ProductInformation

MONOCLONAL ANTI-p14^{ARF}
CLONE DCS-240
Purified Mouse Immunoglobulin

Product Number **P 2610**

Product Description

Monoclonal Anti-p14^{ARF} (mouse IgG1 isotype) is derived from the DCS-240 hybridoma produced by the fusion of mouse myeloma cells and splenocytes from a BALB/c mouse immunized with recombinant human p14^{ARF}. The isotype is determined using Sigma ImmunoType™ Kit (Sigma ISO-1) and by a double diffusion immunoassay using Mouse Monoclonal Antibody Isotyping Reagents (Sigma ISO-2).

Monoclonal Anti-p14^{ARF} reacts specifically with human p14^{ARF}. The antibody may be used in immunoblotting (14 kDa) and imunohistochemistry (formalin-fixed paraffin-embedded).

Inactivation of tumor-suppressor gene p53 leads to deregulated cell proliferation and is a key factor in human tumorigenesis. The ability of p53 to restrain a cell must be reigned in under normal conditions. Several cellular genes have been identified whose expression is activated by p53. One of these, the *mdm2* gene, encodes a protein that interacts directly with p53 and negatively regulates p53 transcriptional activity. p53 and MDM2 function in mutual regulation; activation of p53 results in expression of MDM2, which consequently inhibits p53 transcriptional function.[1] By its physical interaction with p53, MDM2 accomplishes this inhibition in two ways: repressing p53 transcriptional activity and mediating the degradation of p53.[2] Overexpression of MDM2 results in reduced quantities of coexpressed p53, and disruption of the p53-MDM2 interaction by mutation results in both activation and accumulation of p53.[3] MDM2 shuttles p53 from the nucleus to the cytoplasm where it is then degraded.[4] The shuttling of MDM2 between the nucleus and the cytoplasm is essential for MDM2's ability to promote p53 degradation. One way to stabilize and activate p53 in cells is by interfering either with the interaction between MDM2 and p53 or with the ability of MDM2 to target bound p53 for degradation. p53-MDM2 interaction may be regulated through two entirely separate and independent mechanisms that are regulated through distinct signaling pathways involving changes in p53 due to covalent modification, and/or through noncovalent regulators of the p53-MDM2 association. Coexpression of p14^{ARF} (a human homologue of mouse p19^{ARF}) is a product of the alternate reading frame (ARF) located within the p16^{INK4A} locus. p14^{ARF} blocks the nucleo-cytoplasmic shuttling of MDM2, attenuating MDM2-mediated degradation of p53, thereby stabilizing p53.[5] This 'one gene--two products--two pathways' arrangement provides a basis for the prominence of INK4a/ARF in tumorigenesis.[6] p14^{ARF} also links the tumor suppressors Rb and p53. Abnormal proliferative signals, such as loss of Rb is linked with the activation of p53 response, through E2F1 and p14^{ARF}.[7] Functional inactivation of the retinoblastoma (Rb) and p53 pathways appears to be a rite of passage for all cancerous cells and results in disruption of cell-cycle regulation and deactivation of the apoptotic response that normally ensues. Indeed, loss of ARF limits cell-autonomous tumor surveillance in response to particular oncogenic signals, and organism lacking ARF function, such as those lacking p53, are highly tumor prone.[8] Monoclonal antibody reacting specifically with p14^{ARF} is an essential tool in defining the interactions and distributions of p14^{ARF}, and its function in signaling pathways and mutual regulation of p53.

Reagents

Monoclonal Anti-p14^{ARF} is supplied as a solution in 0.01 M phosphate buffered saline pH 7.4, containing 15 mM sodium azide (see MSDS) as a preservative.

Antibody Concentration: Approx. 2 mg/ml.

Precautions and Disclaimer

Due to the sodium azide content a material safety sheet (MSDS) for this product has been sent to the attention of the safety officer of your institution.
Consult the MSDS for information regarding hazardous and safe handling practices.

Storage/Stability

For continuous use, store at 2-8 °C for up to one month. For extended storage, freeze in working aliquots. Repeated freezing and thawing is not recommended. Storage in "frost-free" freezers is 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 HeLa cells.

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

References

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4. Roth, J., et al., EMBO J., **17**, 554-564 (1998).
5. Tao, W., and Levine, A.J., Proc. Natl. Acad. Sci. USA, **96**, 6937-6941 (1999).
6. Chin, L., et al., Trends Bioch. Sci., **23**, 291-296 (1998).
7. Bates, S., et al., Nature, **395**, 124-125 (1998).
8. Kamijo, T., et al., Cell, **91**, 649-659 (1997).

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