Precipio's RevCI™ Procedure Delivers Conclusive Lymphoma Diagnosis

Abstract:
Precipio received a bone marrow biopsy of an 82-year-old male with unexplained anemia and severe thrombocytopenia. The clinician suspected a myelodysplastic syndrome.
Small population of clonal B-cells identified by flow cytometry in addition to lack of dysplasia in the marrow, raised the concern of a possible lymphoproliferative neoplasm. With the Omnia assessment and critical proprietary RevCI technology, the Precipio team further evaluated the submitted biopsy to confirm a diagnosis of a Chronic Lymphocytic Leukemia (CLL). FISH testing by cytogenetics provides valuable information for diagnosing and assessing the prognosis of mature Be cell neoplasms. Cases with only lowe level involvement of the bone marrow or peripheral blood risk having their cytogenetic abnormalities missed if percentages of Be lymphocytes present in the sample submitted are below the required limit to perform conventional FISH testing.
To raise the sensitivity of B-cell detection, Precipio utilized its proprietary cell enrichment technology, RevCI™ or Reversible Cell Isolation. RevCI™ enables the utilization of critical FISH studies on samples with low percentages of B-cells, aiding in properly classifying the malignancy.
The RevCI™ technology can be used to enrich for B-cells in bone marrow or peripheral blood specimens prior to conducting FISH studies. RevCI™ enables the subsequent tests to detect abnormalities in cases with scant B-cells.

Methods:
Precipio conducted its Omnia™ Comprehensive Assessment to properly evaluate the submitted biopsy. First, flow cytometry detected a small monoclonal population of B-cells co-expressing CD5 comprising of only 1% of the total cellularity. This raised the concern of a lymphoproliferative neoplasm rather than the initially suspected MDS. The pathologist requested that the case be tested for CLL panel by FISH. The cytogenetics department considered the flow cytometry results and determined that it would be essential to utilize RevCI™ for such a minute population of B-cells in order to obtain conclusive FISH results.

Results:
The RevCI™ procedure is unique in its ability to reverse the coupling of immunomagnetic beads used to isolate target cells thereby enabling performance of other tests on the sample including FISH studies, flow cytometry and morphologic assessment. By utilizing RevCI™, Precipio is able to successfully provide accurate and conclusive results in 95% of its lymphoma cases. This is in stark contrast to other labs where enrichment is not used and as a result, produces inconclusive or contradictory results at rates as high as 50%.

Key Highlights:
- Omnia evaluation identified abnormal B-cell population, otherwise not part of an MDS work up
- Only 1% abnormal cells identified, which was insufficient for evaluation by conventional FISH to confirm sub-classification of this lymphoid neoplasm
- Proprietary RevCI™ utilized and enabled critical FISH testing and provided conclusive results that confirmed CLL diagnosis

In this case, FISH studies detected an abnormal clone with trisomy 12(CEP12) in about 28% of the cells analyzed. Trisomy 12 is a chromosomal abnormality detected in about 20% of cases of chronic lymphocytic leukemia[1].

Clinical Implications:
Without enrichment, inconclusive or false negative diagnoses of low level B-cell neoplasms have the same likelihood as clear, definitive ones. Inconclusive results hinder the clinician from designing a personalized treatment plan for the patient due to the lack of clarity on a specific diagnosis. Often times these cases without the critical FISH results, are treated with a broader approach with lower chances of success.
Precipio's RevCI™ is a powerful technology that increases the detection rate of genetic abnormalities and enables correlation with flow cytometry and morphology. This results in an accurate and comprehensive diagnosis of B-cell neoplasms for the clinician.

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[1] Swerdlow, Steven H., et al. **WHO classification of tumours of haematopoietic and lymphoid tissues.** International Agency for Research on Cancer, 2017, pp 218.