

IGH-CCND1 Fusion, t(11;14) by FISH

FOR THE DIAGNOSIS OF MANTLE CELL LYMPHOMA

Test Highlights

- *IGH-CCND1* FISH is a sensitive and specific method for the detection of the t(11;14) gene translocation, which aids in the diagnosis of mantle cell lymphoma.

Disease Overview

- Mantle cell lymphoma is a non-Hodgkin lymphoma that originates from malignant B-lymphocytes normally residing in the mantle zone or outer edge of the B-cell follicle. The neoplastic lymphocytes are small in size and have a monoclonal mature B-cell phenotype with co-expression of CD5.
- Mantle cell lymphoma is highly associated with the specific translocation t(11;14), which causes the over-expression of cyclin D1. Demonstration of cyclin D1 over-expression by immunohistochemistry or the t(11;14) by molecular or cytogenetic methods is essential in making a definitive diagnosis of mantle cell lymphoma. It is also important to differentiate it from other small B-cell lymphomas that co-express CD5 (such as chronic lymphocytic leukemia/small lymphocytic lymphoma), as mantle cell lymphoma has a much more aggressive clinical course and requires a more aggressive treatment approach.

Epidemiology

- Mantle cell lymphoma is an uncommon neoplasm representing about 3–10 percent of all non-Hodgkin lymphomas. Approximately 3,300 new cases are diagnosed each year in the United States.
- Mantle cell lymphoma is more common in males and in the elderly population (median age of onset is 58 years old). Both nodal and extranodal (particularly gastrointestinal tract and Waldeyer ring) disease is seen. Most patients will present with widespread stage III or IV disease.

Genetics

- Mantle cell lymphoma is strongly associated with a specific translocation, t(11;14)(q13;q32), which juxtaposes the immunoglobulin heavy chain and the cyclin D1 (*PRAD-1* or *bcl-1*) genes leading to over-expression of cyclin D1.
- A small number of cases may have genetic changes leading to over-expression of other cyclins as an underlying pathogenetic mechanism.

Indications for Ordering

- Diagnosis or suspicion of mantle cell lymphoma from morphology or immunophenotypic studies.
- Non-Hodgkin lymphoma with equivocal or uninterpretable immunophenotyping.

Contraindication

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 *IGH-CCND1* [t(11;14)] translocation is strongly supportive of a diagnosis of mantle cell lymphoma.
- A negative result does not rule out mantle cell lymphoma, since a small percentage of patients may have alternative translocations.

Limitations

Tissues fixed in alcohol-based or non-formalin fixatives have not been tested using this method.

Methodology

The detection of *IGH-CCND1* translocation [t(11;14)] in formalin-fixed, paraffin-embedded tissue uses a commercially available DNA FISH probe.

Related Tests

FISH testing should be performed to confirm a suspected diagnosis of lymphoma. The following tests can be used as an initial screen for lymphoma:

- Leukemia/Lymphoma Phenotyping (Comprehensive—Whole Blood) (0096299)
- Leukemia/Lymphoma Phenotyping (Comprehensive—Bone Marrow) (0095244)
- Leukemia/Lymphoma Phenotyping (Comprehensive—Miscellaneous) (0095243)

References

1. Swerdlow SH, et al. Mantle cell lymphoma. In *WHO classification of tumours of haematopoietic and lymphoid tissues*. Swerdlow SH, et al, eds. 2008; Lyon, France: IARC Press.
2. Belaud-Rotureau MA, et al. A comparative analysis of FISH, RT-PCR, PCR, and immunohistochemistry for the diagnosis of mantle cell lymphomas. *Mod Pathol* 2002;15(5):517–25.
3. Campo E. Genetic and molecular genetic studies in the diagnosis of B-cell lymphomas I: mantle cell lymphoma, follicular lymphoma, and Burkitt's lymphoma. *Hum Pathol* 2003;34:330–5.
4. Frater JL, Hsi ED. Properties of the mantle cell and mantle cell lymphoma. *Curr Opin Hematol* 2002;9:56–62.
5. Package insert. Vysis® LSI IGH/CCND1-XT Dual Color, Dual Fusion Translocation Probe. Des Plaines, IL: Abbott Molecular; 2010.

Test Information

0049381 ***IGH-CCND1* Fusion, t(11;14) by FISH**

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

Michelle Wallander, PhD