Abstract Only:

Clone-specific MYD88 L265P and CXCR4 mutation status can provide clinical utility in suspected Waldenström macroglobulinemia/lymphoplasmacytic lymphoma

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Abstract

MYD88 L265P, a diagnostic marker for lymphoplasmacytic lymphoma (LPL)/Waldenström macroglobulinemia (WM) can also be detected in other hematopoietic malignancies. We demonstrate a novel approach to increase the specificity of this marker for WM/LPL diagnosis by combining flow cytometric cell sorting with molecular analysis.

Clonal B-lymphocyte and co-occurring clonal plasma cell populations of low-grade B-cell lymphomas were sorted by flow cytometry and analyzed for immunoglobulin gene rearrangements (PCR), and for *MYD88* and *CXCR4* mutations.

Identical clonal origin was confirmed by PCR for 21 LPL/WM cases and *MYD88* L265P was detected in both B-cell and plasma cell fractions. 9/20 other B-cell lymphomas with identical light chain restriction on B-cells and plasma cells were genotypically identical by PCR and *MYD88* L265P was detected in both cell fractions in 7/9 whereas in 11/20 specimens with different clonal origin, *MYD88* L265P was absent (5/11), or only found in B-lymphocytes (4/11), or plasma cells (2/11). *CXCR4* mutations were detected in 17/39 cases, but missed in 63% of these without cell sorting.

Confirming *MYD88*L265P in both B-cells and plasma cell fractions can provide a novel and powerful discriminator to distinguish LPL/WM from phenotypically similar disorders. Furthermore, this approach significantly increases *CXCR4* detection sensitivity.

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