Trend MRD in Longitudinal Studies

Accelerate your Minimal Residual Disease Testing with the LymphoTrack® MRD Software

For Research Use Only. Not for use in diagnostic procedures.
Trend MRD in Longitudinal Studies - Accelerate your Minimal Residual Disease Testing with the LymphoTrack® MRD Software
The LymphoTrack MRD Solution can be used in your own laboratory to track levels of MRD in subjects exhibiting IGH or T-cell clonality. The LymphoTrack MRD Solution is used to assess levels of MRD in subjects following therapy and throughout remission in your own laboratory. The National Comprehensive Cancer Network (NCCN) guidelines now recommend MRD testing for several lymphoid cancers, including multiple myeloma (MM), acute lymphoblastic leukemia (ALL), and chronic lymphocytic leukemia (CLL).1,2,3,4 European LeukemiaNet (ELN) guidelines recommend MRD testing following induction and consolidation courses to assess remission status and determine kinetics of disease response, and sequentially beyond consolidation to detect impending morphologic relapse.5

<table>
<thead>
<tr>
<th>LymphoTrack MRD Software</th>
<th>Low Positive Control</th>
<th>Internal Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>LymphoTrack Assay</td>
<td>LymphoTrack® B-Cell Low Positive Control Catalog # 4-088-0098</td>
<td>LymphoQuant® B-Cell Internal Control Catalog # 4-088-0118</td>
</tr>
<tr>
<td>IGHV Leader, IGH FR1/2/3</td>
<td>LymphoTrack® T-Cell Low Positive Control Catalog # 4-088-0108</td>
<td>LymphoQuant® T-Cell Internal Control Catalog # 4-088-0128</td>
</tr>
</tbody>
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LymphoTrack®
MRD Software

Assessment of Minimal Residual Disease using v2.0.2+

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ADVANTAGES OF NGS-BASED MRD TESTING

**Sensitive**
Track clonal sequences in subsequent samples with up to $1 \times 10^{-6}$ sensitivity

**Accurate**
Calculate estimated cell equivalents for accurate MRD assessment and tracking over time

**Efficient**
Simultaneously track up to 5 gene rearrangements

**Standardized**
Offer concordant, objective testing worldwide by tracking sequence specific DNA targets

**Proactive**
Detect refractory and relapsed disease earlier in oncology studies

**Vigilant**
Monitor and assess the effectiveness of therapies and/or remission status in oncology studies
PLAN YOUR EXPERIMENT

Gain Confidence in your Results

The Project Planner is a tool that is integrated in the software to aid in experimental design. The user may use default levels or customize the confidence levels. The tool allows the user to calculate the level of confidence for a specific sensitivity by manipulating experiment parameters:

- # of PCR Replicates
- # of Resequences
- Read Depth
- Amount of DNA (ng)
**ADD A SUBJECT**

**New Subject Setup**

Once clonal sequences are identified using the LymphoTrack (Dx) Software, up to 5 clonal sequences may be simultaneously monitored in longitudinal studies.

**Associate Sequence(s) with Subject Samples**

The Add Subject/Sample window is used to add new Samples to a Subject and associate the Sample information with respective data files.
LOW POSITIVE AND INTERNAL CONTROL SETUP

Low Positive Controls

Designed specifically for MRD testing, the LymphoTrack Low Positive Controls* are optimized to work in concert with the LymphoQuant Internal Controls. B-Cell and T-Cell Low Positive Controls may be run in lieu of the positive controls provided in the LymphoTrack IGHV Leader, IGH FR1, FR2, FR3, TRG and TRB kits to ensure that MRD levels of sensitivity are being confidently interrogated in samples.

LymphoQuant Internal Controls

B-cell or T-cell LymphoQuant Internal Control may be spiked into the PCR to estimate the respective number of clonotype equivalents and percent clonotype present. Consistent use of a LymphoQuant Internal Control enables clinicians to objectively monitor the disease over time with a highly standardized, sensitive method.

* IGK is poorly suited for MRD analyses due to the complexity and low genetic diversity of this locus. If you choose to use IGK for MRD testing, verify the sequence of interest is not detected in a polyclonal negative control and carefully select a low positive control appropriate for IGK.
Create, Load, and Save MRD Subject Projects

Once clonal sequences are associated with a Subject and Samples, a Project can be Saved for future use.

Saved Projects can be loaded when additional time points are added to a study.
LymphoTrack®
MRD Reports

Understanding the LymphoTrack MRD Reports

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The MRD Summary Report provides the status of the clonal sequences that are being tracked. Detailed information is provided for the most recent time point. In this sample, MRD was detected by the software for 2 of the 3 interrogated clonal sequences. If “DETECTED” an estimated Clonal Frequency is displayed. If the sequence is NOT DETECTED (e.g. Sequence #3) the last column of the table displays a quantitative assessment of the % Confidence that the result is a true negative.

**Estimated MRD Levels for Subject**

This chart provides a longitudinal view of the sample-level MRD results for all sequences queried at each collection date/timepoint. Each result is shown as a Clonal Frequency level (estimated clonal cells per total cells analyzed). When MRD is not identified for a clonal sequence, it is graphed as NOT DETECTED (ND).

Note that this chart provides visual representation of the results; please see the Sample Report for specific detection limits.
Subsequent pages of the MRD Summary Report provide details for each of the clonal sequences being tracked. For example, this table provides the following information for sequence #1 (e.g. Primary Clone):

- Collection/Timepoint Date
- Sample Unique Identifier (i.e. First Followup)
- Sample Type (Peripheral Blood, Bone Marrow, etc.)
- DNA Input (in nanograms) per PCR
- Clonal Frequency
- Estimate Clonal Cell Equivalents
- Estimated Clonal cell Equivalents per 1 Million Total Cells

This chart provides a longitudinal view of the sample-level MRD results for individual sequences queried at each collection date/timepoint.
**MRD SAMPLE REPORT**

**Details for each Subject**

The Sample Report begins with the Subject ID and Sample specific information. The overall MRD Result displays how many sequences were DETECTED in the total number of sequences analyzed. This table shows the total number of reads that include the B- or T-cell LymphoQuant Internal Control. The LymphoQuant Status will display whether or not sufficient reads were detected.

**Details for each Collection Date or Timepoint**

This table provides a birds eye view of the MRD results for the Sample Collection Date or Timepoint. Details are summarized for each sequence analyzed including the Clonal Frequency if DETECTED and the % Confidence if NOT DETECTED.
MRD SAMPLE REPORT FOR THE LOW POSITIVE CONTROL
Details for Low Positive Control

A Sample Report is generated for the Low Positive Control and contains the same information as the Subject Sample Report. The only difference is that the Low Positive Control Status will indicate “Passed” if a sufficient number of reads were identified, “Failed” if an insufficient number of reads were identified, or “N/A” if Low Positive Control was not sequenced.

MRD SUMMARY REPORT CONTINUED
Sequence Details

This table provides details about each sequence analyzed.
- The interrogated sequence
- PCR replicate details
- The Cumulative Read
- The Cumulative % Total Reads
- The LymphoQuant Internal Control Cumulative Reads

If the sequence was DETECTED, Clonal Frequencies are shown. If the sequence was NOT DETECTED the % Confidence at 1E-3, 1E-4, 1E-5 and 1E-6 are given. At 1E-3, 1E-4, 1E-5 and 1E-6 are given.
EXPLANATION OF DEFINITION OF TERMS
Definitions for many of the terms used in the MRD Software and Reports.

ASSAY LIMITATIONS
Additional information regarding the capabilities of the LymphoTrack Assays and Software, assay variance, potential for interference, degradation and inhibition, sequencing artifacts and estimations of clonal cell equivalents.
Ask How to Accelerate Your MRD Testing

The LymphoTrack® MRD Solution

For Additional Information
Call +1 858.224.6600 | Email marketing@invivoscribe.com | Visit invivoscribe.com
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