

## BACKGROUND

Members of the NK subfamily of homeobox genes have been implicated in processes of cell fate specification and organogenesis in many species, including *Drosophila*, in which they were first identified. Molecular genetic analyses in *Drosophila* showed that *NK-3* corresponded to the *bagpipe* gene, which is required for visceral mesoderm development, whereas *NK-2* corresponded to *tinman*, which is required for cardiac mesoderm. In amniotes, these functional relationships appear to be conserved among *Nkx* homologs, although the specific functions are parceled out between two or more homologs for each NK ancestor. Thus, two *NK-3* class genes are known in amniotes, corresponding to *Nkx3.1* and *Nkx3.2* (also known as *Bapx1*), with their overall patterns of gene expression during development well-conserved. A third *Nkx3* family member has been identified in urodele amphibians, which contain a clear ortholog of *Nkx3.2*, but not of *Nkx3.1*; instead, a novel *Nkx3.3* gene has been defined that has not been identified in higher vertebrates.<sup>1</sup>

The *Nkx3.1* homeobox gene is a key regulator of prostatic epithelial differentiation, while its loss-of-function in mice has been implicated in prostate cancer initiation. In particular, *Nkx3.1* null mutant mice display abnormal prostatic differentiation as well as epithelial hyperplasia and dysplasia prior to 1 year of age. Human *NKX3.1* maps to chromosome 8p21, which frequently undergoes loss of heterozygosity at early stages of prostate carcinogenesis. Although *NKX3.1* is not mutated in prostate cancer, it undergoes epigenetic inactivation through loss of protein expression in human prostate cancer and in mouse models.<sup>2</sup> It was shown that PTEN loss causes reduced *NKX3.1* expression in both murine and human prostate cancers. Restoration of *Nkx3.1* expression in vivo in *Pten* null epithelium leads to decreased cell proliferation, increased cell death, and prevention of tumor initiation. Whereas androgen receptor (AR) positively regulates *NKX3.1* expression, *NKX3.1* negatively modulates AR transcription and consequently the AR-associated signaling events. Consistent with its tumor suppressor functions, *NKX3.1* engages cell cycle and cell death machinery via association with HDAC1, leading to increased p53 acetylation and half-life through MDM2-dependent mechanisms. Importantly, overexpression of *Nkx3.1* has little effect on *Pten* wild-type epithelium, suggesting that PTEN plays a predominant role in PTEN-*NKX3.1* interplay. Manipulating *NKX3.1* expression may serve as a therapeutic strategy for treating PTEN-deficient prostate cancers.<sup>3</sup> In addition, *NKX3.1* affects DNA damage response and cell survival after DNA damage. It was shown that endogenous *NKX3.1* in LNCaP cells localizes to sites of DNA damage where it affects the recruitment of phosphorylated ATM and the phosphorylation of H2AX. *NKX3.1* expression enhances activation of and activation of ATR.<sup>4</sup> Moreover *NKX3.1* activates expression of

insulin-like growth factor binding protein-3 to attenuate insulin-like growth factor-I signaling and cell proliferation.<sup>5</sup> thus, the growth-suppressive effects of *NKX3.1* in prostate cells are mediated, in part, by activation of IGFBP-3 expression.

### References:

1. Shen, M.M. & Abate-Shen, C.: Dev. Dyn.228:767-78, 2003
2. Bora, G. et al: Am. J. Surg. Path. 34:1097-105, 2010
3. Lei, Q. et al: cancer Cell 9:367-78, 2006
4. Cai, B. & Gelmann, E.P: Cancer Res. 70:3089-97, 2010
5. Muhlbradt, E. et al: Cancer Res. 69:2615-22, 2009

## TECHNICAL INFORMATION

### Source:

*NKX3.1* Antibody is a mouse monoclonal antibody raised against recombinant human *NKX3.1* fragments expressed in *E. coli*.

### Specificity and Sensitivity:

This antibody detects endogenous *NKX3.1* proteins without cross-reactivity with other family members.

**Storage Buffer:** PBS and 30% glycerol

### Storage:

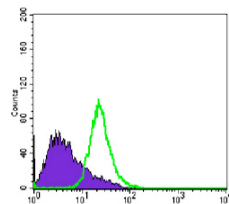
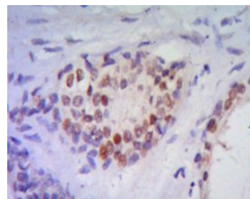
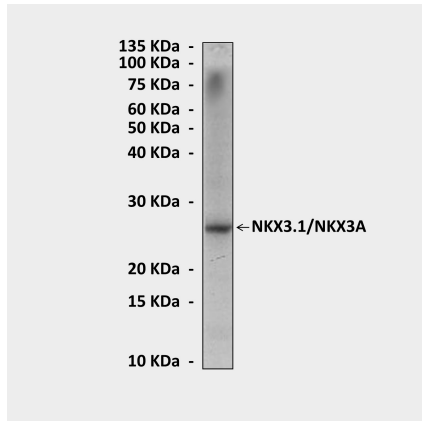
Store at -20°C for at least one year. Store at 4°C for frequent use. Avoid repeated freeze-thaw cycles.

## APPLICATIONS

Application:	*Dilution:
WB	1:1000
IP	1:50
IHC	1:50-200
ICC	n/d
FACS	1:50-200
*Optimal dilutions must be determined by end user.	



### QUALITY CONTROL DATA



**Top:** Western Blot detection of NKX3.1 proteins in LNCap cell lysate using NKX3.1 Antibody. **Middle:** This antibody stains paraffin-embedded human prostate cancer tissue in immunohistochemical analysis. **Bottom:** It also specifically reacts with NKX3.1 proteins in PC-3 cells by FACS testing (NKX3.1 antibody: Green; control; Purple).

