

BACKGROUND

In eukaryotes, the ubiquitin-mediated proteolysis by the 26S proteasome is one of the most fundamental regulatory mechanisms controlling cell cycle progression, transcriptional regulation, signal transduction, and many other cellular processes. The ubiquitination of targets for degradation is a three-enzyme process, in which the E1 ubiquitin-activating enzyme and E2 ubiquitin-conjugating enzyme are relatively nonspecific, whereas different E3 ubiquitin ligases recognize specific substrates. Two distinct ubiquitin conjugation pathways mediate cell division by affecting the transition from G1 to S phase, the separation of sister chromatids during anaphase, and the exit from mitosis. The first event in G1/S requires the ubiquitin-conjugating enzyme Cdc34 (or Ubc3) and a ubiquitin-protein ligase complex termed SCF complex (Skp1-Cullin-F-box protein) in order to activate DNA replication. The two mitotic events involve a large ubiquitin-ligase complex called the anaphase-promoting complex-cyclosome (APC/C) in combination with one of two distinct ubiquitin-conjugating enzymes (Ubc10 or Ubc4). APC/C regulates mitosis by affecting chromosome and spindle dynamics and by regulating the activity of mitotic cyclin-dependent kinase (Cdks).¹

Skp2 (S-phase kinase-associated protein 2) is a key regulator of cell cycle and localizes at 5p13, which has been involved in karyotype transform. The protein SKP2, about 45 kDa and 436 amino acids long, is a nuclear protein. It contains an F-box, leucine-rich repeats (LLR) and a C-terminal motif. The F-box spans about 40 amino acids and comprises of 3 alpha-helix motifs, which can bind Skp1 regulator. Each LRR contains a beta-sheet and an alpha-helix. The LLRs are directly involved in the recognition of substrates during ubiquitination. The function of the N-terminal region (about 100 amino acids) is not clear.

Skp2 were originally found as novel proteins that associated with cyclin A/ CDK2/Cks1 in cancer cells. They were subsequently found to be the critical components of SCFSkp2 (Skp1, Cul1, F-box protein Skp2) ubiquitin E3 ligase complex that targets the CDK inhibitor p27Kip1 and other substrates for ubiquitin-dependent proteolysis. The low expression of p27 in malignant cancers is often inversely correlated with the elevated expression of Skp2. Skp2 normally localizes in the nucleus and many substrates of SCFSkp2, such as p27, p21Cip1 and pRb130, are nuclear proteins. However, cytosolic localization of the elevated Skp2 has been reported in several cancers. Skp2 is rate limiting for p27 degradation. Earlier studies revealed that the PI-3-kinase/Pten pathway plays a pivotal role in regulating Skp2 and p27. It was reported that Akt1, a major effector of the PI-3-kinase/Pten pathway, can not only directly bind to Skp2, but also can phosphorylate serine 72 (S72) in human Skp2. Phosphorylation of S72 by Akt1

causes the translocation of Skp2 from the nucleus to cytoplasm. It was shown that phosphorylation of S72 by Akt1 inhibits Skp2 interaction with Cdh1, which prevents the degradation of Skp2 by the mitotic APC/Cdh1 ubiquitin E3 ligase. The other report indicated that S72 phosphorylation facilitates the assembly of SCFSkp2 E3 ligase complex and promotes the oncogenic potential of Skp2 by enhancing cell proliferation and cell migration.² Several groups showed that Skp2 expression is negatively correlated with the prognosis of various carcinoma, including laryngocarcinoma, gastric cancer, colorectal cancer, breast cancer, urinary tract transitional epithelial carcinoma and certain soft tissue sarcoma.³

References:

1. Vodermaier, H.C.: Curr. Biol. 14:R787-R796, 2004
2. Zhang, H. : Cell Cycle 9:868-9, 2010
3. Guo, H.Q. et al: Chin J Cancer 29:567-71, 2010

TECHNICAL INFORMATION

Source:

Skp2 Antibody is a rabbit antibody raised against a short peptide from human Skp2 sequence.

Specificity and Sensitivity:

This antibody detects endogenous levels of Skp2 proteins without cross-reactivity with other related proteins.

Storage Buffer: PBS and 30% glycerol

Storage:

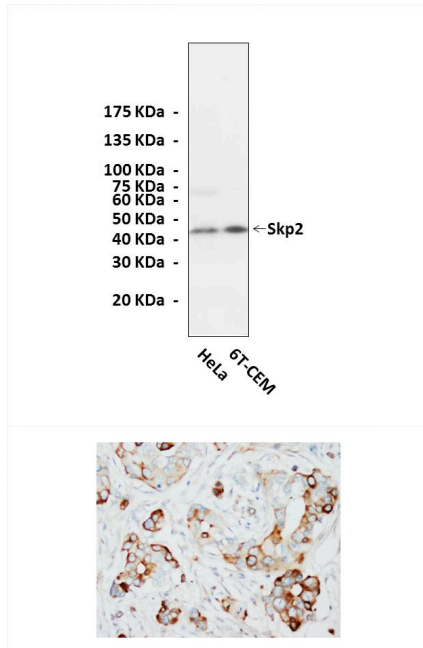
Store at -20°C for at least one year. Store at 4°C for frequent use. Avoid repeated freeze-thaw cycles.

APPLICATIONS

Application:	*Dilution:
WB	1:1000
IP	n/d
IHC	1:50-200
ICC	n/d
FACS	n/d
<i>*Optimal dilutions must be determined by end user.</i>	



QUALITY CONTROL DATA



Top: Western Blot detection of Skp2 proteins in HeLa and 6T-CEM cell lysates using Skp2 Antibody.
Bottom: This antibody stains paraffin-embedded human breast cancer tissue in immunochemical analysis.

