

## IRF4/DUSP22 Gene Rearrangement by FISH

The *IRF4/DUSP22* locus is rearranged in a newly recognized subtype of non-Hodgkin lymphoma, large B-cell lymphoma with *IRF4* rearrangement. These lymphomas are uncommon, but are clinically distinct from morphologically similar lymphomas, including diffuse large B-cell lymphoma, high-grade follicular lymphoma, and pediatric-type follicular lymphoma. The *IRF4/DUSP22* locus is also rearranged in a subset of ALK-negative anaplastic large cell lymphomas (ALCL), where this rearrangement is associated with a significantly better prognosis.

### Disease Overview

#### Incidence

- Large B-cell lymphoma with *IRF4* rearrangement accounts for <1% of all non-Hodgkin B-cell lymphomas overall
  - More common in younger patients, with an incidence of 5-6% under age 18
- *IRF4/DUSP22* rearrangement is found in 30% of ALK-negative ALCLs

#### Symptoms/Findings

Large B-cell lymphoma with *IRF4* rearrangement typically presents with limited stage disease in the head and neck, while the presentation of ALK-negative ALCLs is variable.

#### Disease-Oriented Information

Patients with large B-cell lymphoma with *IRF4* rearrangement typically have a favorable outcome after treatment. Rearrangement of the *IRF4/DUSP22* locus in ALK-negative ALCL is associated with a better prognosis than ALK-negative ALCL without this rearrangement.

### Test Interpretation

#### Analytical Sensitivity

The limit of detection (LOD) for the *IRF4/DUSP22* probe was established by calculating the upper limit of the abnormal signal pattern in normal cells using the Microsoft Excel BETAINV function. The LOD of *IRF4/DUSP22* fluorescence in situ hybridization (FISH) is 11% when 100 cells are enumerated. Using the LOD of 11% the analytical sensitivity was found to be 100% when testing two 6p25 rearranged samples.

#### Tests to Consider

##### [IRF4/DUSP22 \(6p25\) Gene Rearrangement by FISH 3001568](#)

**Method:** Fluorescence in situ Hybridization

- Test is useful in identifying ALK-negative anaplastic large cell lymphomas and large B-cell lymphoma with *IRF4* rearrangement
- The rearrangement is associated with an improved prognosis

See [Related Tests](#)

# Results

## Positive

- Depending on the context of the case, the presence of the 6p25 gene rearrangement supports a diagnosis of large B-cell lymphoma with *IRF4* rearrangement or ALK-negative ALCL with *IRF4/DUSP22* rearrangement.

## Negative

- Absence of the 6p25 gene rearrangement

## Limitations

- *IRF4/DUSP22* FISH testing has not been validated for
  - Tissue fixed in alcohol-based or non-formalin fixatives
  - Decalcified tissue
- Results should be analyzed in conjunction with morphology, immunohistochemistry, and immunophenotyping results.

## References

1. Swerdlow S, Campo E, Jaffe E, Pileri S, Stein H, Thiele J, Arber D, Hasserjian R, Le Beau M. WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues, Revised 4th Ed.. Lyon, France: International Agency for Research on Cancer, 2017.
2. [Translocations activating IRF4 identify a subtype of germinal center-derived B-cell lymphoma affecting predominantly children and young adults.](#) Blood. 2011; 118 (1): 139-47. PubMed
3. [Castellar ERParrilla, Jaffe ES, Said JW, et al. ALK-negative anaplastic large cell lymphoma is a genetically heterogeneous disease with widely disparate clinical outcomes.](#) Blood. 2014; 124 (9): 1473-80. PubMed

## Related Information

[B-Cell Lymphomas](#)  
[T-Cell/NK-Cell Lymphomas](#)

## Related Tests

[MUM1/IRF4 by Immunohistochemistry 2003975](#)

**Method:** Immunohistochemistry

[BCL-6 by Immunohistochemistry 2003457](#)

**Method:** Immunohistochemistry

[BCL-2 by Immunohistochemistry 2004513](#)

**Method:** Immunohistochemistry

ARUP Laboratories is a nonprofit enterprise of the University of Utah and its Department of Pathology. 500 Chipeta Way, Salt Lake City, UT 84108 | (800) 522-2787 | (801) 583-2787 | aruplab.com | arupconsult.com  
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