B-cell MRD Assay

CAP/CLIA-Validated

Clinical Significance

Combinations of radiation, chemotherapy and bone marrow transplantation are potentially curative for several hematologic malignancies. However, in some patients, occult tumor cells exist and are thought to increase the patient's risk of relapse.[1] These subclinical levels of residual cancer cells are termed measurable or minimal residual disease (MRD) and can be evaluated using highly sensitive assays. Tracking antigen-receptor gene rearrangements for clonality and MRD can be applied to virtually all patients.

Cancer cells that arise from alterations in single lymphoid precursors acquire clonal *IGH* junctional regions, which can be used as tumor-specific markers.[2,3] NGS-based MRD assays can generate prognostic and clinically actionable information. Studies have shown that highly sensitive NGS assays can detect MRD up to 6 months before traditional methods[4] which allows early intervention, confirmation of disease status prior to transplant, and increased confidence in remission status.

NextSeq™ 550Dx

Courtesy of Illumina, Inc.

References

1. Rezuke, WN et al. (1997) *Clinical Chemistry.* 43:1814-23.
2. Gazzola, A et al. (2014) *Therapeutic Advances in Hematology.* 5:35-47.
3. González, D et al. (2007) *Blood.* 110:3112-21.
4. Cheng, S et al. (2018) *Journal of Hematology & Oncology.* 11(1):105.

Key Benefits

- 1x10^{-6} sensitivity allows earlier detection of disease relapse and evolution
- Accelerates drug development and exploratory endpoint studies
- Test the same primary sample with NGS and mutiparametric flow cytometry
- Available at LabPMM San Diego, CA; coming soon to Shanghai, China

Indications for Testing

- Identify and track tumor-specific sequences for B-cell proliferations
- NCCN Guidelines (v5.2022) Multiple Myeloma suggest MRD assessments to evaluate:
  - Disease status prior to transplant
  - Following induction, high-dose therapy/ASCT, consolidation and maintenance therapy
- Optimize treatment strategies
- Monitor and evaluate for refractory and relapsed disease

Associated Diseases

Multiple Myeloma (MM)
Chronic Lymphocytic Leukemia (CLL)
B-cell Acute Lymphoblastic Leukemia (B-ALL)
Diffuse Large B-cell Lymphoma (DLBCL)
Mantle Cell Lymphoma (MCL)
Plasma Cell Neoplasms (PCN)
Follicular Lymphoma (FL)
Marginal Zone Lymphoma (MZL)

Method

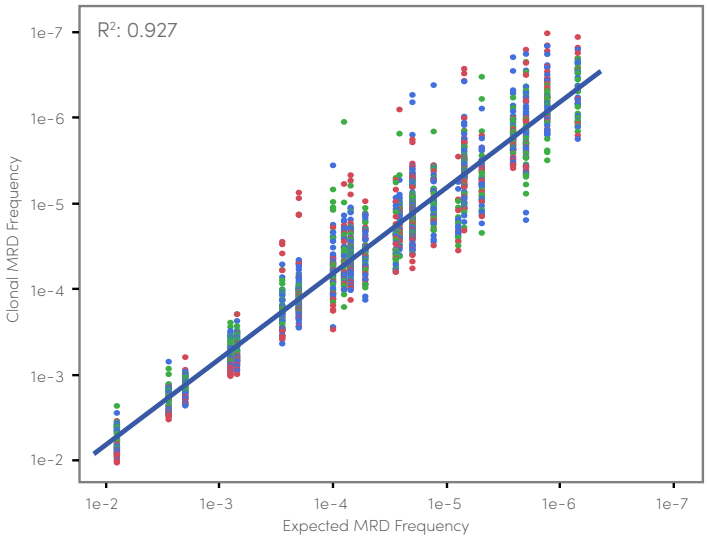
Clonal B-cell gene rearrangement sequences identified at diagnosis, will be tracked in post-treatment follow-up samples for (MRD) status. The conserved framework region 1 (FR1) or framework region 3 (FR3) and joining region is targeted by a multiplex master mix for PCR amplification. The PCR products are then sequenced on a NextSeq™ 550Dx to identify and track FR1 or FR3 clonal sequences previously identified at diagnosis. Bioinformatics tools facilitate the detection of these specific sequences present at MRD levels of 1x10 $^{-6}$ with sufficient DNA input.

This assay requires a sample taken at diagnosis as well as follow-up samples. If the patient has previously been tested by LabPMM for *IGH* clonality, no diagnostic sample is needed.

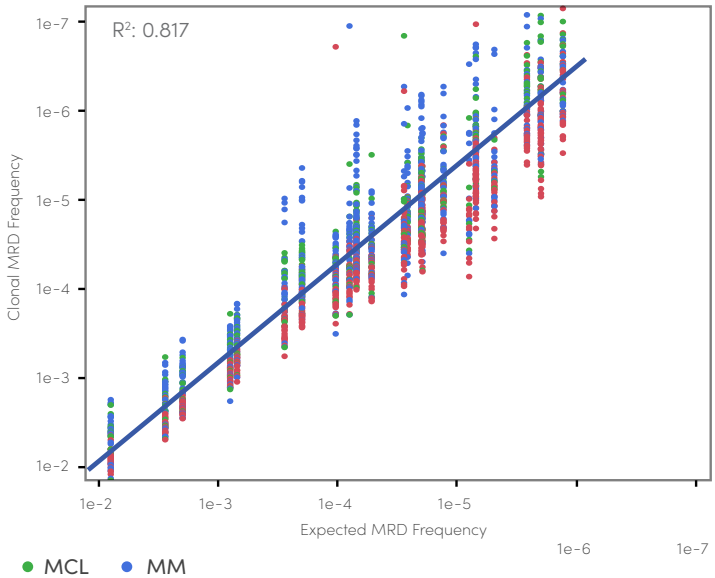
Clinical Performance

Clonal MRD Frequency vs. Expected MRD Frequency

IGH FR1 Performance using 0.5, 2 and 20 µg DNA Input



IGH FR3 Performance using 0.5, 2 and 20 µg DNA Input



Diseases: ● CLL ● MCL ● MM

Specimen Requirements

Interpretation	Turnaround Time	Specimen Requirements	Shipping Conditions	Specimen Stability
An interpretive report will be issued indicating whether *IGH* MRD was detected.	14 to 21 business days	1-2 mL of peripheral blood in EDTA or Heparin 1-2 mL of bone marrow in EDTA or Heparin 0.5 - 20 µg of previously isolated DNA depending on level of sensitivity required*	Peripheral blood ambient or cool; do not freeze Bone marrow** ambient, cool or frozen on dry ice Isolated DNA ambient or frozen on dry ice	15 to 30 °C for up to 3 days 2 to 8 °C up to 7 days -15 to -30 °C for up to 3 months

* If less than 20 µg is provided, the sensitivity of the assay may be impacted.
** Ambient bone marrow may limit the sensitivity that can be achieved.

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