FOXO1 (FKHR) (13q14) Gene Rearrangement by FISH

Indications for Ordering

Use in conjunction with histologic and clinical information for the diagnosis of alveolar rhabdomyosarcoma

Test Description

- Fluorescence in situ hybridization (FISH) analysis on formalin-fixed, paraffin-embedded (FFPE) tissue
- Break-apart DNA probes flank the 13q14 locus
- 100 cells evaluated from regions of tumor identified on histopathologic review of a matching hematoxylin and eosin stained section

Tests to Consider

Primary test

FOXO1 (FKHR) (13q14) Gene Rearrangement by FISH 2001497

Disease Overview

Incidence – rhabdomyosarcomas are the most common soft-tissue sarcoma in children <15 years of age

- Alveolar subtype is rare

Diagnostic/prognostic issues

- Rhabdomyosarcomas are malignant neoplasms showing differentiation toward striated muscle
- Tumors are divided into histomorphologic and prognostic subtypes
  - Embryonal
  - Alveolar
- Differentiating between subtypes is important because the alveolar subtype has a poorer prognosis from the embryonal subtype
- *FOXO1* with a translocation partner of the *PAX* genes is found in alveolar rhabdomyosarcoma, but not the embryonal subtype

Genetics

Gene – *FOXO1*

Function

Translocation involving the *FOXO1* locus can increase the rate of cell division and growth

Variants

FOXO1 can fuse with several translocation partners including *PAX3, PAX7*

Test Interpretation

Results

- Positive – *FOXO1 (FKHR)* rearrangement detected in ≥25% of nuclei
  - Alveolar rhabdomyosarcoma likely
- Negative – *FOXO1 (FKHR)* rearrangement not detected
  - Does not exclude diagnosis of alveolar rhabdomyosarcoma

Limitations

- Results may be compromised if the recommended fixation procedures have not been followed
- This test will not identify the specific translocation partner