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Product Information

Anti-FKHR (FOXO1a) antibody produced in rabbit
affinity isolated antibody, buffered aqueous solution

Product Number F2303

Product Description

Anti-FKHR (FOXO1a) is produced in rabbit using a synthetic peptide corresponding to human FKHR (amino acids 636–651) conjugated to KLH as immunogen. This sequence is conserved in human and mouse FKHR. Anti-FKHR (FOXO1a) is affinity-purified using the immunizing peptide immobilized on agarose.

Anti-FKHR (FOXO1a) recognizes human and mouse FKHR (FOXO1a) by immunoblotting (70–75 kDa). Additional bands of higher molecular weights may be detected in some preparations. Staining of FKHR (FOXO1a) in immunoblotting is specifically inhibited with the immunizing peptide.

The superfamily of Forkhead transcription factors (FOX) consists of more than 100 members, with orthologues expressed in a variety of species ranging from yeast to man.[1,2] They are characterized by a common Forkhead (or Winged Helix) domain, a variant of the helix-turn-helix motif.[2,3] Forkhead family members have been shown to play key regulatory roles in embryonic development, differentiation, apoptosis, and tumorigenesis.[1-5] Three Forkhead family members, termed FKHR (FOXO1a), FKHRL1 (FOXO3a), and AFX (FOXO4) were first identified at chromosomal break-points in human tumors, and consequently linked to tumorigenesis.[5-8] Central to unraveling the role of these proteins was the finding that they are similar in sequence to DAF16 from the nematode *C.elegans.* FKHR, FKHRL1, and AFX represent the mammalian counterparts.[9, 10] DAF16 transduces insulin-like and longevity signals.[9, 10] Similar to its mammalian orthologues, it has at least three putative sites for phosphorylation by PKB/AKT.[10]

Growth factors regulate the activity of FKHR, FKHRL1, and AFX via the PKB/PI3K pathway.[3, 11, 12] These transcription factors are inhibited through phosphor-ylation by PKB, the most likely mechanism being regulation of nuclear localization.[14-16] Phosphorylation of Thr^{32} and Ser^{253} in FKHRL1 (FOXO3a) by PKB after induction with survival factors, [13] results in its retention in the cytoplasm and/or its nuclear exclusion, and thus a subsequent inhibition of FKHRL1 dependent transcription.

Survival factor withdrawal results in FKHRL1 dephosphorylation and translocation to the nucleus. Within the nucleus, the dephosphorylated FKHRL1 induces expression of target genes such as Fas ligand, and triggers apoptosis.[13] FKHR and AFX were later shown to act by a similar mechanism. FKHR contains three residues, Thr^{24}, Ser^{256}, and Ser^{319} that lie within consensus sequences for phosphorylation by PKB. Likewise, induction by insulin-like growth factor (IGF-1) and insulin leads to phosphorylation of one or more of these sites.[14, 15] Two additional consensus sites for PDK1, at Ser^{322} and Ser^{325}, become phosphorylated in IGF-1-stimulated cells. A cluster of phosphorylated Ser^{319}, Ser^{322}, Ser^{325}, and Ser^{329} appears to accelerate nuclear export by controlling the interaction of FKHR with the Ran-containing protein complex that mediates this process.[16] In addition to the involvement of FKHR in apoptosis, it was shown to be involved in glucose homeostasis, cell cycle regulation, and as a nuclear receptor cofactor. Interestingly, FKHR was recently shown to play a role in endometrial differentiation via the protein kinase A (PKA) pathway.[17]

Antibodies reacting specifically with FKHR (FOXO1a) may be useful in studying the expression and function of the protein, as well as in correlating its expression pattern with physiological functions or pathological conditions.

Reagent

Supplied as a solution in 0.01 M phosphate buffered saline, pH 7.4, containing 1% bovine serum albumin (BSA) and 15 mM sodium azide.

Antibody concentration: minimum 0.8 mg/mL

Precautions and Disclaimer

This product is for R&D use only, not for drug, household, or other uses. Please consult the Safety Data Sheet 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, 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 minimum working dilution of 1:2,500 is determined using human FKHR expressed in transfected COS-7 cell extracts or 293-T cell extracts.

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

References

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