

Beta-arrestin 2 Rabbit pAb

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Product Information

Application WB, IHC-P, IHC-F, IF

Primary Accession <u>P32121</u>

Reactivity Pig, Mouse, Rabbit, Horse

Host Rabbit
Clonality Polyclonal
Calculated MW 46106
Physical State Liquid

Immunogen KLH conjugated synthetic peptide derived from human Beta-arrestin 2

Epitope Specificity 251-350/409

Isotype IgG

Purity affinity purified by Protein A

Buffer 0.01M TBS (pH7.4) with 1% BSA, 0.02% Proclin300 and 50% Glycerol.

SUBCELLULAR LOCATION Cytoplasm. Nucleus. Cell membrane. Membrane > clathrin-coated pit.

Cytoplasmic vesicle. Translocates to the plasma membrane and colocalizes

with antagonist-stimulated GPCRs.

SIMILARITY Belongs to the arrestin family.

Post-translational Phosphorylated at Thr-382 in the cytoplasm; probably dephosphorylated at modifications the plasma membrane. The phosphorylation does not regulate internalization

and recycling of ADRB2, interaction with clathrin or AP2B1. The ubiquitination status appears to regulate the formation and trafficking of beta-arrestin-GPCR complexes and signaling. Ubiquitination appears to occurr GPCR-specifc.

Ubiquitinated by MDM2; the ubiquitination is required for rapid

internalization of ADRB2. Deubiquitinated by USP33; the deubiquitination leads to a dissociation of the beta-arrestin-GPCR complex. Stimulation of a

class A GPCR, such as ADRB2, induces transient ubiquitination and

subsequently promotes association with USP33. Stimulation of a class B GPCR

promotes a sustained ubiquitination.

Important Note This product as supplied is intended for research use only, not for use in

human, therapeutic or diagnostic applications.

Background Descriptions Members of arrestin/beta arrestin protein family are thought to participate in

agonist mediated desensitization of G protein coupled receptors and cause specific dampening of cellular responses to stimuli such as hormones, neurotransmitters, or sensory signals. Arrestin beta 2, like arrestin beta 1, was

shown to inhibit beta adrenergic receptor function in vitro. It is expressed at high levels in the central nervous system and may play a role in the regulation

of synaptic receptors

Additional Information

Gene ID 409

Other Names Beta-arrestin-2, Arrestin beta-2, Non-visual arrestin-3, ARRB2, ARB2, ARR2

Dilution WB=1:500-2000,IHC-P=1:100-500,IHC-F=1:100-500

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 ARRB2

Synonyms ARB2, ARR2

Function

Functions in regulating agonist-mediated G-protein coupled receptor (GPCR) signaling by mediating both receptor desensitization and resensitization processes. During homologous desensitization, beta- arrestins bind to the GPRK-phosphorylated receptor and sterically preclude its coupling to the cognate G-protein; the binding appears to require additional receptor determinants exposed only in the active receptor conformation. The beta-arrestins target many receptors for internalization by acting as endocytic adapters (CLASPs, clathrin- associated sorting proteins) and recruiting the GPRCs to the adapter protein 2 complex 2 (AP-2) in clathrin-coated pits (CCPs). However, the extent of beta-arrestin involvement appears to vary significantly depending on the receptor, agonist and cell type. Internalized arrestin-receptor complexes traffic to intracellular endosomes, where they remain uncoupled from G-proteins. Two different modes of arrestinmediated internalization occur. Class A receptors, like ADRB2, OPRM1, ENDRA, D1AR and ADRA1B dissociate from beta-arrestin at or near the plasma membrane and undergo rapid recycling. Class B receptors, like AVPR2, AGTR1, NTSR1, TRHR and TACR1 internalize as a complex with arrestin and traffic with it to endosomal vesicles, presumably as desensitized receptors, for extended periods of time. Receptor resensitization then requires that receptor-bound arrestin is removed so that the receptor can be dephosphorylated and returned to the plasma membrane. Mediates endocytosis of CCR7 following ligation of CCL19 but not CCL21. Involved in internalization of P2RY1, P2RY4, P2RY6 and P2RY11 and ATP-stimulated internalization of P2RY2. Involved in phosphorylation-dependent internalization of OPRD1 and subsequent recycling or degradation. Involved in ubiquitination of IGF1R. Beta- arrestins function as multivalent adapter proteins that can switch the GPCR from a G-protein signaling mode that transmits short-lived signals from the plasma membrane via small molecule second messengers and ion channels to a beta-arrestin signaling mode that transmits a distinct set of signals that are initiated as the receptor internalizes and transits the intracellular compartment. Acts as a signaling scaffold for MAPK pathways such as MAPK1/3 (ERK1/2) and MAPK10 (JNK3). ERK1/2 and JNK3 activated by the beta-arrestin scaffold are largely excluded from the nucleus and confined to cytoplasmic locations such as endocytic vesicles, also called beta-arrestin signalosomes. Acts as a signaling scaffold for the AKT1 pathway. GPCRs for which the beta- arrestin-mediated signaling relies on both ARRB1 and ARRB2 (codependent regulation) include ADRB2, F2RL1 and PTH1R. For some GPCRs the beta- arrestin-mediated signaling relies on either ARRB1 or ARRB2 and is inhibited by the other respective beta-arrestin form (reciprocal regulation). Increases ERK1/2 signaling in AGTR1- and AVPR2-mediated activation (reciprocal regulation). Involved in CCR7-mediated ERK1/2 signaling involving ligand CCL19. Is involved in type-1A angiotensin II receptor/AGTR1-mediated ERK activity. Is involved in type-1A angiotensin II receptor/AGTR1-mediated MAPK10 activity. Is involved in dopamine-stimulated AKT1 activity in the

striatum by disrupting the association of AKT1 with its negative regulator PP2A. Involved in AGTR1-mediated chemotaxis. Appears to function as signaling scaffold involved in regulation of MIP-1-beta-stimulated CCR5-dependent chemotaxis. Involved in attenuation of NF-kappa-B-dependent transcription in response to GPCR or cytokine stimulation by interacting with and stabilizing CHUK. Suppresses UV-induced NF-kappa- B-dependent activation by interacting with CHUK. The function is promoted by stimulation of ADRB2 and dephosphorylation of ARRB2. Involved in p53/TP53-mediated apoptosis by regulating MDM2 and reducing the MDM2-mediated degradation of p53/TP53. May serve as nuclear messenger for GPCRs. Upon stimulation of OR1D2, may be involved in regulation of gene expression during the early processes of fertilization. Also involved in regulation of receptors other than GPCRs. Involved in endocytosis of TGFBR2 and TGFBR3 and down-regulates TGF-beta signaling such as NF-kappa-B activation. Involved in endocytosis of low-density lipoprotein receptor/LDLR. Involved in endocytosis of smoothened homolog/Smo, which also requires GRK2. Involved in endocytosis of SLC9A5. Involved in endocytosis of ENG and subsequent TGF-beta-mediated ERK activation and migration of epithelial cells. Involved in Toll-like receptor and IL-1 receptor signaling through the interaction with TRAF6 which prevents TRAF6 autoubiquitination and oligomerization required for activation of NF- kappa-B and JUN (PubMed: 26839314). Involved in insulin resistance by acting as insulin-induced signaling scaffold for SRC, AKT1 and INSR. Involved in regulation of inhibitory signaling of natural killer cells by recruiting PTPN6 and PTPN11 to KIR2DL1. Involved in IL8-mediated granule release in neutrophils. Involved in the internalization of the atypical chemokine receptor ACKR3. Acts as an adapter protein coupling FFAR4 receptor to specific downstream signaling pathways, as well as mediating receptor endocytosis (PubMed:22282525, PubMed:23809162). During the activation step of NLRP3 inflammasome, directly associates with NLRP3 leading to inhibition of pro-inflammatory cytokine release and inhibition of inflammation (PubMed: <u>23809162</u>).

Cellular Location

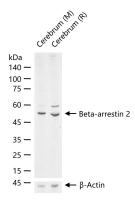
Cytoplasm. Nucleus. Cell membrane. Membrane, clathrin-coated pit. Cytoplasmic vesicle Note=Translocates to the plasma membrane and colocalizes with antagonist-stimulated GPCRs

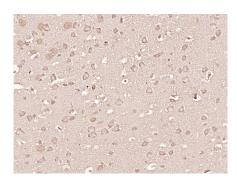
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Images

25 ug total protein per lane of various lysates (see on figure) probed with Beta-arrestin 2 polyclonal antibody, unconjugated (AP57781) at 1:1000 dilution and 4°C overnight incubation. Followed by conjugated secondary antibody incubation at r.t. for 60 min.





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 (Beta-arrestin 2) Polyclonal Antibody, Unconjugated (AP57781) at 1:400 overnight at 4°C, followed by operating according to SP Kit(Rabbit) (sp-0023) instructions and DAB staining.

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