

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

FOR THE DIAGNOSIS OF ALVEOLAR RHABDOMYOSARCOMA

Test Highlights

- FISH analysis is a sensitive and specific detection methodology for the detection of *FOXO1* gene rearrangements, which are associated with alveolar rhabdomyosarcoma.

Disease Overview

- Rhabdomyosarcomas are malignant neoplasms showing differentiation toward striated muscle.
- Rhabdomyosarcoma is the most common soft-tissue sarcoma in children under 15 years of age and is one of the most common soft-tissue sarcomas of adolescents and young adults.
- The most common anatomic sites of origin are the genitourinary tract, head and neck, and retroperitoneum. The pleomorphic variety may arise in the large muscles of the extremities.
- Rhabdomyosarcomas are divided into histomorphologic and prognostic subtypes, including embryonal, alveolar, and pleomorphic. Rhabdomyosarcomas in adults are often of the pleomorphic subtype. The alveolar subtype has a demonstrably poorer prognosis than the embryonal subtype, and its differentiation from the latter is important for therapeutic decisions.
- Immunohistochemically, rhabdomyosarcomas will react positively with antisera against desmin, muscle-specific actin, myogenin, and myo-D1. Anatomic site, age at diagnosis, and histopathologic type are all prognostic factors. Favorable factors include young age, orbital or genitourinary location, size under five centimeters, and a botryoid or spindle-cell pattern.

Genetics

Alveolar rhabdomyosarcoma is strongly associated with a t(1;13) or t(2;13) translocation; both involve the *FOXO1* gene on chromosome 13.

Indications for Ordering

Patients diagnosed with or suspected of having alveolar rhabdomyosarcoma based on morphology or immunophenotypic studies.

Contraindications

This test is not recommended for detection of minimal residual disease.

Additional Ordering Notes

- The biopsy site and fixative used should be provided.
- The submitted sample should contain sufficient viable tumor.

Interpretation

The presence of an *FOXO1* gene rearrangement is strongly supportive of a diagnosis of alveolar rhabdomyosarcoma.

Limitations

- Tissues fixed in alcohol-based or non-formalin fixatives have not been tested using this method.
- The *FOXO1* probe will identify the rearrangement or translocation of 13q14, but not the specific translocation partner.

Methodology

The detection of *FOXO1* gene rearrangements in formalin-fixed, paraffin-embedded tissue uses a commercially available DNA FISH probe.

References

- Vysis[®] LSI FOXO1 Dual Color Break Apart Probe (package insert). Des Plaines, IL: Abbott Molecular; 2010.
- Linardic CM. *PAX3-FOXO1* fusion gene in rhabdomyosarcoma. *Cancer Lett* 2008;270(1):10–8.

Test Information

2001497

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For specific collection, transport, and testing information, refer to the ARUP website at www.aruplab.com.

For information on test selection, ordering, and interpretation, refer to ARUP Consult[®] at www.arupconsult.com.

AUTHOR

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