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HRI Polyclonal Antibody

Catalog # AP70410

Product Information

Application	WB, IHC-P
Primary Accession	Q9BQI3
Reactivity	Human, Mouse, Monkey
Host	Rabbit
Clonality	Polyclonal
Calculated MW	71106

Additional Information

Gene ID	27102
Other Names	EIF2AK1; HRI; KIAA1369; Eukaryotic translation initiation factor 2-alpha kinase 1; Heme-controlled repressor; HCR; Heme-regulated eukaryotic initiation factor eIF-2-alpha kinase; Heme-regulated inhibitor; Hemin-sensitive initiation factor 2
Dilution	WB~~Western Blot: 1/500 - 1/2000. Immunohistochemistry: 1/100 - 1/300. ELISA: 1/40000. Not yet tested in other applications. IHC-P~~N/A
Format	Liquid in PBS containing 50% glycerol, 0.5% BSA and 0.09% (W/V) sodium azide.
Storage Conditions	-20℃

Protein Information

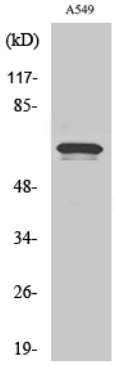
Name	EIF2AK1 (HGNC:24921)
Function	Metabolic-stress sensing protein kinase that phosphorylates the alpha subunit of eukaryotic translation initiation factor 2 (EIF2S1/eIF-2-alpha) in response to various stress conditions (PubMed:32132706, PubMed:32132707, PubMed:37327776, PubMed:37550454, PubMed:38340717). Key activator of the integrated stress response (ISR) required for adaptation to various stress, such as heme deficiency, oxidative stress, osmotic shock, mitochondrial dysfunction and heat shock (PubMed:32132706, PubMed:32132707, PubMed:37327776, PubMed:37550454, PubMed:38340717). EIF2S1/eIF-2-alpha phosphorylation in response to stress converts EIF2S1/eIF-2-alpha in a global protein synthesis inhibitor, leading to a global attenuation of cap-dependent translation, while concomitantly initiating the preferential translation of ISR-specific mRNAs, such as the transcriptional activator ATF4, and hence allowing ATF4-mediated reprogramming (PubMed:32132706, PubMed:32132707, PubMed:37327776). Acts as a key sensor of heme-deficiency: in normal conditions, binds hemin via a cysteine

thiolate and histidine nitrogenous coordination, leading to inhibit the protein kinase activity (By similarity). This binding occurs with moderate affinity, allowing it to sense the heme concentration within the cell: heme depletion relieves inhibition and stimulates kinase activity, activating the ISR (By similarity). Thanks to this unique heme-sensing capacity, plays a crucial role to shut off protein synthesis during acute heme-deficient conditions (By similarity). In red blood cells (RBCs), controls hemoglobin synthesis ensuring a coordinated regulation of the synthesis of its heme and globin moieties (By similarity). It thereby plays an essential protective role for RBC survival in anemias of iron deficiency (By similarity). Iron deficiency also triggers activation by full-length DELE1 (PubMed:37327776). Also activates the ISR in response to mitochondrial dysfunction: HRI/EIF2AK1 protein kinase activity is activated upon binding to the processed form of DELE1 (S-DELE1), thereby promoting the ATF4-mediated reprogramming (PubMed:32132706, PubMed:32132707). Also acts as an activator of mitophagy in response to mitochondrial damage: catalyzes phosphorylation of eIF-2-alpha (EIF2S1) following activation by S-DELE1, thereby promoting mitochondrial localization of EIF2S1, triggering PRKN-independent mitophagy (PubMed:38340717).

Background

Inhibits protein synthesis at the translation initiation level, in response to various stress conditions, including oxidative stress, heme deficiency, osmotic shock and heat shock. Exerts its function through the phosphorylation of EIF2S1 at 'Ser- 48' and 'Ser-51', thus preventing its recycling. Binds hemin forming a 1:1 complex through a cysteine thiolate and histidine nitrogenous coordination. This binding occurs with moderate affinity, allowing it to sense the heme concentration within the cell. Thanks to this unique heme-sensing capacity, plays a crucial role to shut off protein synthesis during acute heme-deficient conditions. In red blood cells (RBCs), controls hemoglobin synthesis ensuring a coordinated regulation of the synthesis of its heme and globin moieties. Thus plays an essential protective role for RBC survival in anemias of iron deficiency. Similarly, in hepatocytes, involved in heme-mediated translational control of CYP2B and CYP3A and possibly other hepatic P450 cytochromes. May also contain ER stress during acute heme-deficient conditions (By similarity).

Images



Western Blot analysis of various cells using HRI Polyclonal Antibody