Gene Section
Mini Review

TFE3 (transcription factor E3)
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Identity
HGNC (Hugo): TFE3
Location: Xp11.2

DNA/RNA

| TFE3 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 |

Description
8 exons.

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

Protein

<table>
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<tr>
<th>t(3;1)(p11;q34)</th>
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<td>inv(3)(p11;q12)</td>
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ATA: acidic transcriptional activation
bHLH: basic helix loop helix
LZ: leucine zipper

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 promoters; 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**

PRCC TFE3 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 transformation.

**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 handful 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' NOHO - 3' TFE3

**Abnormal protein**

N-term NOHO 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

- Xq12 (NONO)
- 17q25 (ASPCR1)
- 17q23 (CLCT)
- 1p34 (PSF)
- 17q25 (ASPCR1)
- Xp11 (TFE3)
- 1q21 (PRCC)

**References**


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*This article should be referenced as such:*