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.\(^1\) 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 (ASPCR1), PRCC, and SFPQ (PSF).

Test Interpretation

Results

- Positive: TFE3 rearrangement detected in \(\geq 15\%\) 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


Additional Resources