

BACKGROUND

Gfi-1 (growth factor independence-1) encodes a nuclear zinc-finger transcription factor and was first identified as an integration site of Moloney murine leukemia virus in a screen for T cell IL-2-independent growth. Subsequently, *Gfi-1* was found to be a frequent target of proviral insertion in T and B cell lymphomas. Overexpression of Gfi-1 abolishes G₁ cell cycle arrest and apoptosis induced by growth factor withdrawal. Transgenic mice that express high levels of Gfi-1 in T cells are predisposed to T cell lymphoma. Gfi-1 has further been shown to cooperate with c-Myc and Pim1 in lymphomagenesis.¹ In addition Gfi-1 may play a role in lung and prostate cancers. Targeted disruption of Gfi-1 in mice has revealed an important role of Gfi-1 in normal hematopoiesis. Gfi-1^{-/-} mice are defective in T and B cell development. Gfi-1^{-/-} mice also lack mature granulocytes because of a block in granulocytic differentiation. Consistent with its role in granulopoiesis, mutations in *Gfi-1*, albeit rare, have been reported in a small group of patients with severe congenital neutropenia (SCN), a disease characterized by an early block in granulocytic differentiation. Gfi-1 also acts to restrict the proliferation of hematopoietic stem cell (HSC) and thereby preserve their functional integrity.² Additionally Gfi-1 has been shown to regulate the development of nonhematopoietic cells including inner ear hair cells, lung neuroendocrine cells and intestinal epithelial cells.

Gfi-1 functions mainly as a repressor of transcription. It represses its target genes by binding to consensus DNA elements containing the AATC core sequence. The Gfi-1 protein consists of an N-terminal SNAG domain required for nuclear localization, a central region and 6 C-terminal zinc fingers (ZFs) involved in DNA binding. The SNAG domain is important for transcriptional repression; however, Gfi-1 may repress transcription through both SNAG domain-dependent and independent mechanisms. The different domains of Gfi-1 have been implicated in recruiting corepressors and histone modifying enzymes, including eight-twenty-one (ETO), CoREST, histone demethylase LSD1, histone deacetylases (HDACs) 1 and 2, and the histone lysine methyltransferase G9a. The mechanisms by which Gfi-1 controls cell proliferation and survival are still poorly understood. It has been shown that Gfi-1 binds to and represses *CDKN1A* encoding the cyclin-dependent kinase inhibitor (CDKI) p21^{Cip}, and the proapoptotic Bcl2 family member *Bax*. Myc-interacting zinc finger protein-1 (Miz-1) is a POZ-ZF transcription factor originally identified as a binding partner of c-Myc. Miz-1 possesses a potent anti-growth activity and has been shown to activate transcription by directly binding to the initiator (*Inr*) elements in its target genes, including *Mad4*, *CDKN1A*, and *CDKN2B* encoding the CDKI p15^{INK4B}. It was shown that Gfi-1 interacts with Miz-1 and is recruited to the core

promoter of *CDKN2B* via Miz-1, leading to transcriptional repression.³ In addition, Gfi1 functions as an antagonist of NF-κB activity at the level of promoter binding. This suggested a new function of Gfi1 as a general negative regulator of the endotoxin-initiated innate immune responses, including septic shock and possibly other severe inflammatory diseases.⁴

References:

1. Wallis, D. et al: Development 130, 221-32, 2003
2. Hock, H. et al: Nature 431:1002-7, 2004
3. Basu, S. et al: Proc. Natl. Acad. Sci. USA 106:1433-8, 2009
4. Sharif-Askari, E. et al: Mol. Cell. Biol. 30:3929-42, 2010

TECHNICAL INFORMATION

Source:

Gfi-1 Antibody is a mouse monoclonal antibody raised against recombinant human Gfi-1 fragments expressed in *E. coli*.

Specificity and Sensitivity:

This antibody detects endogenous Gfi-1 proteins without cross-reactivity with other family members.

Storage Buffer: PBS and 30% glycerol

Storage:

Store at -20°C for at least one year. Store at 4°C for frequent use. Avoid repeated freeze-thaw cycles.

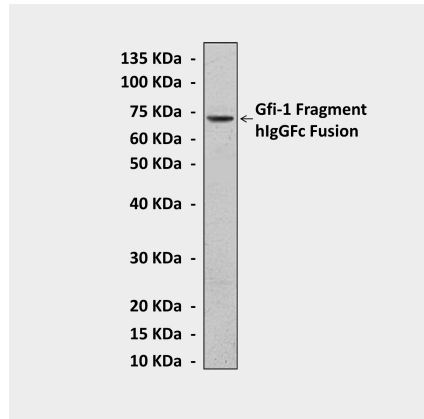
APPLICATIONS

Application:	*Dilution:
WB	1:1000
IP	n/d
IHC	n/d
ICC	n/d
FACS	n/d

*Optimal dilutions must be determined by end user.



QUALITY CONTROL DATA



Western Blot detection of Gfi-1 proteins in 293 cell lysate containing human Gfi-1-hlgGFc fusion proteins using Gfi-1 Antibody.

