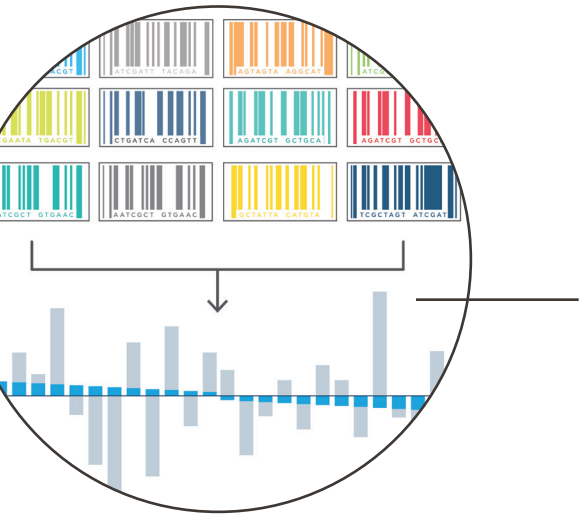
CLONOSEQ TECHNICAL INNOVATIONS



The clonoSEQ Assay is powered by **next-generation sequencing (NGS)** technology and differentiated from other NGS MRD tests by advances in **chemistry** and proprietary **bioinformatics**.[1]

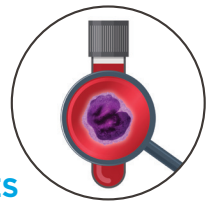
clonoSEQ is the first-ever **FDA-cleared assay** to detect, quantify, and monitor measurable residual disease (MRD) in bone marrow samples from multiple myeloma or B-cell acute lymphoblastic leukemia patients and is the first diagnostic powered by **immunosequencing** to be cleared by the FDA.

ADVANCED BIAS CONTROL

clonoSEQ is the first MRD assay to leverage a synthetic immune repertoire to address the inherent bias that occurs when DNA sequences are amplified using multiplex PCR. These synthetic molecules enable highly accurate and reproducible quantitation of residual disease.[2,3]

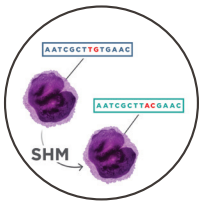
INCREASED ID SUCCESS RATES

With the inclusion of primer sets for IGH, IGK and IGL as well as IGH-BCL1 / IGH-BCL2 translocations, the clonoSEQ Assay provides a comprehensive assessment of immune receptors in a single assay for patients with B-cell malignancies.[4]



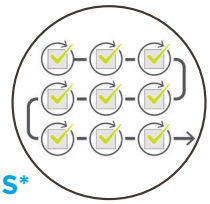
MINIMAL SAMPLE VOLUMES

By evaluating all B-cell receptor loci together in a single PCR reaction, the clonoSEQ Assay conserves sample material, enabling maximum sensitivity to be achieved with less sample material.[4]



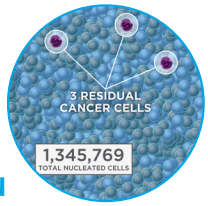
ABILITY TO HANDLE SHM

Somatic hypermutation (SHM) can cause clinical assays to underestimate MRD or even miss it entirely. The clonoSEQ Assay is engineered to minimize the impact of SHM on reporting MRD results.[1,4]



AVOIDANCE OF FALSE NEGATIVES*

Each distinct step in the clonoSEQ Assay is monitored by a corresponding control molecule. That's why when clonoSEQ produces an MRD-negative result, it is clear that the test output is accurate and not the result of an assay failure.[1]



ENHANCED QUANTIFICATION

clonoSEQ uses a robust internal measure to quantify the total nucleated cells (i.e. total input DNA) contained in a tested B-cell malignancy sample. The use of this internal measure ensures the accuracy of a value which is critical to the interpretation of a clinical MRD result.[4]

SOPHISTICATED BIOINFORMATICS

The algorithms that are used to transform raw sequencing data into clonoSEQ results are designed to maximize the assay's ability to distinguish signal vs. noise and to optimally translate raw sequencing reads into contextualized information for clinical use.[4]

***False positive or false negative results may occur for reasons including, but not limited to: contamination, technical, and/or biological factors.**

clonoSEQ is an FDA-cleared in vitro diagnostic (IVD) test service provided by Adaptive Biotechnologies for use in B-cell acute lymphoblastic leukemia and multiple myeloma patients to detect and monitor measurable residual disease (MRD) in bone marrow samples. clonoSEQ is also available for use in other lymphoid cancers as a CLIA-regulated laboratory developed test (LDT) service provided by Adaptive Biotechnologies. Available by prescription only. clonoSEQ results should always be used in combination with clinical examination, patient medical history, and other findings. Results may vary according to sample time within the course of disease or by sampling site location.

REFERENCES

1. Faham M, et al. Blood. 2012;120(26):5173-80. (Study author was an employee of Adaptive at the time of publication).
2. Robins H, et al. Adaptive Biotechnologies. US patent 9,150,905. October 6, 2015.
3. Robins H, et al. Adaptive Biotechnologies. US patent 9,371,558. June 21, 2016.
4. Data on file. Adaptive Biotechnologies. 2018.

INTENDED USE

The clonoSEQ Assay is an in vitro diagnostic that uses multiplex polymerase chain reaction (PCR) and next-generation sequencing (NGS) to identify and quantify rearranged IgH (VDJ), IgH (DJ), IgK, and IgL receptor gene sequences, as well as translocated BCL1/IgH (J) and BCL2/IgH (J) sequences in DNA extracted from bone marrow from patients with B-cell acute lymphoblastic leukemia or multiple myeloma.

clonoSEQ measures minimal residual disease (MRD) to monitor changes in burden of disease during and after treatment. The test is indicated for use by qualified healthcare professionals in accordance with professional guidelines for clinical decision-making and in conjunction with other clinicopathological features.

clonoSEQ is a single-site assay performed at Adaptive Biotechnologies.

SPECIAL CONDITIONS FOR USE

- For *in vitro* diagnostic use.
- For prescription use only (Rx only).

LIMITATIONS

- clonoSEQ is for use with bone marrow specimens collected in EDTA tubes.
- Results should always be used in combination with clinical examination, patient medical history, and other findings.
- Results may vary according to sample time within the course of disease or by sampling site location.
- clonoSEQ may overestimate MRD frequencies near the limit of detection (LoD).
- MRD frequency LoD varies based on the amount of DNA tested; using less DNA input may prevent MRD detection at low frequencies.
- The volume and cellularity of sampled input material may affect the ability to detect low levels of disease.
- Sample processing and cell enrichment strategies may affect the measured MRD frequency.
- False positive or false negative results may occur for reasons including, but not limited to: contamination, technical, and/or biological factors.
- MRD values obtained with different assay methods may not be interchangeable due to differences in assay methods and reagent specificity.

For important information about the FDA-cleared uses of clonoSEQ, including test limitations, visit clonoSEQ.com/technical-summary.

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