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ITCH/AIP4 Polyclonal Antibody

Purified Rabbit Polyclonal Antibody (Pab)
Catalog # AP59068

Product Information

Application	WB, IHC-P, IHC-F, IF, ICC
Primary Accession	Q96J02
Reactivity	Rat, Pig, Dog, Bovine
Host	Rabbit
Clonality	Polyclonal
Calculated MW	102803
Physical State	Liquid
Immunogen	KLH conjugated synthetic peptide derived from human ITCH/AIP4
Epitope Specificity	2-100/903
Isotype	IgG
Purity	affinity purified by Protein A
Buffer	Preservative: 0.02% Proclin300, Constituents: 1% BSA, 0.01M PBS, pH7.4.
SUBCELLULAR LOCATION	Cell membrane. Cytoplasm. Nucleus. Associates with endocytic vesicles. May be recruited to exosomes by NDFIP1.
SIMILARITY	Contains 1 C2 domain. Contains 1 HECT (E6AP-type E3 ubiquitin-protein ligase) domain. Contains 4 WW domains.
Post-translational modifications	On T-cell activation, phosphorylation by the JNK cascade on serine and threonine residues surrounding the PRR domain accelerates the ubiquitination and degradation of JUN and JUNB. The increased ITCH catalytic activity due to phosphorylation by JNK1 may occur due to a conformational change disrupting the interaction between the PRR/WW motifs domain and the HECT domain and, thus exposing the HECT domain (By similarity). Phosphorylation by FYN reduces interaction with JUNB and negatively controls JUN ubiquitination and degradation. Ubiquitinated; autopolyubiquitination with 'Lys-63' linkages which does not lead to protein degradation.
DISEASE	Defects in ITCH are the cause of syndromic multisystem autoimmune disease (SMAD) [MIM:613385]. SMAD is characterized by organomegaly, failure to thrive, developmental delay, dysmorphic features and autoimmune inflammatory cell infiltration of the lungs, liver and gut.
Important Note	This product as supplied is intended for research use only, not for use in human, therapeutic or diagnostic applications.
Background Descriptions	Acts as an 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. It catalyzes 'Lys-29'-, 'Lys-48'- and 'Lys-63'-linked ubiquitin conjugation. It is involved in the control of inflammatory signaling pathways. Is an essential component of a ubiquitin-editing protein complex, comprising also TNFAIP3, TAX1BP1 and RNF11, that ensures the transient nature of inflammatory signaling pathways. Promotes the association of the complex after TNF stimulation. Once the complex is formed, TNFAIP3 deubiquitinates 'Lys-63' polyubiquitin chains on RIPK1 and catalyzes the formation of 'Lys-48'-polyubiquitin chains. This leads to RIPK1 proteosomal degradation and consequently termination of the TNF-

or LPS-mediated activation of NFKB1. Ubiquitinates RIPK2 by 'Lys-63'-linked conjugation and influences NOD2-dependent signal transduction pathways. Regulates the transcriptional activity of several transcription factors, and probably plays an important role in the regulation of immune response. Ubiquitinates NFE2 by 'Lys-63' linkages and is implicated in the control of the development of hematopoietic lineages. Critical regulator of T helper (TH2) cytokine development through its ability to induce JUNB ubiquitination and degradation (By similarity). Ubiquitinates SNX9. Ubiquitinates CXCR4 and HGS/HRS and regulates sorting of CXCR4 to the degradative pathway. It is involved in the negative regulation of MAVS-dependent cellular antiviral responses. Ubiquitinates MAVS through 'Lys-48'-linked conjugation resulting in MAVS proteosomal degradation. Involved in the regulation of apoptosis and reactive oxygen species levels through the ubiquitination and proteosomal degradation of TXNIP. Mediates the antiapoptotic activity of epidermal growth factor through the ubiquitination and proteosomal degradation of p15 BID. Targets DTX1 for lysosomal degradation and controls NOTCH1 degradation, in the absence of ligand, through 'Lys-29'-linked polyubiquitination.

Additional Information

Gene ID	83737
Other Names	E3 ubiquitin-protein ligase Itchy homolog, Itch, 2.3.2.26, Atrophin-1-interacting protein 4, AIP4, HECT-type E3 ubiquitin transferase Itchy homolog, NFE2-associated polypeptide 1, NAPP1, ITCH
Target/Specificity	Widely expressed.
Dilution	WB=1:500-2000,IHC-P=1:100-500,IHC-F=1:100-500,ICC=1:100-500,IF=1:100-500
Format	0.01M TBS(pH7.4) with 1% BSA, 0.09% (W/V) sodium azide and 50% Glyce
Storage	Store at -20 °C for one year. Avoid repeated freeze/thaw cycles. When reconstituted in sterile pH 7.4 0.01M PBS or diluent of antibody the antibody is stable for at least two weeks at 2-4 °C.

Protein Information

Name	ITCH
Function	Acts as an Acts as an 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 (PubMed:11046148, PubMed:14602072, PubMed:15051726, PubMed:16387660, PubMed:17028573, PubMed:18718448, PubMed:18718449, PubMed:19116316, PubMed:19592251, PubMed:19881509, PubMed:20068034, PubMed:20392206, PubMed:20491914, PubMed:23146885, PubMed:24790097, PubMed:25631046). Catalyzes 'Lys-29'-, 'Lys-48'- and 'Lys-63'-linked ubiquitin conjugation (PubMed:17028573, PubMed:18718448, PubMed:19131965, PubMed:19881509). Involved in the control of inflammatory signaling pathways (PubMed:19131965). Essential component of a ubiquitin-editing protein complex, comprising also TNFAIP3, TAX1BP1 and RNF11, that ensures the transient nature of inflammatory signaling pathways (PubMed:19131965).

Promotes the association of the complex after TNF stimulation (PubMed:19131965). Once the complex is formed, TNFAIP3 deubiquitinates 'Lys-63' polyubiquitin chains on RIPK1 and catalyzes the formation of 'Lys-48'-polyubiquitin chains (PubMed:19131965). This leads to RIPK1 proteasomal degradation and consequently termination of the TNF- or LPS-mediated activation of NFKB1 (PubMed:19131965). Ubiquitinates RIPK2 by 'Lys-63'-linked conjugation and influences NOD2-dependent signal transduction pathways (PubMed:19592251). Regulates the transcriptional activity of several transcription factors, and probably plays an important role in the regulation of immune response (PubMed:18718448, PubMed:20491914). Ubiquitinates NFE2 by 'Lys-63' linkages and is implicated in the control of the development of hematopoietic lineages (PubMed:18718448). Mediates JUN ubiquitination and degradation (By similarity). Mediates JUNB ubiquitination and degradation (PubMed:16387660). Critical regulator of type 2 helper T (Th2) cell cytokine production by inducing JUNB ubiquitination and degradation (By similarity). Involved in the negative regulation of MAVS-dependent cellular antiviral responses (PubMed:19881509). Ubiquitinates MAVS through 'Lys-48'-linked conjugation resulting in MAVS proteasomal degradation (PubMed:19881509). Following ligand stimulation, regulates sorting of Wnt receptor FZD4 to the degradative endocytic pathway probably by modulating PI42KA activity (PubMed:23146885). Ubiquitinates PI4K2A and negatively regulates its catalytic activity (PubMed:23146885). Ubiquitinates chemokine receptor CXCR4 and regulates sorting of CXCR4 to the degradative endocytic pathway following ligand stimulation by ubiquitinating endosomal sorting complex required for transport ESCRT-0 components HGS and STAM (PubMed:14602072, PubMed:23146885, PubMed:34927784). Targets DTX1 for lysosomal degradation and controls NOTCH1 degradation, in the absence of ligand, through 'Lys-29'-linked polyubiquitination (PubMed:17028573, PubMed:18628966, PubMed:23886940). Ubiquitinates SNX9 (PubMed:20491914). Ubiquitinates MAP3K7 through 'Lys-48'-linked conjugation (By similarity). Together with UBR5, involved in the regulation of apoptosis and reactive oxygen species levels through the ubiquitination and proteasomal degradation of TXNIP: catalyzes 'Lys-48'-/'Lys-63'-branched ubiquitination of TXNIP (PubMed:20068034, PubMed:29378950). ITCH synthesizes 'Lys-63'-linked chains, while UBR5 is branching multiple 'Lys-48'-linked chains of substrate initially modified (PubMed:29378950). Mediates the antiapoptotic activity of epidermal growth factor through the ubiquitination and proteasomal degradation of p15 BID (PubMed:20392206). Ubiquitinates BRAT1 and this ubiquitination is enhanced in the presence of NDFIP1 (PubMed:25631046). Inhibits the replication of influenza A virus (IAV) via ubiquitination of IAV matrix protein 1 (M1) through 'Lys-48'-linked conjugation resulting in M1 proteasomal degradation (PubMed:30328013). Ubiquitinates NEDD9/HEF1, resulting in proteasomal degradation of NEDD9/HEF1 (PubMed:15051726).

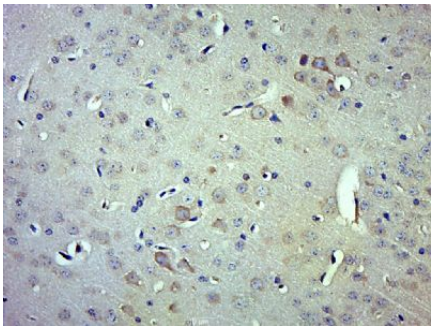
Cellular Location

Cell membrane; Peripheral membrane protein; Cytoplasmic side. Cytoplasm. Nucleus Early endosome membrane; Peripheral membrane protein; Cytoplasmic side. Endosome membrane; Peripheral membrane protein; Cytoplasmic side. Note=May be recruited to exosomes by NDFIP1 (PubMed:18819914). Localizes to plasma membrane upon CXCL12 stimulation where it co-localizes with CXCL4 (PubMed:14602072) Localization to early endosomes is increased upon CXCL12 stimulation where it co-localizes with DTX3L and CXCL4 (PubMed:24790097)

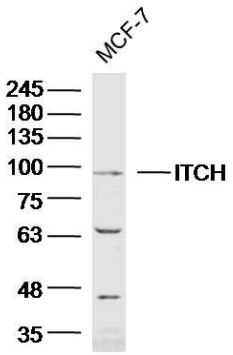
Tissue Location

Widely expressed.

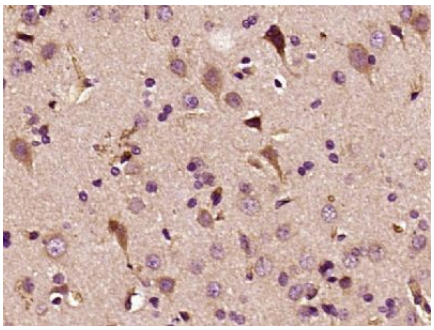
Images



Paraformaldehyde-fixed, paraffin embedded (Mouse brain); Antigen retrieval by boiling in sodium citrate buffer (pH6.0) for 15min; Block endogenous peroxidase by 3% hydrogen peroxide for 20 minutes; Blocking buffer (normal goat serum) at 37°C for 30min; Antibody incubation with (ITCH) Polyclonal Antibody, Unconjugated (AP59068) at 1:500 overnight at 4°C, followed by a conjugated secondary (sp-0023) for 20 minutes and DAB staining.



Sample:
MCF-7 Cell (Human) Lysate at 40 ug
Primary: Anti-ITCH/AIP4 (AP59068) at 1/300 dilution
Secondary: IRDye800CW Goat Anti-Rabbit IgG at 1/20000 dilution
Predicted band size: 103 kD
Observed band size: 98 kD



Paraformaldehyde-fixed, paraffin embedded (Rat brain); Antigen retrieval by boiling in sodium citrate buffer (pH6.0) for 15min; Block endogenous peroxidase by 3% hydrogen peroxide for 20 minutes; Blocking buffer (normal goat serum) at 37°C for 30min; Antibody incubation with (ITCH AIP4) Polyclonal Antibody, Unconjugated (AP59068) at 1:400 overnight at 4°C, followed by operating according to SP Kit(Rabbit) (sp-0023) instructionsand DAB staining.