most cancer tissues showed weak to moderate cytoplasmic and nuclear staining. Few cases of pancreas and renal cancers displayed additional membranous positivity. Lymphoma were negative.

### Immunofluorescence

**IF Overlay:** antibody (green) and anti-tubuline (red)

**IF Localization:** Positivity in cytoplasm.

**IF Validation:** The subcellular location is supported by literature

### Western blot

**WB Size markers (kDa):** 250, 130, 95, 72, 55, 36, 28, 17, 10

**WB Lanes:** Marker(1), RT-4(2), U251 MG(3), Plasma(4), Liver(5), Tonsil(6)

**WB Target weight (kDa):** 147, 104, 149, 141, 101

**WB Validation:** Not supportive (Weak band of predicted size but with additional bands of higher intensity also present)

