

BACKGROUND

The Kelch-related proteins are a superfamily of proteins conserved in a wide range of organisms, from viruses to mammals. At least 60 Kelch-related proteins have been identified, but their physiological and biochemical functions remain largely uncharacterized. Rearrangement of the actin-based cytoskeleton is regulated by a large number of actin-binding proteins. The kelch-related proteins are believed to be important for the maintenance of the ordered cytoskeleton. The *Drosophila* Kelch proteins colocalize with actin filaments in a structure called the ring canal, which bridges 15 nurse cells and the oocyte. *Drosophila* Kelch protein plays an important role in maintaining actin organization during the development of ring canals. The Kelch-related proteins have diverse functions in cell morphology, cell organization, and gene expression, and function in multiprotein complexes through contact sites in their β -propeller domains. Recently, a new member of the BTB/Kelch repeat family, gigaxonin, was reported to be a pathological target for neurodegenerative disorders in which alterations were found to contain multiple mutations in the Kelch repeats in the neurofilament network. Alterations and mutations of these proteins were found in brain tumors and neurodegenerative disorders¹

KLHL21 is a substrate-specific adapter of a BCR (BTB-CUL3-RBX1) E3 ubiquitin-protein ligase complex required for efficient chromosome alignment and cytokinesis. The KLHL21 E3 ubiquitin ligase complex regulates localization of the chromosomal passenger complex (CPC) from chromosomes to the spindle midzone in anaphase and mediates the ubiquitination of AURKB. Ubiquitination of AURKB by BCR(KLHL21) E3 ubiquitin ligase complex may not lead to its degradation by the proteasome. Aurora B is a member of the CPC together with the inner centromere protein (INCENP), Borealin/Dasra B, and survivin. Aurora B kinase activity depends on association with its coactivator INCENP and on autophosphorylation of Thr232. Importantly, the CPC is also regulated at the level of subcellular localization. In early mitosis, it localizes to centromeres, where it regulates kinetochore assembly and function and thereby plays essential roles in chromosome alignment, segregation, and the spindle assembly checkpoint. After anaphase onset, the CPC accumulates at the spindle midzone and the midbody, where it ensures completion of cytokinesis.² Studies suggest a critical role for the ubiquitination of CPC components. Ubiquitination of survivin may trigger CPC binding to centromeres, whereas Cul3-KLHL9-KLHL13 E3 ligase-dependent ubiquitination of Aurora B may regulate recruitment of the CPC to the spindle midzone. Indeed, KLHL9 and KLHL13 bind Aurora B *in vivo* and *in vitro*, and Aurora B is ubiquitinated in a KLHL9- and KLHL13-dependent manner. In *Xenopus laevis* egg extracts, the AAA-

ATPase p97 in complex with the cofactors Ufd1-Npl4 binds ubiquitinated Aurora B and may extract it from mitotic chromosomes. Therefore, it is possible that Cul3-KLHL9-KLHL13 ubiquitinates Aurora B, thereby promoting translocation of the CPC to the spindle midzone. KLHL21 and KLHL22 are other two novel regulators of mitosis. Unlike KLHL22, KLHL21 regulates CPC translocation at the onset of anaphase and is required for completion of cytokinesis. KLHL21 directly interacts with Aurora B and mediates ubiquitination of Aurora B *in vitro*. In contrast to KLHL9 and KLHL13, KLHL21 localizes to midzone microtubules during anaphase and targets Cul3 and Aurora B to this region. Thus, differential localization of distinct Cul3 complexes with KLHL9, KLHL13, and KLHL21 may target different pools of Aurora B during mitosis. KLHL21 may function as a specificity factor to ubiquitinate Aurora B on the midzone, whereas KLHL9 and KLHL13 may mainly target the cytoplasmic pool of Aurora B at this stage.³

References:

1. Seng, S. et al: Mol. Cell. Biol. 26:8371-84, 2006
2. Sumara, I. et al: Trends Cell Biol. 18:84-94, 2008
3. Maerki, S. et al: J. Cell Biol. 187:791-800, 2009

TECHNICAL INFORMATION

Source:

KLHL21 Antibody is a mouse monoclonal antibody raised against recombinant human KLHL21 fragments expressed in *E. coli*.

Specificity and Sensitivity:

This antibody detects endogenous KLHL21 proteins without cross-reactivity with other family members.

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.

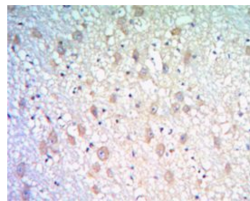
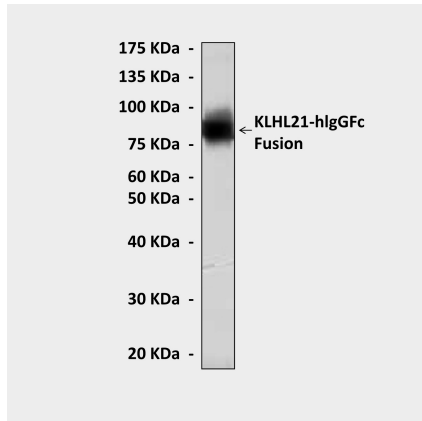
APPLICATIONS

Application:	*Dilution:
WB	1:1000
IP	n/d
IHC	1:50-200
ICC	n/d
FACS	n/d

**Optimal dilutions must be determined by end user.*



QUALITY CONTROL DATA



Top: Western Blot detection of KLHL21-hlgGfc fusion proteins in HEK293 cell lysate containing recombinant human KLHL21-hlgGfc fusion proteins using KLHL21 Antibody. **Bottom:** This antibody stains paraffin-embedded human brain tissue in immunohistochemical analysis.

