

Product Information

Anti-Chk1 antibody, Mouse Monoclonal

Clone DCS-310, purified from hybridoma cell culture

C9358

Product Description

Monoclonal Anti-Chk1 (mouse IgG2b isotype) is derived from the DCS-310 hybridoma produced by the fusion of mouse myeloma cells and splenocytes from a BALB/c mouse immunized with a recombinant human Chk1. The isotype is determined using ImmunoType™ Kit (C9358 ISO-1) and by a double diffusion immunoassay using Mouse Monoclonal Antibody Isotyping Reagents (C9358 ISO-2).

Monoclonal Anti-Chk1 recognizes human Chk1. The product is useful in immunoblotting (54 kDa), immunoprecipitation, and immunohistochemistry (formalin-fixed, paraffin-embedded tissues).

The survival of organisms depends on the accurate transmission of genetic information from one cell to its daughters. Such faithful transmission requires the ability to survive spontaneous and induced DNA damage while minimizing the number of heritable mutations. To achieve this fidelity, cells have evolved surveillance mechanisms that monitor the structure of chromosomes and coordinate repair and cell-cycle progression.¹ When the DNA of a cell is damaged, a network of checkpoint proteins tell the cell to stop at the nearest cell cycle checkpoint, so that the DNA repair machinery can set about shoring up the damage, allowing time for repair prior to proliferation.^{2,3} Several checkpoint genes are essential for cell and organism survival, implying that these pathways are not only surveyors of occasional damage, but are firmly integrated components of cellular physiology.^{1,3}

There are two manifestations of the delays that cells experience in G1, S, or G2 phases of the cell cycle after damage to DNA. The first is the transient arrest seen at G1, S, or G2 (independent of the key tumor suppressor protein p53) that gives the DNA repair machinery time to shore up the damage before division continues.

The second (dependent on p53) is apoptosis or prolonged, probably permanent, G1 delay that results in removal of damaged cells from the population. A failure to halt at these checkpoints leads to genomic instability and an increased likelihood that the cell will become cancerous.

Studies in yeast have identified a network of DNA integrity checkpoint proteins (including four conserved kinases) that regulate the cell's entry into and exit from these cell cycle checkpoints. Mammalian homologs of the four yeast checkpoint kinases have been identified, suggesting that organisms from yeast to human have similar protein pathways for regulating these checkpoints.^{2,4} The DNA damage response network of interacting pathways are signal transduction agents consisting of sensors, transducers, and effectors. The signal transducers are composed of sets of conserved proteins with recognizable motifs. One class is composed of phospho-inositide kinase (PIK)-related proteins which include ATM and ATM-Rad3-related (ATR) in mammals and their homologues in budding and fission yeast. These proteins are central to the entire DNA damage response. Downstream of these proteins are two families of checkpoint kinases (CHK), the Chk1 (54 kDa) and Chk2 (61 kDa, also known as hCds1) kinases, and their homologues.^{5,6}

Studies have established that mammalian Chk1 is structurally unrelated to Chk2, but performs an analogous role in propagating signals from damaged or unreplicated DNA¹. Chk1 is expressed and active only in S-G2 phases of the cell cycle, while Chk2, the human homologue of *S. cerevisiae* Rad53 and *S. pombe* Cds1, is expressed throughout the cell cycle⁷.

Arrest in G2 is mainly regulated by the maintenance of inhibitory phosphorylation of Cdc2. Cdc2 dephosphorylation and activation is catalyzed by the dual specificity phosphatase Cdc25. Evidence indicates that part of the G2M DNA checkpoint mechanism involves inactivation and translocation of Cdc25C into the cytoplasm. This is at least partially mediated by phosphorylation of Cdc25C on Ser²¹⁶ and its consequent binding with 14-3-3 proteins. Chk1 and Chk2 have been shown to phosphorylate Cdc25C at Ser²¹⁶.^{8,9} This modification is thought to maintain Cdc25C phosphorylation in cells arrested at G2M in response to DNA damage.¹ It has also been shown that Chk1 can phosphorylate Wee1, a negative regulator of G2 to M transition⁹.

Monoclonal antibody reacting specifically with Chk1 is a useful tool to study the role and importance of Chk1 as a checkpoint kinase in preventing genomic instability.

Reagent

Monoclonal Anti-CHK2 (hCDS1) is supplied as an approximately 2 mg/mL solution in 0.01 M phosphate buffered saline, pH 7.4, containing 15 mM sodium azide.

Precautions and Disclaimer

Due to the sodium azide content, a Safety Data Sheet (SDS) for this product has been sent to the attention of the safety officer of your institution. Consult the SDS for information regarding hazards and safe handling practices.

Storage/Stability

For continuous use, store at 2-8 °C for up to one month. For prolonged storage, freeze in working aliquots at -20 °C. Repeated freezing and thawing is not recommended. Storage in "frost-free" freezers is also not recommended. If slight turbidity occurs upon prolonged storage, clarify the solution by centrifugation before use. Working dilution samples should be discarded if not used within 12 hours.

Product Profile

A working concentration of 1-2 µg/mL is determined by immunoblotting, using a whole extract of 293T (human embryonal kidney) cells.

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Note: In order to obtain best results in different techniques and preparations we recommend determining optimal working dilutions by titration test.

References

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