Revision 1

Store at -20C

#4617

KEAP1 (H436) Antibody

Cell Signaling TECHNOLOGY®

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For Research Use Only. Not for Use in Diagnostic Procedures.

Applications:	Reactivity:	Sensitivity:	MW (kDa):	Source:	UniProt ID:	Entrez-Gene Id:
WB, IP	H M R Mk	Endogenous	60-64	Rabbit	#Q14145	9817

Product Usage Information

Application	Dilution
Western Blotting	1:1000
Immunoprecipitation	1:50

Storage

Supplied in 10 mM sodium HEPES (pH 7.5), 150 mM NaCl, 100 µg/ml BSA and 50% glycerol. Store at –20°C. Do not aliquot the antibody.

Specificity / Sensitivity

KEAP1 (H436) Antibody detects endogenous levels of total KEAP1 protein.

Source / Purification

Polyclonal antibodies are produced by immunizing animals with a synthetic peptide corresponding to residues surrounding His436 of human KEAP1 protein. Antibodies were purified by protein A and peptide affinity chromatography.

Background

The nuclear factor-like 2 (NRF2) transcriptional activator binds antioxidant response elements (ARE) of target gene promoter regions to regulate expression of oxidative stress response genes. Under basal conditions, the NRF2 inhibitor INrf2 (also called KEAP1) binds and retains NRF2 in the cytoplasm where it can be targeted for ubiquitin-mediated degradation (1). Small amounts of constitutive nuclear NRF2 maintain cellular homeostasis through regulation of basal expression of antioxidant response genes. Following oxidative or electrophilic stress, KEAP1 releases NRF2, thereby allowing the activator to translocate to the nucleus and bind to ARE-containing genes (2). The coordinated action of NRF2 and other transcription factors mediates the response to oxidative stress (3). Altered expression of NRF2 is associated with chronic obstructive pulmonary disease (COPD) (4). NRF2 activity in lung cancer cell lines directly correlates with cell proliferation rates, and inhibition of NRF2 expression by siRNA enhances anti-cancer drug-induced apoptosis (5).
The NRF2 repressor KEAP1 contains an amino terminal BTB/POZ domain and a carboxyl terminal KELCH domain (6,7). The KELCH domain is required for interacting with NRF2 and the BTB/POZ domain functions in binding Cul3 E3 ubiquitin ligase (8-10). Under normal conditions, the complex leads to the cytoplasmic sequestration and ubiquitin-mediated proteasomal degradation of NRF2. Electrophilic modification of KEAP1 leads to disassociation of the NRF2/KEAP1 complex. KEAP1 also targets the down regulation of NF-κB activity by targeting IKKβ degradation (11). Mutation of the corresponding KEAP1 gene is seen in lung cancer cases and can lead to uncontrolled activation of NRF2 (12-14).

Background References

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12. Padmanabhan, B. et al. (2006) *Mol Cell* 21, 689-700.
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Species Reactivity

Species reactivity is determined by testing in at least one approved application (e.g., western blot).

Western Blot Buffer

IMPORTANT: For western blots, incubate membrane with diluted primary antibody in 5% w/v BSA, 1X TBS, 0.1% Tween® 20 at 4°C with gentle shaking, overnight.

Applications Key

WB: Western Blotting **IP:** Immunoprecipitation

Cross-Reactivity Key

H: human **M:** mouse **R:** rat **Hm:** hamster **Mk:** monkey **Vir:** virus **Mi:** mink **C:** chicken **Dm:** D. melanogaster **X:** Xenopus **Z:** zebrafish **B:** bovine **Dg:** dog **Pg:** pig **Sc:** S. cerevisiae **Ce:** C. elegans **Hr:** horse **GP:** Guinea Pig **Rab:** rabbit **All:** all species expected

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Limited Uses