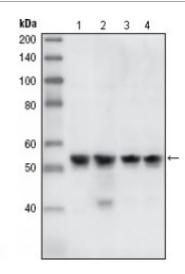


Anti-Chk1 antibody



Description

4

Mouse monoclonal to Chk1.

Model STJ97955

Host Mouse

Reactivity Human, Mouse

Applications ELISA, WB

Immunogen Purified recombinant fragment of Chk1 expressed in E. Coli.

Gene ID <u>1111</u>

Gene Symbol CHEK1

Dilution range WB 1:500-1:2000ELISA 1:10000

Specificity Chk1 Monoclonal Antibody detects endogenous levels of Chk1 protein.

Tissue Specificity Expressed ubiquitously with the most abundant expression in thymus, testis,

small intestine and colon.

Purification Affinity purification

Clone ID 2G1D5

Note For Research Use Only (RUO).

Protein Name Serine/threonine-protein kinase Chk1 CHK1 checkpoint homolog Cell cycle

checkpoint kinase Checkpoint kinase-1

Clonality Monoclonal

Conjugation Unconjugated

Isotype IgG1

Formulation Purified antibody in PBS containing 0.03% sodium azide.

Concentration 1 mg/ml

Storage Instruction Store at -20°C, and avoid repeat freeze-thaw cycles.

Database Links <u>HGNC:1925OMIM:603078</u>

Alternative Names Serine/threonine-protein kinase Chk1 CHK1 checkpoint homolog Cell cycle

checkpoint kinase Checkpoint kinase-1

Function Serine/threonine-protein kinase which is required for checkpoint-mediated cell

cycle arrest and activation of DNA repair in response to the presence of DNA damage or unreplicated DNA. May also negatively regulate cell cycle progression during unperturbed cell cycles. This regulation is achieved by a number of mechanisms that together help to preserve the integrity of the genome. Recognizes the substrate consensus sequence [R-X-X-S/T]. Binds to and phosphorylates CDC25A, CDC25B and CDC25C. Phosphorylation of CDC25A at 'Ser-178' and 'Thr-507' and phosphorylation of CDC25C at 'Ser-216' creates binding sites for 14-3-3 proteins which inhibit CDC25A and CDC25C. Phosphorylation of CDC25A at 'Ser-76', 'Ser-124', 'Ser-178', 'Ser-279' and 'Ser-293' promotes proteolysis of CDC25A. Phosphorylation of CDC25A at 'Ser-76' primes the protein for subsequent phosphorylation at 'Ser-79', 'Ser-82' and 'Ser-88' by NEK11, which is required for

polyubiquitination and degradation of CDCD25A. Inhibition of CDC25 leads to increased inhibitory tyrosine phosphorylation of CDK-cyclin complexes and blocks cell cycle progression. Also phosphorylates NEK6. Binds to and phosphorylates RAD51 at 'Thr-309', which promotes the release of RAD51 from BRCA2 and enhances the association of RAD51 with chromatin, thereby promoting DNA repair by homologous recombination. Phosphorylates multiple sites within the C-terminus of TP53, which promotes activation of TP53 by acetylation and promotes cell cycle arrest and suppression of cellular proliferation. Also promotes repair of DNA cross-links through

phosphorylation of FANCE. Binds to and phosphorylates TLK1 at 'Ser-743', which prevents the TLK1-dependent phosphorylation of the chromatin assembly factor ASF1A. This may enhance chromatin assembly both in the presence or absence of DNA damage. May also play a role in replication fork maintenance through regulation of PCNA. May regulate the transcription of genes that regulate cell-cycle progression through the phosphorylation of histones. Phosphorylates histone H3.1 (to form H3T11ph), which leads to epigenetic inhibition of a subset of genes. May also phosphorylate RB1 to promote its interaction with the E2F family of transcription factors and subsequent cell cycle arrest.; Isoform 2: Endogenous repressor of isoform 1, interacts with, and antagonizes CHK1 to promote the S to G2/M phase transition.

Sequence and Domain Family

The autoinhibitory region (AIR) inhibits the activity of the kinase domain.

Cellular Localization

Nucleus. Cytoplasm. Cytoplasm, cytoskeleton, microtubule organizing center, centrosome. Nuclear export is mediated at least in part by XPO1/CRM1. Also localizes to the centrosome specifically during interphase, where it may protect centrosomal CDC2 kinase from inappropriate activation by cytoplasmic CDC25B.

Post-translational

Phosphorylated by ATR in a RAD17-dependent manner in response to

Modifications

ultraviolet irradiation and inhibition of DNA replication. Phosphorylated by ATM in response to ionizing irradiation. ATM and ATR can both phosphorylate Ser-317 and Ser-345 and this results in enhanced kinase activity. Phosphorylation at Ser-345 induces a change in the conformation of the protein, activates the kinase activity and is a prerequisite for interaction with FBXO6 and subsequent ubiquitination at Lys-436. Phosphorylation at Ser-345 also increases binding to 14-3-3 proteins and promotes nuclear retention. Conversely, dephosphorylation at Ser-345 by PPM1D may contribute to exit from checkpoint mediated cell cycle arrest. Phosphorylation at Ser-280 by AKT1/PKB, may promote mono and/or diubiquitination. Also phosphorylated at undefined residues during mitotic arrest, resulting in decreased activity. Ubiquitinated. Mono or diubiquitination promotes nuclear exclusion. The activated form (phosphorylated on Ser-345) is polyubiquitinated at Lys-436 by some SCF-type E3 ubiquitin ligase complex containing FBXO6 promoting its degradation. Ubiquitination and degradation are required to terminate the checkpoint and ensure that activated CHEK1 does not accumulate as cells progress through S phase, when replication forks encounter transient impediments during normal DNA replication.

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