

# TFE3 (Xp11.2) Gene Rearrangement by FISH

The *TFE3* gene belongs to the microphthalmia transcription factor (MiT) gene family, and encodes a protein that promotes TGF-beta signaling expression of downstream genes.<sup>1</sup> 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).

## Tests to Consider

### TFE3 Gene Rearrangement by FISH 3002633

**Method:** Fluorescence in situ Hybridization (FISH)

Use for the diagnosis of Xp11 translocation  
RCC (TRCC) and 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. Calìo 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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Schöffski P, Wozniak A, Kasper B, et al. [Activity and safety of crizotinib in patients with alveolar soft part sarcoma with rearrangement of TFE3: European Organization for Research and Treatment of Cancer \(EORTC\) phase II trial 90101 'CREATE'](#). *Ann Oncol*. 2018;29(3):758-765.

Sukov WR, Hodge JC, Lohse CM, et al. [TFE3 rearrangements in adult renal cell carcinoma: clinical and pathologic features with outcome in a large series of consecutively treated patients](#). *Am J Surg Pathol*. 2012;36(5):663-670.

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