

DEDICATED TO PROVIDING ADVANCED TESTING

Genitourinary Tumors

Renal, Prostate, and Testicular Cancers

<10

DAYS TURNAROUND TIME

7

ASSAYS

6

GENITOURINARY EXPERTS

CLINICAL DESIGN AND IMPLEMENTATION

The genitourinary service line laboratory at Michigan Medicine Laboratories currently offers fluorescent in situ hybridization (FISH) assays for TFE3, TFEB and ERG gene aberrations and is actively working on new assays for inclusion in its clinical menu. Renal cell cancer is less common than prostate cancer but twice as lethal, with advanced metastatic renal tumors demonstrating a very dismal prognosis. The tremendous evolution in classification of renal tumors has been associated with the development of diverse therapeutic choices, wherein specific subtypes of renal tumors might dictate availability and response to specific treatments.

Our Methodology

FISH is performed on unstained formalin fixed paraffin embedded (FFPE) tissue sections of cases under investigation using a dual color break-apart probe set specific to the TFE3 gene locus at Xp11.2. Similar methodology is applied to detect the break-apart probe patterns specific to the TFEB gene locus at 6p21. The probe mixture includes one probe that is located centromeric and one probe located telomeric to the TFE3 or TFEB gene breakpoint region. Splitting of the probes is observed when a rearrangement involving these genes is present (Figure 1). Probe signals are evaluated in interphase nuclei and cases are interpreted according to normal cutoff values determined by the laboratory.

BENEFITS

- Control specimens are run concurrently to ensure quality control.
- 6 Available experts that specialist in Genitourinary Cancers.
- 10 days or less for turn around times, with STAT available.

TWO MAIN CLASSES OF T-RCC ARE CURRENTLY RECOGNIZED

Translocations involving the TFE3 locus on chromosome Xp11 and a t(6;11) translocation generating the TFEB gene fusion. Xp11 RCCs often morphologically demonstrate high nuclear grade, prominent papillary and/or alveolar pattern and clear to granular eosinophilic cytoplasm (Figure 1). The t(6;11) carcinomas may exhibit nests, sheets and tubules of cells with clear to eosinophilic cytoplasm separated by thin vascular septae. These tumors may also present with a biphasic morphology with a minor subpopulation of smaller cells with high nuclear/cytoplasmic ratio with or without the presence of associated basement membrane material. While morphologic features often correlate with translocation category and subtype, significant morphologic overlap exists among different translocation groups and non-translocation associated tumors. Our morphologic recognition of these renal tumors is undoubtedly improving and newer patterns have recently been associated with t-RCC9, 3. Still, these renal tumors can be diagnostically challenging without the aid of appropriate ancillary studies. Whereas immunohistochemistry (IHC) for TFE3 or TFEB proteins (or their common transcriptional target cathepsin K) is specific for t-RCC, there is poor reproducibility of TFE3 or TFEB IHC, and the sensitivity is not high enough to exclude the possibility of false-negative results. FISH, however, has been robustly validated for the accurate diagnosis of these renal tumor subtypes and exhibits a high degree of sensitivity and specificity 2-4. Importantly, because it shares molecular rearrangement of the 4 Michigan Medicine Laboratory TFE3 gene locus, the TFE3 FISH assay can also be used to confirm the diagnosis of alveolar soft part sarcoma, if indicated.



SEARCH TEST MENU

- KIDNEY – TFEB Rearrangements by FISH
- KIDNEY – TFE3 Rearrangements by FISH
- PROSTATE – ERG Rearrangements by FISH
- TESTICULAR – Cancer Cytogenomic Array for i12p, FFPE tissue

QUESTIONS?

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READY TO ORDER?
800.862.7284



FISH FOR TFE3/TFEB GENE ABERRATIONS

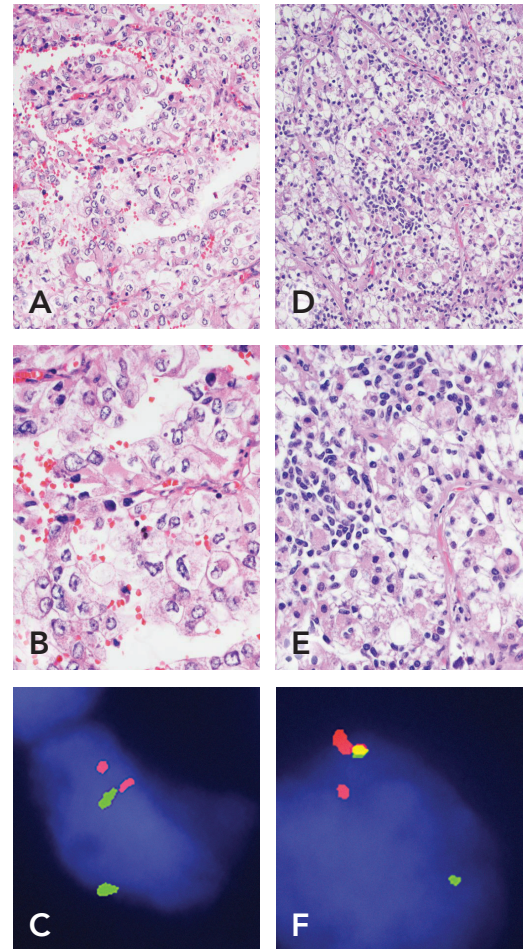


Figure 1. A and B, H&E images of Xp11 t-RCC demonstrates papillary architecture with cells exhibiting voluminous clear and eosinophilic cytoplasm (A - 200x, B - 400X). C, TFE3 FISH employing TFE3 break-apart FISH probe strategy demonstrates TFE3 translocation - co-localized green and red signal indicate wild-type TFE3 allele, TFE3 translocation is indicated by a single green signal and single red signal. D and E, H&E images of t(6;11) t-RCC with nests and sheets of cells separated by thin vascular septae; biphasic morphology with clusters of smaller cells dispersed between larger cells (D - 200x, E - 400X). F, TFEB FISH employing TFEB break-apart FISH probe strategy demonstrates TFEB translocation - co-localized green and red signal indicate wild-type TFEB allele, TFEB translocation is indicated by a single green signal and single red signal.

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