

# *EWSR1* Gene Rearrangement by FISH

## FOR THE DIAGNOSIS OF EWING SARCOMA

### Test Highlights

*EWSR1* FISH is a sensitive and specific method used to detect *EWSR1* gene rearrangements and aid in the diagnosis of Ewing sarcoma.

#### Disease Overview

- Ewing sarcoma is a round-cell tumor occurring in children and young adults.
- The tumor most often presents in the long bones of the body, such as the arms, legs, pelvis, or chest, and frequently metastasizes to the lungs or other bones.

#### Epidemiology

- Ewing sarcoma is more common in males, with a peak age for occurrence between 10 and 20 years.
- About four cases of Ewing sarcoma per 1,000,000 children are diagnosed each year in the United States.

#### Genetics

Ewing sarcoma is strongly associated with t(11;22) and, in some cases, t(7;22) or t(21;22) involving the *EWSR1* gene on chromosome 22.

#### Pathophysiology

- The exact cause of Ewing sarcoma is not known. Translocations within the *EWSR1* gene on chromosome 22 can increase the rate of cell division and growth.
- The distinction of Ewing sarcoma from other sarcomas provides prognostic and therapeutically relevant information.

#### Indication for Ordering

Patients diagnosed with or suspected of having Ewing sarcoma based on morphology or immunophenotypic studies.

#### Contraindication

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

#### Additional Ordering Note

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

#### Interpretation

Presence of an *EWSR1* gene rearrangement is strongly supportive of a diagnosis of Ewing sarcoma.

#### Limitations

- Tissues fixed in alcohol-based or non-formalin fixatives have not been tested using this method.
- This test will not identify the specific *EWSR* translocation partner.

#### Methodology

- The detection of *EWSR1* gene rearrangements in formalin-fixed, paraffin-embedded tissue uses a commercially available DNA FISH probe. The presence of two fusion signals per nucleus indicates an intact *EWSR1* gene. The presence of a single orange and single green signal indicates a rearranged *EWSR1* gene.
- This test is conducted by noting the probe-signal configuration within the nuclei and reporting the result as rearranged or normal.

#### References

1. Vysis<sup>®</sup> LSI *EWSR1* Dual Color Breakapart Probe (package insert). Des Plaines, IL: Abbott Molecular, Inc.; 2002.
2. Sandberg AA, Bridge JA. Updates on cytogenetics and molecular genetics of bone and soft tissue tumors; Ewing sarcoma and peripheral primitive neuroectodermal tumors. *Cancer genet cytogenet* 2002;123(1):1–26.
3. Balamuth NJ, Womer RB. Ewing's sarcoma. *Lancet Oncol* 2010; 11(2):184–92.
4. Osuna D and de Alava E. Molecular pathology of sarcomas. *Rev Recent Clin Trials* 2009; 4(1):12–26.
5. Toomey EC, Schiffman JD, Lessnick SL. Recent advances in the molecular pathogenesis of Ewing's sarcoma. *Oncogene* 2010;29(32):4504–16.
6. Khoury JD. Ewing sarcoma family of tumors. *Adv Anat Pathol* 2005; 12(4):212–20.

## Test Information

0049335

*EWSR1 (22q12) Gene Rearrangement by FISH*

For specific collection, transport, and testing information, refer to the ARUP website at [www.aruplab.com](http://www.aruplab.com).

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

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