10320 Camino Santa Fe, Suite G
San Diego, CA 92121
Tel: 858.875.1900 Fax: 858.875.1999

FLCN Recombinant Rabbit mAb

Catalog # AP100308

Product Information

Application	WB, IHC-P, IHC-F, IF, IP, E
Primary Accession	Q8NFG4
Other Accession	Q8NFG4
Reactivity	Human
Host	Rabbit
Clonality	Recombinant
Calculated MW	64473
Isotype	IgG
Purity	affinity purified by Protein A
Buffer	0.01M TBS (pH7.4) with 1% BSA, 0.02% Proclin300 and 50% Glycerol.
SIMILARITY	Belongs to the folliculin family.
SUBUNIT	Interacts (via C-terminus) with FNIP1 and FNIP2 (via C-terminus). This mediates indirect interaction with the PRKAA1, PRKAB1 and PRKAG1 subunits of 5'-AMP-activated protein kinase.
Post-translational modifications	Phosphorylated. Several different phosphorylated forms exist.
DISEASE	Defects in FLCN are the cause of Birt-Hogg-Dube syndrome (BHD) [MIM:135150]. BHD is a rare autosomal dominant genodermatosis characterized by hair follicle hamartomas (fibrofolliculomas), kidney tumors, and spontaneous pneumothorax. Fibrofolliculomas are part of the triad of BHD skin lesions that also includes trichodiscomas and acrochordons. Onset of this dermatologic condition is invariably in adulthood. BHD is associated with a variety of histologic types of renal tumors, including chromophobe renal cell carcinoma (RCC), benign renal oncocytoma, clear-cell RCC and papillary type I RCC. Multiple lipomas, angiolipomas, and parathyroid adenomas are also seen in patients affected with this disease. The majority of mutations are predicted to prematurely terminate the protein. Defects in FLCN are in some cases a cause of primary spontaneous pneumothorax (PSP) [MIM:173600]. PSP is a condition in which air is present in the pleural space in the absence of a precipitating event, such as trauma or lung disease. This results in secondary collapse of the lung, either partially or completely, and some degree of hypoxia. PSP is relatively common, with an incidence between 7.4-18/100'000 for men and 1.2-6/100'000 for women and a dose-dependent, increased risk among smokers. Most cases are sporadic, typically occurring in tall, thin men aged 10-30 years and generally while at rest. Familial PSP is rarer and usually is inherited as an autosomal dominant condition with reduced penetrance, although X-linked recessive and autosomal recessive inheritance have also been suggested. Defects in FLCN may be a cause of renal cell carcinoma (RCC) [MIM:144700]. Renal cell carcinoma is a heterogeneous group of sporadic or hereditary carcinoma derived from cells of the proximal renal tubular epithelium. It is subclassified into clear cell renal carcinoma (non-papillary carcinoma), papillary renal cell carcinoma, chromophobe renal cell carcinoma, collecting duct carcinoma with medullary carcinoma of the kidney, and unclassified renal cell carcinoma. Clear cell renal cell carcinoma is the most common subtype.

Background Descriptions	This gene is located within the Smith-Magenis syndrome region on chromosome 17. Mutations in this gene are associated with Birt-Hogg-Dube syndrome, which is characterized by fibrofolliculomas, renal tumors, lung cysts, and pneumothorax. Alternative splicing of this gene results in three transcript variants encoding different isoforms.

Additional Information

Gene ID	201163
Other Names	BHD; DENND8B; FLCL; FLCN_HUMAN; FLCN; BHD skin lesion fibrofolliculoma protein; Birt-Hogg-Dube syndrome protein; folliculin; Folliculin (BHD skin lesion fibrofolliculoma protein) (Birt-Hogg-Dube syndrome protein)
Dilution	IHC-P=1:50-200,IHC-F=1:50-200,WB=1:500-2000,IF=1:50-200,ELISA=1:5000-10000,IP=1:50-200
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	FLCN {ECO:0000303|PubMed:15657874, ECO:0000312|HGNC:HGNC:27310}
Function	Multi-functional protein, involved in both the cellular response to amino acid availability and in the regulation of glycolysis (PubMed:17028174, PubMed:18663353, PubMed:21209915, PubMed:24081491, PubMed:24095279, PubMed:31672913, PubMed:31704029, PubMed:32612235, PubMed:34381247, PubMed:36103527, PubMed:37079666). GTPase-activating protein that plays a key role in the cellular response to amino acid availability through regulation of the non-canonical mTORC1 signaling cascade controlling the MiT/TFE factors TFEB and TFE3 (PubMed:17028174, PubMed:18663353, PubMed:21209915, PubMed:24081491, PubMed:24095279, PubMed:24448649, PubMed:31672913, PubMed:31704029, PubMed:32612235, PubMed:36103527, PubMed:37079666). Activates mTORC1 by acting as a GTPase-activating protein: specifically stimulates GTP hydrolysis by RagC/RRAGC or RagD/RRAGD, promoting the conversion to the GDP-bound state of RagC/RRAGC or RagD/RRAGD, and thereby activating the kinase activity of mTORC1 (PubMed:24095279, PubMed:31672913, PubMed:31704029, PubMed:32612235, PubMed:37079666). The GTPase-activating activity is inhibited during starvation and activated in presence of nutrients (PubMed:31672913, PubMed:32612235). Acts as a key component for non- canonical mTORC1-dependent control of the MiT/TFE factors TFEB and TFE3, while it is not involved in mTORC1-dependent phosphorylation of canonical RPS6KB1/S6K1 and EIF4EBP1/4E-BP1 (PubMed:21209915, PubMed:24081491, PubMed:31672913, PubMed:32612235). In low-amino acid conditions, the lysosomal folliculin complex (LFC) is formed on the membrane of lysosomes, which inhibits the GTPase-activating activity of FLCN, inactivates mTORC1 and maximizes nuclear translocation of TFEB and TFE3 (PubMed:31672913). Upon amino acid restimulation, RagA/RRAGA (or RagB/RRAGB) nucleotide exchange promotes disassembly of the LFC complex and liberates the GTPase-activating activity of FLCN, leading to activation of mTORC1 and subsequent cytoplasmic retention of TFEB and TFE3 (PubMed:31672913). Indirectly acts as a positive regulator of

Wnt signaling by promoting mTOR-dependent cytoplasmic retention of MiT/TFE factor TFE3 (PubMed:31272105). Required for the exit of hematopoietic stem cell from pluripotency by promoting mTOR-dependent cytoplasmic retention of TFE3, thereby increasing Wnt signaling (PubMed:30733432). Acts as an inhibitor of browning of adipose tissue by regulating mTOR-dependent cytoplasmic retention of TFE3 (By similarity). Involved in the control of embryonic stem cells differentiation; together with LAMTOR1 it is necessary to recruit and activate RagC/RRAGC and RagD/RRAGD at the lysosomes, and to induce exit of embryonic stem cells from pluripotency via non-canonical, mTOR- independent TFE3 inactivation (By similarity). In response to flow stress, regulates STK11/LKB1 accumulation and mTORC1 activation through primary cilia: may act by recruiting STK11/LKB1 to primary cilia for activation of AMPK resided at basal bodies, causing mTORC1 down- regulation (PubMed:27072130). Together with FNIP1 and/or FNIP2, regulates autophagy: following phosphorylation by ULK1, interacts with GABARAP and promotes autophagy (PubMed:25126726). Interaction with GABARAP also inhibits the non-canonical mTORC1 signaling cascade: GABARAP sequesters FLCN, thereby inactivating mTORC1 and promoting nuclear translocation of TFEB and TFE3 (PubMed:34597140, PubMed:39423796). Required for starvation-induced perinuclear clustering of lysosomes by promoting association of RILP with its effector RAB34 (PubMed:27113757). Regulates glycolysis by binding to lactate dehydrogenase LDHA, acting as an uncompetitive inhibitor (PubMed:34381247).

Cellular Location

Lysosome membrane. Cytoplasm, cytosol. Cell projection, cilium. Cytoplasm, cytoskeleton, microtubule organizing center, centrosome. Cytoplasm, cytoskeleton, spindle. Nucleus Note=Localizes to lysosome membrane in amino acid-depleted conditions and relocalizes to the cytosol upon refeeding (PubMed:24095279, PubMed:29848618, PubMed:31672913). Colocalizes with FNIP1 and FNIP2 in the cytoplasm (PubMed:17028174, PubMed:18663353). Also localizes to motile and non-motile cilia, centrosomes and the mitotic spindle (PubMed:23784378).

Tissue Location

Expressed in most tissues tested, including skin, lung, kidney, heart, testis and stomach.

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