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PARK8 (LRRK2) Antibody

Purified Mouse Monoclonal Antibody (Mab)
Catalog # AM7099a

Product Information

Application	WB, IHC-P, E
Primary Accession	Q5S007
Reactivity	Human, Mouse
Host	Mouse
Clonality	Monoclonal
Isotype	Mouse IgG1
Clone Names	133AT1218
Calculated MW	286103

Additional Information

Gene ID	120892
Other Names	Leucine-rich repeat serine/threonine-protein kinase 2, Dardarin, LRRK2, PARK8
Target/Specificity	This PARK8 (LRRK2) antibody was raised in mice using purified His-tagged recombinant protein comprised of the C-terminal 261 residues of LRRK2.
Dilution	WB~~1:100~500 IHC-P~~1:100~500 E~~Use at an assay dependent concentration.
Format	Purified monoclonal antibody supplied in PBS with 0.09% (W/V) sodium azide. This antibody is purified through a protein G column, 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	PARK8 (LRRK2) Antibody is for research use only and not for use in diagnostic or therapeutic procedures.

Protein Information

Name	LRRK2
Synonyms	PARK8
Function	Serine/threonine-protein kinase which phosphorylates a broad range of proteins involved in multiple processes such as neuronal plasticity, innate immunity, autophagy, and vesicle trafficking (PubMed:17114044,

PubMed:20949042, PubMed:21850687, PubMed:22012985, PubMed:23395371, PubMed:24687852, PubMed:25201882, PubMed:26014385, PubMed:26824392, PubMed:27830463, PubMed:28720718, PubMed:29125462, PubMed:29127255, PubMed:29212815, PubMed:30398148, PubMed:30635421). Is a key regulator of RAB GTPases by regulating the GTP/GDP exchange and interaction partners of RABs through phosphorylation (PubMed:26824392, PubMed:28720718, PubMed:29125462, PubMed:29127255, PubMed:29212815, PubMed:30398148, PubMed:30635421). Phosphorylates RAB3A, RAB3B, RAB3C, RAB3D, RAB5A, RAB5B, RAB5C, RAB8A, RAB8B, RAB10, RAB12, RAB29, RAB35, and RAB43 (PubMed:23395371, PubMed:26824392, PubMed:28720718, PubMed:29125462, PubMed:29127255, PubMed:29212815, PubMed:30398148, PubMed:30635421, PubMed:38127736). Regulates the RAB3IP-catalyzed GDP/GTP exchange for RAB8A through the phosphorylation of 'Thr-72' on RAB8A (PubMed:26824392). Inhibits the interaction between RAB8A and GDI1 and/or GDI2 by phosphorylating 'Thr-72' on RAB8A (PubMed:26824392). Regulates primary ciliogenesis through phosphorylation of RAB8A and RAB10, which promotes SHH signaling in the brain (PubMed:29125462, PubMed:30398148). Together with RAB29, plays a role in the retrograde trafficking pathway for recycling proteins, such as mannose-6-phosphate receptor (M6PR), between lysosomes and the Golgi apparatus in a retromer-dependent manner (PubMed:23395371). Regulates neuronal process morphology in the intact central nervous system (CNS) (PubMed:17114044). Plays a role in synaptic vesicle trafficking (PubMed:24687852). Plays an important role in recruiting SEC16A to endoplasmic reticulum exit sites (ERES) and in regulating ER to Golgi vesicle-mediated transport and ERES organization (PubMed:25201882). Positively regulates autophagy through a calcium-dependent activation of the CaMKK/AMPK signaling pathway (PubMed:22012985). The process involves activation of nicotinic acid adenine dinucleotide phosphate (NAADP) receptors, increase in lysosomal pH, and calcium release from lysosomes (PubMed:22012985). Phosphorylates PRDX3 (PubMed:21850687). By phosphorylating APP on 'Thr-743', which promotes the production and the nuclear translocation of the APP intracellular domain (AICD), regulates dopaminergic neuron apoptosis (PubMed:28720718). Acts as a positive regulator of innate immunity by mediating phosphorylation of RIPK2 downstream of NOD1 and NOD2, thereby enhancing RIPK2 activation (PubMed:27830463). Independent of its kinase activity, inhibits the proteasomal degradation of MAPT, thus promoting MAPT oligomerization and secretion (PubMed:26014385). In addition, has GTPase activity via its Roc domain which regulates LRRK2 kinase activity (PubMed:18230735, PubMed:26824392, PubMed:28720718, PubMed:29125462, PubMed:29212815). Recruited by RAB29/RAB7L1 to overloaded lysosomes where it phosphorylates and stabilizes RAB8A and RAB10 which promote lysosomal content release and suppress lysosomal enlargement through the EHBP1 and EHBP1L1 effector proteins (PubMed:30209220, PubMed:38227290).

Cellular Location

Cytoplasmic vesicle. Perikaryon. Golgi apparatus membrane; Peripheral membrane protein. Cell projection, axon. Cell projection, dendrite. Endoplasmic reticulum membrane; Peripheral membrane protein. Cytoplasmic vesicle, secretory vesicle, synaptic vesicle membrane. Endosome {ECO:0000250|UniProtKB:Q5S006}. Lysosome Mitochondrion outer membrane; Peripheral membrane protein. Cytoplasm, cytoskeleton. Cytoplasmic vesicle, phagosome {ECO:0000250|UniProtKB:Q5S006}. Note=Colocalized with RAB29 along tubular structures emerging from Golgi apparatus (PubMed:23395371, PubMed:38127736). Localizes to endoplasmic reticulum exit sites (ERES), also known as transitional endoplasmic reticulum (tER) (PubMed:25201882). Detected on phagosomes and stressed lysosomes but not detected on autophagosomes induced by starvation (By similarity).

	Recruitment to stressed lysosomes is dependent on the ATG8 conjugation system composed of ATG5, ATG12 and ATG16L1 and leads to lysosomal stress-induced activation of LRRK2 (By similarity) {ECO:0000250|UniProtKB:Q5S006, ECO:0000269|PubMed:23395371, ECO:0000269|PubMed:25201882, ECO:0000269|PubMed:38127736}
Tissue Location	Expressed in pyramidal neurons in all cortical laminae of the visual cortex, in neurons of the substantia nigra pars compacta and caudate putamen (at protein level). Expressed in neutrophils (at protein level) (PubMed:29127255). Expressed in the brain. Expressed throughout the adult brain, but at a lower level than in heart and liver. Also expressed in placenta, lung, skeletal muscle, kidney and pancreas. In the brain, expressed in the cerebellum, cerebral cortex, medulla, spinal cord occipital pole, frontal lobe, temporal lobe and putamen. Expression is particularly high in brain dopaminoceptive areas.

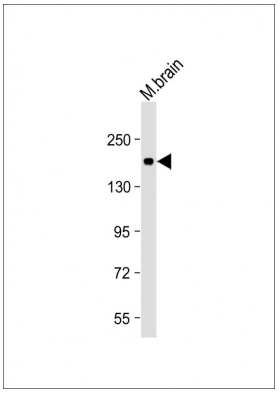
Background

This gene is a member of the leucine-rich repeat kinase family and encodes a protein with an ankryin repeat region, a leucine-rich repeat (LRR) domain, a kinase domain, a DFG-like motif, a RAS domain, a GTPase domain, a MLK-like domain, and a WD40 domain. The protein is present largely in the cytoplasm but also associates with the mitochondrial outer membrane. Mutations in this gene have been associated with Parkinson disease-8.

References

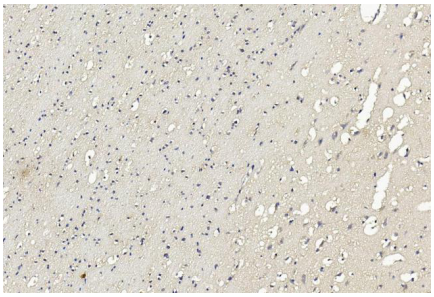
Olfactory heterogeneity in LRRK2 related Parkinsonism. Silveira-Moriyama L, et al. Mov Disord, 2010 Sep 3. PMID 20818658.
LRRK2 G2019S mutations are associated with an increased cancer risk in Parkinson disease. Saunders-Pullman R, et al. Mov Disord, 2010 Sep 3. PMID 20818610.
Low frequency of common LRRK2 mutations in Mexican patients with Parkinson's disease. Yescas P, et al. Neurosci Lett, 2010 Aug 18. PMID 20727385.
Absence of Commonly Reported Leucine-Rich Repeat Kinase 2 Mutations in Eastern Indian Parkinson's Disease Patients. Sanyal J, et al. Genet Test Mol Biomarkers, 2010 Aug 19. PMID 20722494.
Penetrance in Parkinson's disease related to the LRRK2 R1441G mutation in the Basque country (Spain). Ruiz-Martínez J, et al. Mov Disord, 2010 Aug 18. PMID 20721916.

Images



Anti-PARK8 (LRRK2) Antibody at 1:2000 dilution + Mouse brain lysate Lysates/proteins at 20 µg per lane. Secondary Goat Anti-mouse IgG, (H+L), Peroxidase conjugated at 1/10000 dilution. Predicted band size : 286 kDa Blocking/Dilution buffer: 5% NFDM/TBST.

Immunohistochemical analysis of paraffin-embedded Human brain section using Pink1(Cat#am7099a). am7099a was diluted at 1:50 dilution. A undiluted biotinylated goat polyvalent antibody was used as the secondary, followed by DAB staining.



Citations

- Dynamic and redundant regulation of LRRK2 and LRRK1 expression.
- Curcumin exposure induces expression of the Parkinson's disease-associated leucine-rich repeat kinase 2 (LRRK2) in rat mesencephalic cells.

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