Revision 4

Store at -20C

#12117

ITCH (D8Q6D) Rabbit mAb

Cell Signaling TECHNOLOGY®

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Applications:	Reactivity:	Sensitivity:	MW (kDa):	Source/Isotype:	UniProt ID:	Entrez-Gene Id:
W, IP	H M R	Endogenous	105	Rabbit IgG	#Q96J02	83737

Product Usage Information

Application	Dilution
Western Blotting	1:1000
Immunoprecipitation	1:200

Storage

Supplied in 10 mM sodium HEPES (pH 7.5), 150 mM NaCl, 100 µg/ml BSA, 50% glycerol and less than 0.02% sodium azide. Store at –20°C. Do not aliquot the antibody.

Specificity/Sensitivity

ITCH (D8Q6D) Rabbit mAb recognizes endogenous levels of total ITCH protein.

Source / Purification

Monoclonal antibody is produced by immunizing animals with a synthetic peptide corresponding to residues surrounding Asp125 of human ITCH protein.

Background

ITCH is a HECT domain-containing E3 ubiquitin ligase, first identified in genetic studies of the mouse *agouti* locus, in which mutations result in characteristic coat color changes. One particular *agouti* mutation (non-agouti-lethal 18H) is notable for the development of immunological defects not observed in other *agouti* mutant mice; these include lymphoid hyperplasia and chronic stomach, lung and skin inflammation (manifest as constant itching). The 18H *agouti* mutation was traced to a chromosomal inversion that disrupted expression of an adjacent gene in the *agouti* locus, subsequently termed *Itch* to reflect the chronic itching phenotype (1-3).
Further characterizations revealed that *Itch* encoded a NEDD4-like E3-ubiquitin ligase capable of catalyzing Lys29, Lys48, and/or Lys63-linked ubiquitination of target proteins, leading to their degradation by the proteosome pathway (4-6). The distinct phenotypes of *Itch* mutant mice led to the identification of an important regulatory role for ITCH-mediated ubiquitination in inflammatory signaling pathways. For example, ITCH-mediated ubiquitination of the transcription factor JunB was shown to play a direct inhibitory role in regulating expression of the proinflammatory cytokine IL-4. ITCH-null T lymphocytes consequently exhibit increased production of IL-4, leading to biased differentiation of naive $CD4^+$ cells towards the proinflammatory Th2 lineage (7). In accordance with the findings from mutant *Itch* mouse models, a genetic linkage study in humans identified loss-of-function mutations in *ITCH* as a direct cause of syndromic multisystem autoimmune disease (SMAD) (8).
Notably, targets of ITCH-mediated ubiquitination are not restricted to immune signaling pathways. For example, key mediators of the Hedgehog (9,10), Wnt/β-catenin (11), Hippo (12), and Notch signaling pathways (13,14) have been identified as important targets of ITCH-mediated ubiquitination (2).

Background References

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12. Salah, Z. et al. (2011) *Cancer Res* 71, 2010-20.
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14. McGill, M.A. and McGlade, C.J. (2003) *J Biol Chem* 278, 23196-203.

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 nonfat dry milk, 1X TBS, 0.1% Tween® 20 at 4°C with gentle shaking, overnight.

Applications Key

W: Western Blotting **IP:** Immunoprecipitation

Cross-Reactivity Key

H: Human **M:** Mouse **R:** Rat

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