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Phospho-TOPBP1(S1159) Antibody

Affinity Purified Rabbit Polyclonal Antibody (Pab)
Catalog # AP3774a

Product Information

Application	DB, E
Primary Accession	Q92547
Other Accession	Q6ZQF0, NP_008958.2
Reactivity	Human
Predicted	Mouse
Host	Rabbit
Clonality	Polyclonal
Isotype	Rabbit IgG
Clone Names	RB36342
Calculated MW	170679

Additional Information

Gene ID	11073
Other Names	DNA topoisomerase 2-binding protein 1, DNA topoisomerase II-beta-binding protein 1, TopBP1, DNA topoisomerase II-binding protein 1, TOPBP1, KIAA0259
Target/Specificity	This TOPBP1 Antibody is generated from rabbits immunized with a KLH conjugated synthetic phosphopeptide corresponding to amino acid residues surrounding S1159 of human TOPBP1.
Dilution	DB~~1:500 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-TOPBP1(S1159) Antibody is for research use only and not for use in diagnostic or therapeutic procedures.

Protein Information

Name	TOPBP1 {ECO:0000303|PubMed:9461304, ECO:0000312|HGNC:HGNC:17008}
Function	Scaffold protein that acts as a key protein-protein adapter in DNA

replication and DNA repair (PubMed:10498869, PubMed:11395493, PubMed:11714696, PubMed:17575048, PubMed:20545769, PubMed:21777809, PubMed:26811421, PubMed:30898438, PubMed:31135337, PubMed:33592542, PubMed:35597237, PubMed:37674080). Composed of multiple BRCT domains, which specifically recognize and bind phosphorylated proteins, bringing proteins together into functional combinations (PubMed:17575048, PubMed:20545769, PubMed:21777809, PubMed:26811421, PubMed:30898438, PubMed:31135337, PubMed:35597237, PubMed:37674080). Required for DNA replication initiation but not for the formation of pre-replicative complexes or the elongation stages (By similarity). Necessary for the loading of replication factors onto chromatin, including GMNC, CDC45, DNA polymerases and components of the GINS complex (By similarity). Plays a central role in DNA repair by bridging proteins and promoting recruitment of proteins to DNA damage sites (PubMed:30898438, PubMed:35597237, PubMed:37674080). Involved in double-strand break (DSB) repair via homologous recombination in S-phase by promoting the exchange between the DNA replication factor A (RPA) complex and RAD51 (PubMed:26811421, PubMed:35597237). Mechanistically, TOPBP1 is recruited to DNA damage sites in S-phase via interaction with phosphorylated HTATSF1, and promotes the loading of RAD51, thereby facilitating RAD51 nucleofilaments formation and RPA displacement, followed by homologous recombination (PubMed:35597237). Involved in microhomology-mediated end-joining (MMEJ) DNA repair by promoting recruitment of polymerase theta (POLQ) to DNA damage sites during mitosis (PubMed:37674080). MMEJ is an alternative non-homologous end- joining (NHEJ) machinery that takes place during mitosis to repair DSBs in DNA that originate in S-phase (PubMed:37674080). Recognizes and binds POLQ phosphorylated by PLK1, enabling its recruitment to DSBs for subsequent repair (PubMed:37674080). Involved in G1 DNA damage checkpoint by acting as a molecular adapter that couples TP53BP1 and the 9-1-1 complex (PubMed:31135337). In response to DNA damage, triggers the recruitment of checkpoint signaling proteins on chromatin, which activate the CHEK1 signaling pathway and block S-phase progression (PubMed:16530042, PubMed:21777809). Acts as an activator of the kinase activity of ATR (PubMed:16530042, PubMed:21777809). Also required for chromosomal stability when DSBs occur during mitosis by forming filamentous assemblies that bridge MDC1 and tether broken chromosomes during mitosis (PubMed:30898438). Together with CIP2A, plays an essential role in the response to genome instability generated by the presence of acentric chromosome fragments derived from shattered chromosomes within micronuclei (PubMed:35121901, PubMed:35842428, PubMed:37165191, PubMed:37316668). Micronuclei, which are frequently found in cancer cells, consist of chromatin surrounded by their own nuclear membrane: following breakdown of the micronuclear envelope, a process associated with chromothripsis, the CIP2A-TOPBP1 complex tethers chromosome fragments during mitosis to ensure clustered segregation of the fragments to a single daughter cell nucleus, facilitating re-ligation with limited chromosome scattering and loss (PubMed:37165191, PubMed:37316668). Recruits the SWI/SNF chromatin remodeling complex to E2F1-responsive promoters, thereby down- regulating E2F1 activity and inhibiting E2F1-dependent apoptosis during G1/S transition and after DNA damage (PubMed:12697828, PubMed:15075294).

Cellular Location

Nucleus. Chromosome. Cytoplasm, cytoskeleton, microtubule organizing center, centrosome. Cytoplasm, cytoskeleton, spindle pole. Note=Localizes to sites of DNA damage, such as double-stranded breaks (DSBs) (PubMed:10498869, PubMed:21482717, PubMed:21659603, PubMed:21777809, PubMed:30898438, PubMed:35842428, PubMed:37674080). Recruited to DNA double-strand break (DSBs) during S-phase following interaction with phosphorylated HTATSF1

(PubMed:35597237). Recruited to DSBs during mitosis following interaction with phosphorylated MDC1 (PubMed:30898438). Has a uniform nuclear distribution during G phase (PubMed:11395493). Colocalizes with BRCA1 at stalled replication forks during S phase (PubMed:11395493). In mitotic cells it colocalizes with BRCA1 at spindle poles and centrosomes during metaphase and anaphase (PubMed:11395493). Detected in discrete foci together with PML and numerous DNA repair enzymes after DNA damage by alkylating agents, UV or gamma irradiation (PubMed:12773567). Detected on unpaired autosomes in meiotic prophase cells (By similarity). Detected on X and Y chromosomes during later stages of prophase (By similarity). Colocalizes with ATR and H2AX at unsynapsed chromosome cores during prophase (By similarity). Localizes to broken chromosomes within micronuclei during interphase and following chromothripsis (PubMed:37165191, PubMed:37316668) Localization to broken chromosomes is mainly independent of MDC1 (PubMed:35121901, PubMed:37165191). {ECO:0000250|UniProtKB:Q6ZQF0, ECO:0000269|PubMed:10498869, ECO:0000269|PubMed:11395493, ECO:0000269|PubMed:12773567, ECO:0000269|PubMed:21482717, ECO:0000269|PubMed:21659603, ECO:0000269|PubMed:21777809, ECO:0000269|PubMed:30898438, ECO:0000269|PubMed:35121901, ECO:0000269|PubMed:35597237, ECO:0000269|PubMed:35842428, ECO:0000269|PubMed:37165191, ECO:0000269|PubMed:37316668, ECO:0000269|PubMed:37674080}

Tissue Location Highly expressed in heart, brain, placenta, lung and kidney.

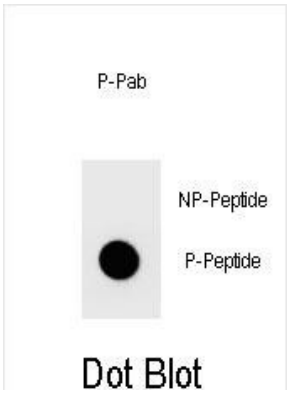
Background

This gene encodes a binding protein which interacts with the C-terminal region of topoisomerase II beta. This interaction suggests a supportive role for this protein in the catalytic reactions of topoisomerase II beta through transient breakages of DNA strands.

References

Huo, Y.G., et al. Biochem. Biophys. Res. Commun. 401(3):401-405(2010)
Blackford, A.N., et al. Proc. Natl. Acad. Sci. U.S.A. 107(27):12251-12256(2010)
Takeishi, Y., et al. Genes Cells 15(7):761-771(2010)
Gong, Z., et al. Mol. Cell 37(3):438-446(2010)
Couch, F.J., et al. Cancer Epidemiol. Biomarkers Prev. 19(1):251-257(2010)

Images



Dot blot analysis of Phospho-TOPBP1-S1159 Antibody Phospho-specific Pab (Cat. #AP3774a) on nitrocellulose membrane. 50ng of Phospho-peptide or Non Phospho-peptide per dot were adsorbed. Antibody working concentrations are 0.6ug per ml.

Citations

- Oocytes can repair DNA damage during meiosis via a microtubule-dependent recruitment of CIP2A-MDC1-TOPBP1 complex from spindle pole to chromosomes
- Overexpression of TopBP1, a canonical ATR/Chk1 activator, paradoxically hinders ATR/Chk1 activation in cancer
- Cell Cycle-Dependent Switch of TopBP1 Functions by Cdk2 and Akt
- AKT signaling promotes DNA damage accumulation and proliferation in polycystic kidney disease
- Akt switches TopBP1 function from checkpoint activation to transcriptional regulation through phosphoserine binding-mediated oligomerization.