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MYD88 L265P Mutation Detection

Background Information

Lymphoplasmacytic lymphoma (LPL) is a small B-cell neoplasm with plasmacytic differentiation that typically involves the bone marrow and may also involve spleen and lymph nodes. In most cases, LPL is associated with an IgM paraprotein (Waldenstrom's macroglobulinemia).[1,2] Distinguishing LPL from other small B-cell neoplasms that may show plasmacytic differentiation, especially marginal zone lymphomas, is often challenging.

Recently, the *MYD88* L265P mutation has been identified in >90% of cases of LPL.[3] This mutation may also be found in diffuse large B-cell lymphomas, especially those with a non-germinal center phenotype, but the mutation is only rarely found in other small B-cell neoplasms. The detection of a *MYD88* L265P mutation can therefore assist in establishing the diagnosis of LPL.[3-5]

Cleveland Clinic Laboratories has developed, validated and implemented a sensitive PCR assay for the detection of *MYD88* L265P in peripheral blood, bone marrow or formalin-fixed, paraffin-embedded tissues.

Clinical Indications

MYD88 L265P mutation testing is useful in the evaluation of small B-cell neoplasms, especially those with plasmacytic differentiation.

Interpretation

Normal results are reported as "*MYD88* L265P mutation not detected." Positive results are as "*MYD88* L265P mutation detected," and an interpretation provided.

Methodology

DNA is extracted from the sample, and real-time PCR is performed using primers specific for the L265P mutation and a reference primer set for a non-mutated portion of the *MYD88* gene.

Limitations

This assay has a sensitivity of 0.5% mutant alleles. This assay detects only the L265P point mutation, and a negative result does not exclude a diagnosis of lymphoplasmacytic lymphoma.

References

1. Swerdlow S.H., Berger F., Pileri S.A., et al. Lymphoplasmacytic lymphoma. In: *WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues.* IARC: Lyon 2008. Swerdlow SH, Campo E. Harris EL, et al (Eds). Pp 194-195.
2. Treon SP, Hunter ZR, Castillo JJ, et al. Waldenström macroglobulinemia. *Hematol Oncol Clin North Am.* 2014 Oct;28(5):945-70.
3. Treon SP, Xu L, Yang G, et al. *MYD88* L265P somatic mutation in Waldenström's macroglobulinemia. *N Engl J Med.* 2012 Aug 30;367(9):826-33.
4. Hamadeh F, MacNamara SP, Aguilera NS, et al. *MYD88* L265P mutation analysis helps define nodal lymphoplasmacytic lymphoma. *Mod Pathol.* 2014 Sep 12. [Epub ahead of print]
5. Ondrejka SL, Lin JJ, Warden DW, et al. *MYD88* L265P somatic mutation: its usefulness in the differential diagnosis of bone marrow involvement by B-cell lymphoproliferative disorders. *Am J Clin Pathol.* 2013 Sep;140(3):387-94.

9500 Euclid Avenue | Cleveland, Ohio 44195 | 216.444.5755 | 800.628.6816 | clevelandcliniclabs.com

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Test Overview

Test Name	*MYD88* L265P Mutation Analysis
Ordering Mnemonic	*MYD88*
Specimen Requirements	Whole blood: • Volume: 4 ml • Container: EDTA (Lavender) • Transport temperature: Refrigerated Bone marrow: • Volume: 2 ml • Container: EDTA (Lavender) • Transport temperature: Refrigerated Formalin-fixed paraffin embedded tissue/bone marrow clot • Size: one block • Transport: Ambient
Minimum Specimen Requirements	Whole blood: Volume: 2 ml Bone marrow: Volume: 1 ml
Stability	Ambient: • Blood/bone marrow: 24 hours • Formalin-fixed paraffin embedded tissue/bone marrow clot: indefinitely Frozen: • Blood/bone marrow: unacceptable • Formalin-fixed paraffin embedded tissue/bone marrow clot: indefinitely Refrigerated: • Blood/bone marrow: 5 days • Formalin-fixed paraffin embedded tissue/bone marrow clot: indefinitely
Clinical Information	This test is designed to detect the point mutation c.794T>C, p.L265P in the *MYD88* gene. *MYD88* L265P mutations are present in the majority of cases of lymphoplasmacytic lymphoma and, less commonly, in other B-cell lymphoproliferative disorders.
Reference Range	*MYD88* L265P mutation not detected
Billing Code	89733
CPT Code	81479; G0452

Technical Information Contact:

Lisa Buhrow, MT(ASCP)
216.444.8034
buhrowl@ccf.org

Scientific Information Contact:

James R. Cook, MD, PhD
216.444.4435
cookj2@ccf.org