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Phospho-CHK1(S317) Antibody

Affinity Purified Rabbit Polyclonal Antibody (Pab)
Catalog # AP3070a

Product Information

Application	DB, WB, IHC-P, E
Primary Accession	O14757
Reactivity	Human, Mouse
Host	Rabbit
Clonality	Polyclonal
Isotype	Rabbit IgG
Clone Names	RB7845, RB18425
Calculated MW	54434

Additional Information

Gene ID	1111
Other Names	Serine/threonine-protein kinase Chk1, CHK1 checkpoint homolog, Cell cycle checkpoint kinase, Checkpoint kinase-1, CHEK1, CHK1
Target/Specificity	This CHK1 Antibody is generated from rabbits immunized with a KLH conjugated synthetic phosphopeptide corresponding to amino acid residues surrounding S317 of human CHK1.
Dilution	DB~~1:500 WB~~1:1000 IHC-P~~1:100~500 E~~Use at an assay dependent concentration.
Format	Purified polyclonal antibody supplied in PBS with 0.09% (W/V) sodium azide. This antibody is purified through a protein A column, followed by peptide affinity purification.
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	Phospho-CHK1(S317) Antibody is for research use only and not for use in diagnostic or therapeutic procedures.

Protein Information

Name	CHEK1
Synonyms	CHK1
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 (PubMed:11535615, PubMed:12399544, PubMed:12446774, PubMed:14559997, PubMed:14988723, PubMed:15311285, PubMed:15650047, PubMed:15665856, PubMed:32357935). May also negatively regulate cell cycle progression during unperturbed cell cycles (PubMed:11535615, PubMed:12399544, PubMed:12446774, PubMed:14559997, PubMed:14988723, PubMed:15311285, PubMed:15650047, PubMed:15665856). This regulation is achieved by a number of mechanisms that together help to preserve the integrity of the genome (PubMed:11535615, PubMed:12399544, PubMed:12446774, PubMed:14559997, PubMed:14988723, PubMed:15311285, PubMed:15650047, PubMed:15665856). Recognizes the substrate consensus sequence [R-X-X- S/T] (PubMed:11535615, PubMed:12399544, PubMed:12446774, PubMed:14559997, PubMed:14988723, PubMed:15311285, PubMed:15650047, PubMed:15665856). Binds to and phosphorylates CDC25A, CDC25B and CDC25C (PubMed:12676583, PubMed:12676925, PubMed:12759351, PubMed:14559997, PubMed:14681206, PubMed:19734889, PubMed:9278511). 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 (PubMed:9278511). Phosphorylation of CDC25A at 'Ser- 76', 'Ser-124', 'Ser-178', 'Ser-279' and 'Ser-293' promotes proteolysis of CDC25A (PubMed:12676583, PubMed:12676925, PubMed:12759351, PubMed:14681206, PubMed:19734889, PubMed:9278511). 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 (PubMed:19734889, PubMed:20090422, PubMed:9278511). Inhibition of CDC25 leads to increased inhibitory tyrosine phosphorylation of CDK-cyclin complexes and blocks cell cycle progression (PubMed:9278511). Also phosphorylates NEK6 (PubMed:18728393). 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 (PubMed:15665856). 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 (PubMed:10673501, PubMed:15659650, PubMed:16511572). Also promotes repair of DNA cross-links through phosphorylation of FANCE (PubMed:17296736). Binds to and phosphorylates TLK1 at 'Ser-743', which prevents the TLK1-dependent phosphorylation of the chromatin assembly factor ASF1A (PubMed:12660173, PubMed:12955071). This may enhance chromatin assembly both in the presence or absence of DNA damage (PubMed:12660173, PubMed:12955071). May also play a role in replication fork maintenance through regulation of PCNA (PubMed:18451105). May regulate the transcription of genes that regulate cell-cycle progression through the phosphorylation of histones (By similarity). Phosphorylates histone H3.1 (to form H3T11ph), which leads to epigenetic inhibition of a subset of genes (By similarity). May also phosphorylate RB1 to promote its interaction with the E2F family of transcription factors and subsequent cell cycle arrest (PubMed:17380128). Phosphorylates SPRTN, promoting SPRTN recruitment to chromatin (PubMed:31316063). Reduces replication stress and activates the G2/M checkpoint, by phosphorylating and inactivating PABIR1/FAM122A and promoting the serine/threonine-protein phosphatase 2A-mediated dephosphorylation and stabilization of WEE1 levels and activity (PubMed:33108758).

Cellular Location

Nucleus. Chromosome. Cytoplasm Cytoplasm, cytoskeleton, microtubule organizing center, centrosome. Note=Nuclear export is mediated at least in part by XPO1/CRM1 (PubMed:12676962). Also localizes to the centrosome specifically during interphase, where it may protect centrosomal CDC2 kinase from inappropriate activation by cytoplasmic CDC25B (PubMed:15311285).

	Proteolytic cleavage at the C-terminus by SPRTN promotes removal from chromatin (PubMed:31316063)
Tissue Location	Expressed ubiquitously with the most abundant expression in thymus, testis, small intestine and colon

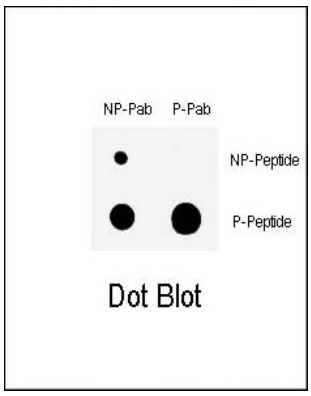
Background

Checkpoint pathways control the order and timing of cell cycle transitions and ensure that critical events, such as DNA replication and chromosome segregation, are completed with high fidelity. The S. pombe Chk1 gene encodes a protein kinase that is required for the DNA damage checkpoint. Antibodies against CHK1 recognized a 54-kD protein on immunoblots of mammalian cell extracts. However,CHK1 is modified in response to DNA damage. In vitro, CHK1 directly phosphorylated a regulator of CDC2 tyrosine phosphorylation, CDC25C. In response to DNA damage, CHK1 phosphorylates and inhibits CDC25C, thus preventing activation of the CDC2-cyclin B complex and mitotic entry. CHK1 directly phosphorylates CDC25A during an unperturbed cell cycle, and that phosphorylation of CDC25A by CHK1 is required for cells to delay cell cycle progression in response to double-strand DNA breaks.

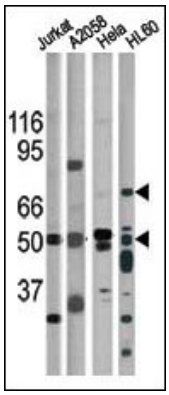
References

Kramer, A., et al., Nat. Cell Biol. 6(9):884-891 (2004).
Xu, X., et al., J. Biol. Chem. 279(33):34091-34094 (2004).
Ng, C.P., et al., J. Biol. Chem. 279(10):8808-8819 (2004).
Chen, M.S., et al., Mol. Cell. Biol. 23(21):7488-7497 (2003).
Groth, A., et al., EMBO J. 22(7):1676-1687 (2003).

Images

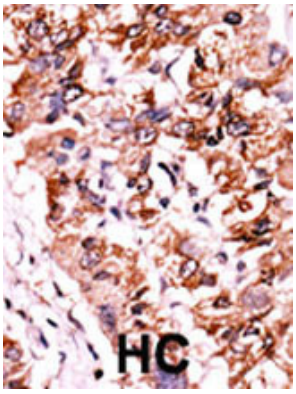


Dot blot analysis of anti-Phospho-CHK1-S317 Antibody (Cat. #AP3070a) on nitrocellulose membrane. 50ng of Phospho-peptide or Non Phospho-peptide per dot were adsorbed. Antobodies working concentration was 0.5ug per ml.



The anti-Phospho-CHK1-S317 Pab (Cat. #AP7219b) is used in Western blot for detection in, from left to right, Jurkat, A2058, Hela, and HL60 tissue lysates.

Formalin-fixed and paraffin-embedded human cancer tissue reacted with the primary antibody, which was



peroxidase-conjugated to the secondary antibody, followed by AEC staining. This data demonstrates the use of this antibody for immunohistochemistry; clinical relevance has not been evaluated. BC = breast carcinoma; HC = hepatocarcinoma.

Citations

- TLK1B mediated phosphorylation of Rad9 regulates its nuclear/cytoplasmic localization and cell cycle checkpoint.

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