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 3001297

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 three histomorphologic and prognostic subtypes
  o Embryonal
  o Alveolar
  o Pleomorphic (primarily occurs in adults)
• Differentiating between subtypes is important because the alveolar subtype has a poorer prognosis than the embryonal subtype
• FOXO1 with a translocation partner of the PAX genes is found in alveolar rhabdomyosarcoma, but not the embryonal or pleomorphic subtypes

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
  o Alveolar rhabdomyosarcoma likely
• Negative – FOXO1 (FKHR) rearrangement not detected
  o 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