

PAX-FKHR Translocations by RT-PCR

USED TO DETECT THE PRESENCE OF PAX3-FKHR AND PAX7-FKHR TRANSCRIPTS IN TUMOR TISSUE WHERE ALVEOLAR RHABDOMYOSARCOMA IS SUSPECTED

Disease Overview

- Rhabdomyosarcomas are the most common childhood soft tissue malignancy, accounting for 60 percent of soft tissue sarcoma cases among children younger than 5 years of age.
- Incidence of rhabdomyosarcoma decreases with age, thus accounting for only 25 percent of soft tissue sarcomas in 15- to 19-year-olds.
- Histologically, rhabdomyosarcomas are divided into two major categories: embryonal and alveolar. The alveolar subtype accounts for one-fourth of cases and has a worse prognosis than the embryonal subtype.
- The detection of a *PAX-FKHR* transcript is specific for alveolar rhabdomyosarcoma, differentiating this tumor type from embryonal and spindle-cell rhabdomyosarcomas.

Genetics

- Alveolar rhabdomyosarcoma (ARMS) is associated with two chromosomal translocations specific for the disease. The t(2;13) (q35;q14) translocation juxtaposes the *PAX3* gene with the *FKHR* gene in approximately 55 percent of cases, whereas the t(1;13) (p36;q14) translocation fuses the *PAX7* gene with the *FKHR* gene in about 22 percent of cases. The resulting gene fusions produce novel transcription factors with oncogenic activity.
- Studies suggest that the *PAX7-FKHR* gene fusion has a better prognosis than the *PAX3-FKHR* gene fusion, with four-year overall survival rates being 77 percent and 52 percent, respectively.

Interpretation

- A negative result does not exclude the presence of a rare *PAX-FKHR* transcript.
- A positive result indicates the presence of either a *PAX3-FKHR* or *PAX7-FKHR* translocation indicative of ARMS.

Methodology

- Patient tumor RNA is isolated from formalin-fixed, paraffin-embedded tissue blocks and reverse transcribed into cDNA. The cDNA is then PCR-amplified using oligonucleotide primers specific for the *PAX* genes and the *FKHR* gene.
- Each sample is also amplified for the *MRPL19* gene, which serves as a PCR control.

Indications for Ordering

- The principle use for the assay is to differentiate alveolar rhabdomyosarcomas from other types of rhabdomyosarcomas in tumor tissue by the detection of a *PAX-FKHR* transcript.
- Results of this test should be interpreted in the context of histology and other relevant data, and should not be used alone for a diagnosis of malignancy.
- As currently configured, this assay is intended to serve as a qualitative test and should not be used to detect minimal residual disease.

References

1. Barr FG, Xiong QB, Kelly K. A consensus polymerase chain reaction oligonucleotide hybridization approach for the detection of chromosomal translocations in pediatric bone and soft tissue sarcomas. *Am J Clin Pathol* 1995;104: 627–33.
2. Reichmuth C, et al. The diagnostic potential of the chromosome translocation of t(2;13) in rhabdomyosarcoma. *J Pathology* 1996;180:50–7.
3. Sorenson P, et al. *PAX3-FKHR* and *PAX7-FKHR* gene fusions are prognostic indicators in alveolar rhabdomyosarcoma: a report from the children's oncology group. *J Clin Oncology* 2002;20:2672–9.

Test Information

0040113 *PAX-FKHR* Translocation by RT-PCR

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.

AUTHORS

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