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Gene Section
Mini Review

TFE3 (transcription factor E3)

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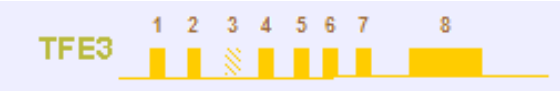
Identity

HGNC (Hugo): TFE3

Location: Xp11.2

DNA/RNA



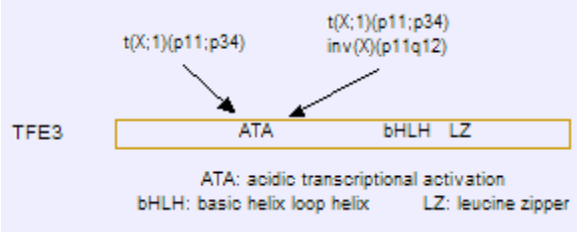
Description

8 exons.

Transcription

Differential splicing removing exon 3 (with dominant negative activity of the resulting protein).

Protein



Description

743 amino acids; 80 kDa; N-term acidic transcriptional activation domain (domain 260-271, exon 3), helix-loop-helix (344 -400), leucine zipper (409-430), and a proline/arginine rich sequence (575-743) C-term.

Expression

Wide; in fetal and adult tissues.

Localisation

Nucleus.

Function

Transcription factor; member of the basic helix-loop-helix family (b-HLH) of transcription factors primarily found to bind to the immunoglobulin enchancer muE3 motif, Ig K enhancers and Ig H variable regions promotors; the helix-loop-helix - leucine zipper region is implicated in DNA binding and dimerization (homo and heterodimerizations); mice which lack TFE3 in their B and T lymphocytes reconstitute the B- and T-cell compartments, but IgM levels are reduced.

Homology

To other members of the myc family of helix-loop-helix transcription factors.

Implicated in

t(X;1)(p11.2;q21.2) in renal cell carcinoma --> PRCC/TFE3

Prognosis

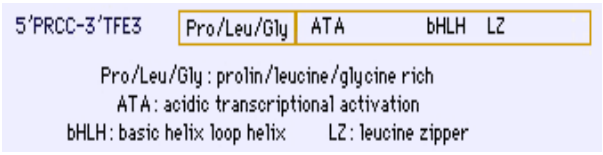
Overall 5-yr survival rate around 85%.

Hybrid/Mutated gene

5' PRCC- 3' TFE3; variable breakpoint in PRCC; breakpoint in the 1st intron of TFE3.

Abnormal protein

N-term PRCC with the proline rich sequence fused to most of TFE3, including the acidic transcriptional activation domain, the helix-loop-helix, and the leucine zipper; the reciprocal TFE3-PRCC is expressed; it is to be noted that the normal TFE3 transcript is lost in female patients



Oncogenesis

PRCCTFE3 appears to be the fusion product that is most critical for the development of papillary renal cell carcinomas; it is a three-fold better trans-activator than wild-type TFE3 and shows the characteristics associated with malignant trans-formation.

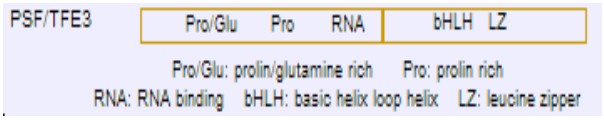
t(X;1)(p11.2;p34) in renal cell carcinoma --> PSF/TFE3

Disease

t(X;1)(p11.2;p34) has only been found in a handfull cases of papillary renal cell carcinoma.

Hybrid/Mutated gene

5' PSF- 3' TFE3



Abnormal protein

N-term PSF and most of it fused to the DNA binding domains of TFE3 (excluding the acidic transcriptional activation domain, including the C-term helix-loop-helix, and the leucine zipper); no TFE3-PSF reciprocal transcript, as the der(X) t(X;1) is missing; the normal TFE3 transcript is found.

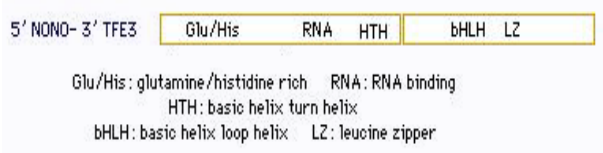
inv(X)(p11.2q12) in renal cell carcinoma --> NonO/TFE3

Disease

Only one case of papillary renal cell carcinoma.

Hybrid/Mutated gene

5' NONO- 3' TFE3



Abnormal protein

N-term NONO and most of it except the C-term proline rich sequence fused to the DNA binding domains of TFE3 (excluding the acidic trans-criptional activation domain, including the C-term helix-loop-helix, and the leucine zipper); the reciprocal transcript is found.

Alveolar soft part sarcoma with ASPSCR1 -TFE3 fusion

Cytogenetics

der(X)t(X;17)(p11;q25) is consistently involved; it implicates: 1- the formation of a hybrid gene at the breakpoint, and also, 2- gain in Xp11-pter sequences, and loss of heterozygocity in 11q25-qter, with possible implications.

Hybrid/Mutated gene

5' ASPSCR1-3' TFE3; the reciprocal 5' TFE3 - 3' ASPSCR1 is most often absent. ASPSCR1 is fused in frame to TFE3 exon 3 or 4.

Abnormal protein

NH2 term ASPSCR1, fused to the C term of TFE3.

Oncogenesis

Might combine the effect of a fusion protein to that of gene(s) dosage.

Primary renal ASPSCR1-TFE3 tumour

Disease

A subset of renal cell carcinoma, which presents with a combination of alveolar soft part sarcoma-like features and epithelial features is found to carry this anomaly.

Cytogenetics

Balanced t(X;17)(p11.2;q25), in contrast with what is found in the alveolar soft part sarcoma (see above).

Hybrid/Mutated gene

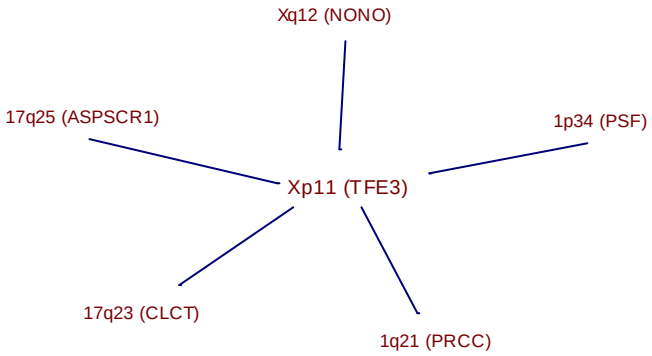
5' ASPSCR1-3' TFE3.

Abnormal protein

NH2 term ASPSCR1, fused to the C term of TFE3.

Other Xp11 involvements in renal cell carcinoma (t(X;10)(p11;q23), etc.) are likely to implicate TFE3

Breakpoints



TFE3 and partners. Editor 08/2001 updated 08/2004.

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