

PARK8 (LRRK2) Antibody (E519)

Purified Rabbit Polyclonal Antibody (Pab) Catalog # AP7099e

Product Information

Application WB, E **Primary Accession Q5S007 Other Accession** NP 940980 Reactivity Human Host Rabbit Clonality Polyclonal Isotype Rabbit IgG **Calculated MW** 286103 **Antigen Region** 504-536

Additional Information

Gene ID 120892

Other Names Leucine-rich repeat serine/threonine-protein kinase 2, Dardarin, LRRK2,

PARK8

Target/Specificity This PARK8(LRRK2) antibody is generated from rabbits immunized with a KLH

conjugated synthetic peptide between 504-536 amino acids from human

PARK8(LRRK2).

Dilution WB~~1:1000 E~~Use at an assay dependent concentration.

Format Purified polyclonal antibody supplied in PBS with 0.05% (V/V) Proclin 300. 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 PARK8 (LRRK2) Antibody (E519) 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: <u>29212815</u>, PubMed: <u>30398148</u>, PubMed: <u>30635421</u>, 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: <u>23395371</u>). Regulates neuronal process morphology in the intact central nervous system (CNS) (PubMed: 17114044). Plays a role in synaptic vesicle trafficking (PubMed: <u>24687852</u>). 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.

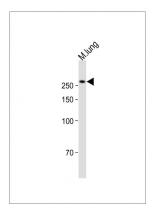
Background

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's disease identified to date. LRRK2, a genetic mutation, was recently found linked to about 5 percent of inherited cases of Parkinson's disease. By high-resolution recombination mapping and candidate gene sequencing in 46 families, 6 disease-segregating mutations (5 missense and 1 putative splice site mutation). It may be central to the pathogenesis of several major neurodegenerative disorders associated with parkinsonism. LRRK2 belongs to the ROCO protein family and includes a protein kinase domain of the MAPKKK class and several other major functional domains.

References

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Bonifati V. Lancet Neurol. 2002. 1:83.
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Images



All lanes: PARK8 (LRRK2) Antibody (E519) at 1:1000 dilution + Mouse lung lysate Lysates/proteins at 20 µg per lane. Secondary: Goat Anti-Rabbit IgG, (H+L), Peroxidase conjugated (ASP1615) at 1/15000 dilution. Observed band size: 280kDa Blocking/Dilution buffer: 5% NFDM/TBST.

Citations

• Dynamic and redundant regulation of LRRK2 and LRRK1 expression.

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