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ProductInformation

Anti-FANCD2
produced in rabbit, IgG fraction of antiserum

Catalog Number **F0305**

Product Description

Anti-FANC2 is developed in rabbit using a synthetic peptide corresponding to amino acids 1-18 of human FANCD2, conjugated to KLH via a C-terminal added cysteine residue, as immunogen. The immunizing peptide is present in isoforms a and b of FANCD2. Whole antiserum is fractionated and then further purified by ion-exchange chromatography to provide the IgG fraction of antiserum that is essentially free of other rabbit serum proteins.

Anti-FANCD2 specifically recognizes human FANCD2 by immunoblotting, doublet at 170 kDa, and immunofluorescence. Staining of the FANCD2 band in immunoblotting is specifically inhibited by the immunizing peptide.

DNA damage checkpoints are biochemical pathways that delay or arrest cell cycle progression in response to DNA damage.[1, 2] Key checkpoint regulators are conserved throughout eukaryotes.[3, 4] Fanconi anemia (FA) is a disease with autosomal recessive inheritance, characterized by developmental abnormalites, progressive bone marrow failure, and cancer predisposition. Cells from FA patients exhibit hypersensitivity to DNA cross-linking agents, such as mitomycin C and cisplatin, suggesting a role for these proteins in the repair of damaged DNA.[5-7] At least 11 FA complementation groups are known to exist and nine genes have been identified, cloned, and referred to as FA subtypes A, B, C, D1/BRCA2, D2, E, F, G, and L.[8] The members of the Fanconi anemia complementation groups do not share sequence similarity and are related by their assembly into a common nuclear protein complex.[9,10] The FA complementation group D is heterogeneous consisting of 2 distinct genes, FANCD1 and FANCD2. FANCD2 is a nuclear protein consisting of two splicing isoforms of 1471 and 1451 amino acids (isoforms a and b respectively).[11] FA proteins A, C, E, F, D2, and G assemble in a multisubunit nuclear complex, which A, C, E, F, and G are required for the activation by monoubiquitination of the downstream FANCD2 protein after exposure to DNA damaging agents such as mitomycin C. After monoubiquitination, FANCD2 is targeted to nuclear foci with other proteins (BRCA1 and FANCD1/BRCA2) involved in homology-directed DNA repair.[12] Following IR, FANCD2 is phosphorylated by ATM, a central component of the S-phase checkpoint pathway on Ser^{222}. This phosphorylation activates the S phase checkpoint. The ATM-dependent phosphorylation of FANCD2 and the FA-pathway dependent monoubiquitination of FANCD2 are independent post-translatonal modifications both regulating discrete cellular signaling pathways. The enzyme/substrate interactions of ATM and FANCD2 account (at least in part) for the common clinical and cellular phenotypes of ataxia-telangiectasia patients (presenting mutations in ATM), and FA patients.[12]

Reagent

Supplied as a 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 material safety data 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, or storage in “frost-free” freezers, is not recommended. If slight turbidity occurs upon prolonged storage, clarify the solution by centrifugation before use. Working dilutions should be discarded if not used within 12 hours.

Product Profile

Immunoblotting: a working dilution of 1:2,000-1:4,000 is recommended using extracts of the U2OS cell line.

Indirect immunofluorescence: a working dilution of 1:250-1:500 is recommended using HEK 293-T cells fixed with paraformaldehyde-Triton®.

Note: In order to obtain the best results using various techniques and preparations, we recommend determining the optimal working dilutions by titration.

References

1. Sancar, A., et al., *Annu. Rev. Biochem*., **73**, 39-85 (2004).
2. Elledge, S.J., *Science*, **274**, 1664-1672 (1996).
3. Weinert, T., *Cell*, **94**, 555-558 (1998).
4. Savitsky, K., et al., *Science*, **268**, 1749-1753 (1995).
5. Bagby, G.C. Jr., *Curr. Opin. Hematol*., **10**, 68-76 (2003).
6. D'Andrea, A.D., and Grompe, M., *Nature Rev. Cancer*, **3**, 23-24 (2003).
7. Woo-Hyun Park, et al., *J. Biol. Chem*., **280**, 23593-23598 (2005).
8. Collins, N., and Kupfer, G.M., *Int. J. Hematol*., **82**, 176-183 (2005).
9. D'Andrea, A.D., *Genes & Dev.*, **17**, 1933-1936 (2003).
10. Joenje, H., and Patel, K.J., *Nature Rev. Genet*., **2**, 446-457 (2001).
11. Timmers, C., et al., *Molec. Cell*, **7**, 241-248 (2001).
12. Taniguchi, T., et al., *Cell*, **109**, 459-472 (2002).

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