TFE3 (Xp11.2) Gene Rearrangement by FISH

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The *TFE3* gene belongs to the micropthalmia transcription factor (MiT) gene family, and encodes a protein that promotes TGF-beta signaling expression of downstream genes.[1] Translocations involving the *TFE3* locus can increase the rate of cell division and growth. *TFE3* may be involved in gene translocations in certain cancers, particularly renal cell carcinoma (RCC) and alveolar soft part sarcoma (ASPS).

Disease Overview

Incidence

Xp11-TRCC is a rare RCC subtype that comprises 20-40% of childhood RCC and 1-4% of adult RCC. ASPS is a rare sarcoma of deep soft tissue that accounts for <1% of all soft tissue sarcomas.

Diagnostic/Prognostic Issues

- Xp11-TRCC tend to exhibit uncommon RCC morphologies such as clear, papillary, and chromophobe-like.
- Adult Xp11-TRCC tend to have more frequent lymph node metastasis and may be more clinically aggressive than other RCC subtypes.
- Childhood Xp11-TRCC tends to have a more indolent course.
- Xp11-TRCC may benefit from mTOR inhibitor drug therapy.
- ASPS are highly malignant, although with an indolent course. They tend to metastasize, especially to the brain and lungs, and conventional chemotherapy has limited benefit.
- ASPS has been shown to also have abnormal *MET* gene expression and patients may benefit from crizotinib therapy.

Genetics

Gene

TFE3

Function

Translocation involving the *TFE3* locus can increase the rate of cell division and growth.

Variants

TFE3 can fuse with over a dozen translocation partners. The most common partners include *ASPL* (*ASPSCR1*), *PRCC*, and *SFPQ* (*PSF*).

Test Interpretation

Results

- Positive: *TFE3* rearrangement detected in ≥15% of nuclei
  - Diagnosis of Xp11-TRCC or ASPS
- Negative: *TFE3* rearrangement not detected
  - Does not exclude diagnosis of Xp11-TRCC or ASPS

Limitations

- Results may be compromised if the recommended fixation procedures have not been followed.
- This test will not identify the specific translocation partner.
- Rare intrachromosomal rearrangements may not be detectable by conventional FISH assays.

References

1. Caliò A, Segala D, Munari E, Brunelli M, Martignoni G. MiT family translocation renal cell carcinoma: from the early descriptions to the current knowledge. *Cancers (Basel)*. 2019;11(8):1110.

Additional Resources

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