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Parkin Antibody (N-term)

Purified Rabbit Polyclonal Antibody (Pab)
Catalog # AP6402a

Product Information

Application	WB, E
Primary Accession	O60260
Other Accession	NP_004553
Reactivity	Human
Predicted	Bovine
Host	Rabbit
Clonality	Polyclonal
Isotype	Rabbit IgG
Clone Names	RB7371
Calculated MW	51641
Antigen Region	111-140

Additional Information

Gene ID	5071
Other Names	E3 ubiquitin-protein ligase parkin, 632-, Parkinson juvenile disease protein 2, Parkinson disease protein 2, PARK2, PRKN
Target/Specificity	This Parkin antibody is generated from rabbits immunized with a KLH conjugated synthetic peptide between 111-140 amino acids from the N-terminal region of human Parkin.
Dilution	WB~~1:2000 E~~Use at an assay dependent concentration.
Format	Purified polyclonal antibody supplied in PBS with 0.09% (W/V) sodium azide. This antibody is prepared by Saturated Ammonium Sulfate (SAS) precipitation followed by dialysis against PBS.
Storage	Maintain refrigerated at 2-8°C for up to 2 weeks. For long term storage store at -20°C in small aliquots to prevent freeze-thaw cycles.
Precautions	Parkin Antibody (N-term) is for research use only and not for use in diagnostic or therapeutic procedures.

Protein Information

Name	PRKN (HGNC:8607)
Synonyms	PARK2

Function

Functions within a multiprotein E3 ubiquitin ligase complex, catalyzing the covalent attachment of ubiquitin moieties onto substrate proteins (PubMed:10888878, PubMed:10973942, PubMed:11431533, PubMed:12150907, PubMed:12628165, PubMed:15105460, PubMed:16135753, PubMed:21376232, PubMed:21532592, PubMed:22396657, PubMed:23620051, PubMed:23754282, PubMed:24660806, PubMed:24751536, PubMed:29311685, PubMed:32047033). Substrates include SYT11 and VDAC1 (PubMed:29311685, PubMed:32047033). Other substrates are BCL2, CCNE1, GPR37, RHOT1/MIRO1, MFN1, MFN2, STUB1, SNCAIP, SEPTIN5, TOMM20, USP30, ZNF746, MIRO1 and AIMP2 (PubMed:10888878, PubMed:10973942, PubMed:11431533, PubMed:12150907, PubMed:12628165, PubMed:15105460, PubMed:16135753, PubMed:21376232, PubMed:21532592, PubMed:22396657, PubMed:23620051, PubMed:23754282, PubMed:24660806, PubMed:24751536). Mediates monoubiquitination as well as 'Lys-6', 'Lys-11', 'Lys-48'-linked and 'Lys-63'-linked polyubiquitination of substrates depending on the context (PubMed:19229105, PubMed:20889974, PubMed:25474007, PubMed:25621951, PubMed:32047033). Participates in the removal and/or detoxification of abnormally folded or damaged protein by mediating 'Lys-63'-linked polyubiquitination of misfolded proteins such as PARK7: 'Lys-63'-linked polyubiquitinated misfolded proteins are then recognized by HDAC6, leading to their recruitment to aggresomes, followed by degradation (PubMed:17846173, PubMed:19229105). Mediates 'Lys-63'-linked polyubiquitination of a 22 kDa O-linked glycosylated isoform of SNCAIP, possibly playing a role in Lewy-body formation (PubMed:11431533, PubMed:11590439, PubMed:15105460, PubMed:15728840, PubMed:19229105). Mediates monoubiquitination of BCL2, thereby acting as a positive regulator of autophagy (PubMed:20889974). Protects against mitochondrial dysfunction during cellular stress, by acting downstream of PINK1 to coordinate mitochondrial quality control mechanisms that remove and replace dysfunctional mitochondrial components (PubMed:11439185, PubMed:18957282, PubMed:19029340, PubMed:19966284, PubMed:21376232, PubMed:22082830, PubMed:22396657, PubMed:23620051, PubMed:23933751, PubMed:24660806, PubMed:24784582, PubMed:24896179, PubMed:25474007, PubMed:25527291, PubMed:32047033). Depending on the severity of mitochondrial damage and/or dysfunction, activity ranges from preventing apoptosis and stimulating mitochondrial biogenesis to regulating mitochondrial dynamics and eliminating severely damaged mitochondria via mitophagy (PubMed:11439185, PubMed:19029340, PubMed:19801972, PubMed:19966284, PubMed:21376232, PubMed:22082830, PubMed:22396657, PubMed:23620051, PubMed:23685073, PubMed:23933751, PubMed:24896179, PubMed:25527291, PubMed:32047033, PubMed:33499712). Activation and recruitment onto the outer membrane of damaged/dysfunctional mitochondria (OMM) requires PINK1-mediated phosphorylation of both PRKN and ubiquitin (PubMed:24660806, PubMed:24784582, PubMed:25474007, PubMed:25527291). After mitochondrial damage, functions with PINK1 to mediate the decision between mitophagy or preventing apoptosis by inducing either the poly- or monoubiquitination of VDAC1, respectively; polyubiquitination of VDAC1 promotes mitophagy, while monoubiquitination of VDAC1 decreases mitochondrial calcium influx which ultimately inhibits apoptosis (PubMed:27534820, PubMed:32047033). When cellular stress results in irreversible mitochondrial damage, promotes the autophagic degradation of dysfunctional depolarized mitochondria (mitophagy) by promoting the ubiquitination of mitochondrial proteins such as TOMM20, RHOT1/MIRO1, MFN1 and USP30 (PubMed:19029340, PubMed:19966284, PubMed:21753002, PubMed:22396657, PubMed:23620051, PubMed:23685073, PubMed:23933751, PubMed:24896179,

PubMed:25527291). Preferentially assembles 'Lys-6'-, 'Lys-11'- and 'Lys-63'-linked polyubiquitin chains, leading to mitophagy (PubMed:25621951, PubMed:32047033). The PINK1-PRKN pathway also promotes fission of damaged mitochondria by PINK1-mediated phosphorylation which promotes the PRKN-dependent degradation of mitochondrial proteins involved in fission such as MFN2 (PubMed:23620051). This prevents the refusion of unhealthy mitochondria with the mitochondrial network or initiates mitochondrial fragmentation facilitating their later engulfment by autophagosomes (PubMed:23620051). Regulates motility of damaged mitochondria via the ubiquitination and subsequent degradation of MIRO1 and MIRO2; in motor neurons, this likely inhibits mitochondrial intracellular anterograde transport along the axons which probably increases the chance of the mitochondria undergoing mitophagy in the soma (PubMed:22396657). Involved in mitochondrial biogenesis via the 'Lys-48'-linked polyubiquitination of transcriptional repressor ZNF746/PARIS which leads to its subsequent proteasomal degradation and allows activation of the transcription factor PPARGC1A (PubMed:21376232). Limits the production of reactive oxygen species (ROS) (PubMed:18541373). Regulates cyclin-E during neuronal apoptosis (PubMed:12628165). In collaboration with CHPF isoform 2, may enhance cell viability and protect cells from oxidative stress (PubMed:22082830). Independently of its ubiquitin ligase activity, protects from apoptosis by the transcriptional repression of p53/TP53 (PubMed:19801972). May protect neurons against alpha synuclein toxicity, proteasomal dysfunction, GPR37 accumulation, and kainate-induced excitotoxicity (PubMed:11439185). May play a role in controlling neurotransmitter trafficking at the presynaptic terminal and in calcium-dependent exocytosis. May represent a tumor suppressor gene (PubMed:12719539).

Cellular Location

Cytoplasm, cytosol. Nucleus. Endoplasmic reticulum. Mitochondrion. Mitochondrion outer membrane {ECO:0000250|UniProtKB:Q9WVS6}. Cell projection, neuron projection. Postsynaptic density {ECO:0000250|UniProtKB:Q9WVS6}. Presynapse {ECO:0000250|UniProtKB:Q9WVS6}. Note=Mainly localizes in the cytosol (PubMed:19029340, PubMed:19229105). Co-localizes with SYT11 in neutrites (PubMed:12925569). Co-localizes with SNCAIP in brainstem Lewy bodies (PubMed:10319893, PubMed:11431533). Translocates to dysfunctional mitochondria that have lost the mitochondrial membrane potential; recruitment to mitochondria is PINK1-dependent (PubMed:18957282, PubMed:19966284, PubMed:23620051, PubMed:24898855) Mitochondrial localization also gradually increases with cellular growth (PubMed:22082830).

Tissue Location

Highly expressed in the brain including the substantia nigra (PubMed:19501131, PubMed:9560156). Expressed in heart, testis and skeletal muscle (PubMed:9560156). Expression is down- regulated or absent in tumor biopsies, and absent in the brain of PARK2 patients (PubMed:12719539, PubMed:14614460). Overexpression protects dopamine neurons from kainate-mediated apoptosis (PubMed:12628165) Found in serum (at protein level) (PubMed:19501131)

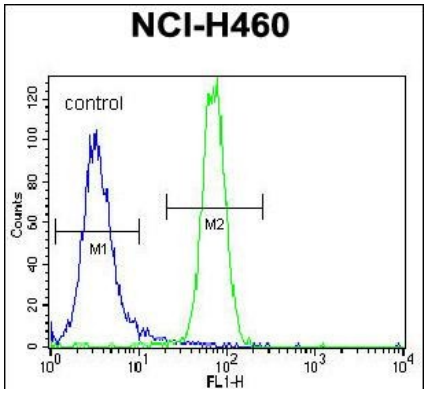
Background

Parkinson is the second most common neurodegenerative disease after Alzheimers. About 1 percent of people over the age of 65 and 3 percent of people over the age of 75 are affected by the disease. The mutation is the most common cause of Parkinson disease identified to date. The function of Park2 is not well-known; however, it may play a role in the ubiquitin-mediated proteolytic pathway. Mutations in this gene are known to cause autosomal recessive juvenile parkinsonism. Alternative splicing of this gene produces three known products of undetermined function.

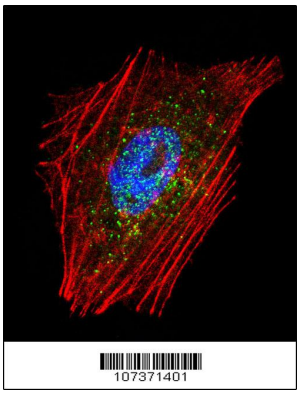
References

Kumru, H., et al., Ann. Neurol. 56(4):599-603 (2004). Pigullo, S., et al., Parkinsonism Relat. Disord. 10(6):357-362 (2004). Yao, D., et al., Proc. Natl. Acad. Sci. U.S.A. 101(29):10810-10814 (2004). West, A.B., et al., J. Biol. Chem. 279(28):28896-28902 (2004). Wang, F., et al., Genes Chromosomes Cancer 40(2):85-96 (2004).

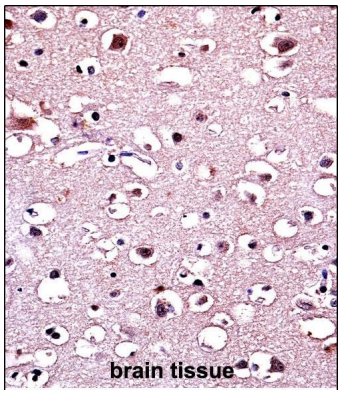
Images



Parkin Antibody (N-term) (Cat. #AP6402a) flow cytometric analysis of NCI-H460 cells (right histogram) compared to a negative control cell (left histogram).FITC-conjugated goat-anti-rabbit secondary antibodies were used for the analysis.

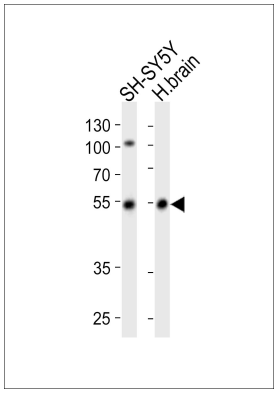


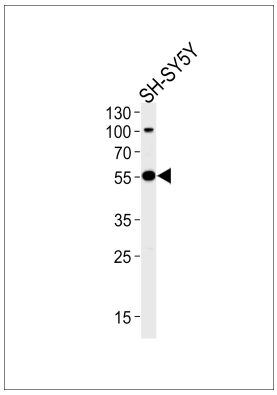
Confocal immunofluorescent analysis of Parkin Antibody (N-term)(Cat#AP6402a) with NCI-H460 cell followed by Alexa Fluor 488-conjugated goat anti-rabbit lgG (green).Actin filaments have been labeled with Alexa Fluor 555 phalloidin (red).DAPI was used to stain the cell nuclear (blue).



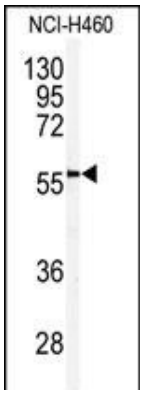
Parkin Antibody (N-term) (AP6402a)immunohistochemistry analysis in formalin fixed and paraffin embedded human brain tissue followed by peroxidase conjugation of the secondary antibody and DAB staining.This data demonstrates the use of Parkin Antibody (N-term) for immunohistochemistry. Clinical relevance has not been evaluated.

Western blot analysis of lysates from SH-SY5Y cell line, human brain tissue lysate (from left to right), using Park2 Antibody (N-term)(Cat. #AP6402a). AP6402a was diluted at 1:1000 at each lane. A goat anti-rabbit IgG H&L(HRP) at 1:10000 dilution was used as the secondary antibody. Lysates at 20ug per lane.





Western blot analysis of lysate from SH-SY5Y cell line, using Park2 Antibody (N-term) (Cat. #AP6402a). AP6402a was diluted at 1:1000 at each lane. A goat anti-rabbit (HRP) at 1:5000 dilution was used as the secondary antibody. Lysate at 35ug.



Western blot analysis of anti-PARK2 (Parkin) Antibody (N-term) (Cat.#AP6402a) in NCI-H460 cell line lysates (35ug/lane). PARK2 (Parkin)(arrow) was detected using the purified Pab.

Please note: All products are 'FOR RESEARCH USE ONLY. NOT FOR USE IN DIAGNOSTIC OR THERAPEUTIC PROCEDURES'.