AML Express Testing :

Leveraging Next-Generation Sequencing for Critical Gene Analysis

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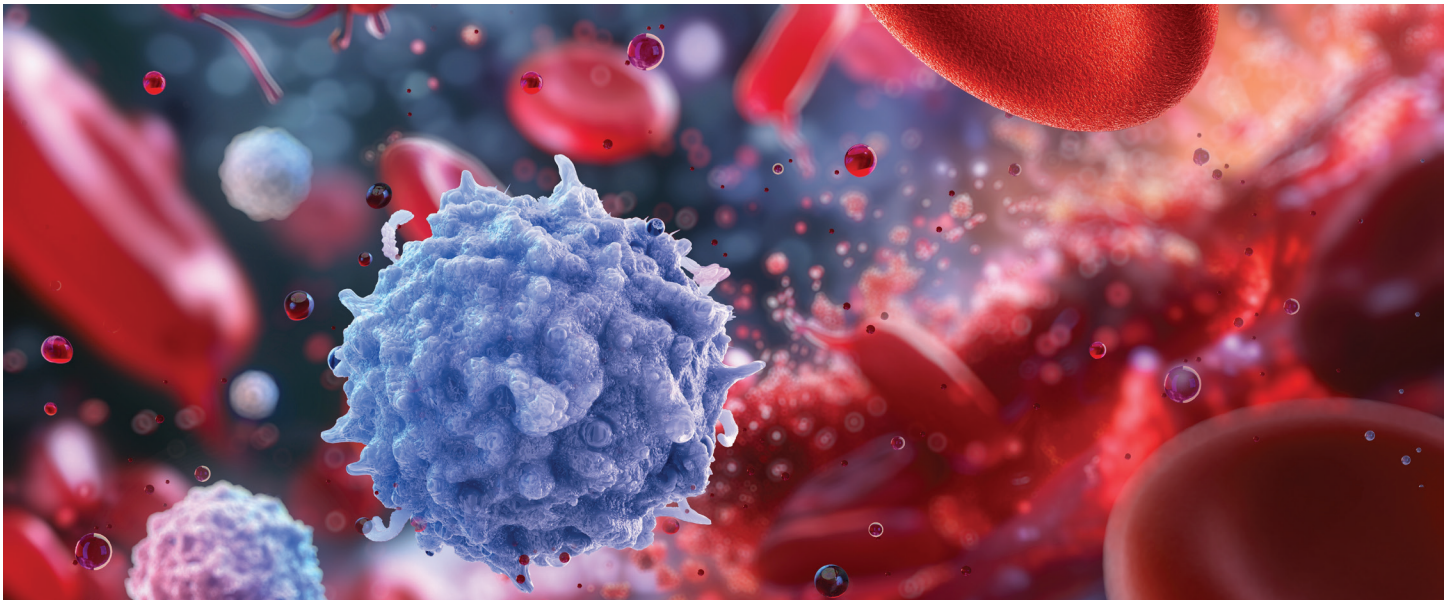
Acute Myeloid Leukemia (AML) is the most common form of leukemia, with approximately 20,800 new cases expected in the United States in 2024 and a five-year survival rate of only 32%.[1] This aggressive cancer is characterized by rapid and uncontrolled proliferation of immature myeloid cells, called blasts, in the blood and bone marrow. The unchecked growth disrupts normal blood cell production, leading to severe bone marrow failure and diminished levels of blood cells including red cells, white cells, and/or platelets. AML progresses rapidly, often within weeks or months, and requires prompt diagnosis and intervention to avoid life-threatening complications.

The Urgency of AML Diagnosis and Treatment.

Given its aggressive nature and rapid progression, AML is considered an oncology emergency. Urgent diagnosis and treatment are crucial, and patients with acute symptoms should be admitted to the hospital for immediate diagnostic testing to minimize delays in care. Patients with AML are at high risk for complications such as severe infections, bleeding disorders, and organ failure, and effective management involves prompt treatment to prevent severe complications.[2] A significant proportion of AML cases are identified in emergency settings, reflecting the severity of acute symptoms. Early and effective intervention allows for better management and adjustment of tailored treatment regimens, including chemotherapy, targeted therapy, or stem cell transplantation, which are essential for optimizing therapeutic outcomes and preventing rapid deterioration. Many AML treatment regimens depend on the expedited return of genetic test results to determine and initiate appropriate therapies.

The Impact of Genetic Testing.

Somatic mutations and fusions are central to AML development, and identifying these specific mutations is crucial for guiding prognosis and therapeutic decisions.[3] Advances in genetic profiling have led to the identification of distinct AML subtypes, each with unique genetic alternations, where both primary and co-occurring mutations significantly impact disease progression and patient outcomes.[4] Molecular characterization is vital for the accurate diagnosis, subtype classification, and treatment planning of AML. Improved access to molecular testing and faster result turnaround times have been key factors in enhancing treatment outcomes.[5]



The AML Express Advantage.

The AML Express Assay provides a turnaround time of just 3-5 days using Next-Generation Sequencing (NGS) technology to test 47 clinically relevant AML biomarkers. NGS analyzes multiple genes or genomes for comprehensive data, whereas PCR targets specific DNA sequences quickly and is routinely used for the analysis of single genes in the acute setting. AML Express combines PCR's rapid turnaround with NGS's broad analysis to provide swift, detailed genetic insights for AML treatment. Recent recommendations emphasize the importance of NGS for accurate risk stratification of AML and personalized treatment.[6]

The assay provides rapid analysis of 38 genes by DNA analysis and 9 fusion genes by RNA sequencing, to ensure precise genetic characterization of relevant genes. Using NGS panels of this size reveals that over 77% of AML patients harbor at least one clinically significant mutation.[7] Therefore, a comprehensive assay that covers these important biomarkers is crucial for optimal clinical workup, facilitating accurate diagnosis, risk assessment, prognosis, and the customization of therapeutic strategies, including the use of therapies targeting specific mutations. Diagnostic accuracy is improved by identifying specific genomic alterations, with RNA sequencing for fusion genes being the preferred method in guidelines due to its greater sensitivity and precision.[8] Optimizing fusion detection through RNA sequencing significantly enhances sensitivity, increasing it from 80% to 100% compared to DNA sequencing.[9] This approach identifies gene fusions that DNA methods may miss, with 21% of myeloid patients, including those with AML, showing guideline-recommended tested fusions.[10] Clinical guidelines advocate for incorporating RNA testing for a comprehensive assessment of gene fusions.

The AML Express Assay provides rapid and accurate genetic testing of key genes that are essential for precise diagnosis and tailored treatment of AML in emergency settings where rapid turnaround is crucial. This enables timely, informed decision-making and facilitates more personalized and effective treatment strategies for AML patients and their physicians.

DNA Sequencing of 38 genes – *Detection of SNVs/ InDels*

ABL1	*ASXL1*	*BCOR*	*BRAF*	*CALR*	*CBL*	*CEBPA*	*CSF3R*	*DDX41*	*DNMT3A*
ETV6	*EZH2*	*FLT3*	*GATA2*	*HRAS*	*IDH1*	*IDH2*	*JAK2*	*KIT*	*KRAS*
MPL	*NF1*	*NPM1*	*NRAS*	*PHF6*	*PPM1D*	*PRPF8*	*PTPN11*	*RUNX1*	*SETBP1*
SF3B1	*SRSF2*	*STAG2*	*TET2*	*TP53*	*U2AF1*	*WT1*	*ZRSR2*		

RNA Sequencing of 9 genes – *Detection of fusions*

ABL1	*KAT6A*	*KMT2A*	*MECOM*	*MYH11*	*NUP98*	*NUP214*	*RUNX1*	*RARA*	

AML Express *analyzes 47 clinically relevant AML biomarkers using NGS for both DNA & RNA, providing results within 3-5 days.*

1. SEER Cancer Stat Facts: Acute Myeloid Leukemia. National Cancer Institute. Bethesda, MD. Updated 2024. https://seer.cancer.gov/statfacts/html/amyl.html
2. Genç EE, Saraç İS, Arslan H, Eşkazan AE. Diagnostic and Treatment Obstacles in Acute Myeloid Leukemia: Social, Operational, and Financial. Oncol Ther. 2023 Jun;11(2):145-152. doi: 10.1007/s40487-023-00229-4. Epub 2023 May 13. PMID: 37178373; PMCID: PMC10182356.
3. Döhner H, Wei AH, Appelbaum FR, et al. Diagnosis and management of AML in adults: 2022 recommendations from an international expert panel on behalf of the ELN. Blood. 2022;140(12):1345-1377. doi:10.1182/blood.2022016867
4. Papaemmanuil E, Gerstung M, Bullinger L, Gaidzik VI, Paschka P, Roberts ND, Potter NE, Heuser M, Thol F, Bolli N, Gundem G, Van Loo P, Martincorena I, Ganly P, Mudie L, McLaren S, O'Meara S, Raine K, Jones DR, Teague JW, Butler AP, Greaves MF, Ganser A, Döhner K, Schlenk RF, Döhner H, Campbell PJ. Genomic Classification and Prognosis in Acute Myeloid Leukemia. N Engl J Med. 2016 Jun 9;374(23):2209-2221. doi: 10.1056/NEJMoa1516192. PMID: 27276561; PMCID: PMC4979995.
5. Halpern AB, Walter RB. Practice patterns and outcomes for adults with acute myeloid leukemia receiving care in community vs academic settings. Hematology Am Soc Hematol Educ Program. 2020;2020(1):129-134. doi:10.1182/hematology.2020000097
6. Rosenthal SH, Gerasimova A, Ma C, et al. Analytical validation and performance characteristics of a 48-gene next-generation sequencing panel for detecting potentially actionable genomic alterations in myeloid neoplasms. PLoS One. 2021;16(4):e0243683. Published 2021 Apr 28. doi:10.1371/journal.pone.0243683
7. Rosenthal SH, Gerasimova A, Ma C, et al. Analytical validation and performance characteristics of a 48-gene next-generation sequencing panel for detecting potentially actionable genomic alterations in myeloid neoplasms. PLoS One. 2021;16(4):e0243683. Published 2021 Apr 28. doi:10.1371/journal.pone.0243683
8. Arber DA, Orazi A, Hasserjian RP, et al. International Consensus Classification of Myeloid Neoplasms and Acute Leukemias: integrating morphologic, clinical, and genomic data. Blood. 2022 Sep 15;140(11):1200-1228. doi: 10.1182/blood.2022015850. PMID: 35767897; PMCID: PMC9479031.
9. Mertens F, et al. Nat Rev Cancer. 2015;15:371-381.
10. Michal Krawczyk, Lina Zelinger, Cynthie Wong, Hyunjun Nam, Brad Thomas, Nathan D Montgomery, Derek D Lyle, Fernando Lopez-Diaz; RNA Fusions and Their Association with DNA Alterations in Myeloid Neoplasia Patients Identified By a Single Tube Multimodal Comprehensive Genomic Profiling Test. Blood 2023; 142 (Supplement 1): 1556. doi: https://doi.org/10.1182/blood-2023-190505

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