Gene Section

Mini Review

NKX3-1 (NK3 homeobox 1)
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Identity
Other names: NKX3 BAPX2; NKX3A; NKX3.1
HGNC (Hugo): NKX3-1
Location: 8p21.2
Local order: Gene orientation: telomere-3' NKX3.1 5'-centromere.

DNA/RNA
Description
The gene has two exons and one intron.

Transcription
Transcription takes place in a centromere --+ telomere orientation. The length of the processed mRNA is about 3200 bp.

Pseudogene
Not known.

Protein
Description
234 amino acids; 35-38 kDa, contains one N-terminal domain (residues 1-123), one homeo-domain (residues 124-183), and one C-terminal domain (residues 184-234).

Expression
Expression is restricted to the adult murine prostate and bulbourethral gland. During early murine embryogenesis NKX3-1 expression has also been detected in developing somites and testes. In the adult human expression is seen in prostate epithelium, testis, ureter, and pulmonary bronchial mucous glands.

Localisation
Nuclear.

Function
Binds to DNA to suppress transcription. Interacts with transcription factors, e.g. serum response factor, to enhance transcriptional activation. Binds to and potentiates topoisomerase I DNA resolving activity. Acts as prostate tumor suppressor.

Homology
Homeodomain protein with membership of the NKX family.

The gene for NKX3-1 comprises two exons of 334 and 2947 bp, respectively. The length of the intron is 964 bp. Positions of start and stop codons are indicated.

NKX3-1 contains two exons encoding a 234-amino acid protein including a homeodomain (grey).


Mutations

Germinal

Twenty-one germ-line variants have been identified in 159 probands of hereditary prostate cancer families. These variants were linked to prostate cancer risk in hereditary prostate cancer families. For example, the C154T (11% of the population) polymorphism mutation is associated with prostatic enlargement and prostate cancer risk. A T164A mutations in one family cosegregates with prostate cancer in three affected brothers. For a more complete list of identified mutations, please visit http://cancerres.aacrjournals.org/cgi/content/full/66/1/69.

Somatic

None.

Implicated in

Prostate Cancer

Disease

Prostate cancer is the most commonly diagnosed cancer in American men and the second leading cause of cancer-related deaths. Prostate cancer predominantly occurs in the peripheral zone of the human prostate, with roughly 5 to 10% of cases found in the central zone. Disease development involves the temporal and spatial loss of the basal epithelial compartment accompanied by increased proliferation and dedifferentiation of the luminal (secretory) epithelial cells. Prostate cancer is a slow developing disease that is typically found in men greater than 60 years of age and incidence increases with increasing age.

Prognosis

PSA test combined with digital-rectal exams are used to screen for the presence of disease. If the digital-rectal exams are positive, additional tests including needle core biopsies are taken to assess disease stage and grade. Patients with localized, prostate-restricted cancers are theoretically curable with complete removal of the prostate (radical prostatectomy). Patients with extra-prostatic disease are treated with hormone (androgen ablation) therapy, radiation, and/or antiandrogens; however, no curative treatments are available for nonorgan confined metastatic disease.

Cytogenetics

Various forms of aneuploidy.

Oncogenesis

Nkx3.1 plays an essential role in normal murine prostate development. Loss of function of Nkx3.1 leads to defects in prostatic protein secretions and in ductal morphogenesis. Loss-of-function of Nkx3.1 also contributes to prostate carcinogenesis. For example, Nkx3.1 mutant mice develop prostatic dysplasia. Nkx3.1 loss potentiates prostate carcinogenesis in a Pten-/- background. Further-more, by a variety of mechanisms Nkx3.1 expression is reduced in noninvasive and early stage human prostate cancer, suggesting that its decreased expression is one of the earliest steps in the majority of human prostate cancers.

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