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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

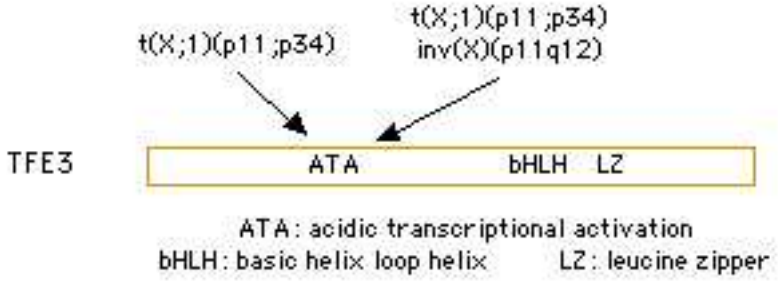
Nucleus.

Function

Transcription factor; member of the basic helix-loop-helix family (b-HLH) of transcription factors primarily found to bind to the immunoglobulin enhancer 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%.

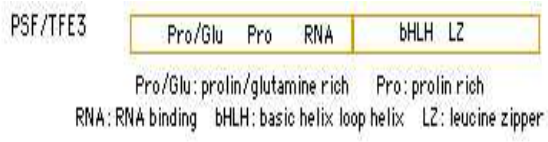
Hybrid/Mutated gene
5' PRCC - 3' TFE3; variable breakpoint in PRCC; breakpoint in the 1st intron of TFE3.

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.

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.

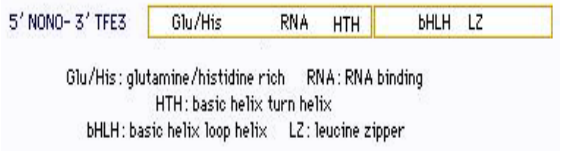


Abnormal protein
N-term PSF and most of it fused to the DNA binding domains of TFE3 (excluding the acidic transcriptional activation domain, including the C-term helix-loop-helix, and the leucine zipper); no TFE3-PSF reciprocal transcript, as the der(X) t(X;1) is missing; the normal TFE3 transcript is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

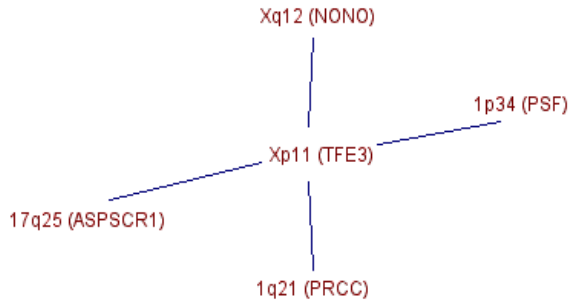
Cytogenetics
Balanced t(X;17)(p11.2;q25), in contrast with what is found in the alveolar soft part sarcoma (see above).

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

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Huret JL. TFE3 (transcription factor E3). Atlas Genet Cytogenet Oncol Haematol. 2001; 5(4):268-270.