Editorial

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Measurable Residual Disease Testing Using Next-Generation Sequencing in Acute Myeloid Leukemia

Measurable residual disease (MRD) is an important prognostic indicator of AML and is critical for risk stratification of treatment decisions [1]. Detecting MRD in patients with morphologically determined marrow with <5% blasts is important for refining the risk classification of AML [1, 2]. MRD detection in AML enables refined outcome prediction, impending relapse identification, and early intervention [1]. Several laboratory techniques can be utilized for the sensitive and accurate detection of MRD in AML and other hematologic malignancies. In clinical laboratories, molecular diagnostic methods, such as FISH and reverse transcription (RT)-PCR, have been used for the detection of recurrent fusion genes [3-4]. Newer diagnostic technologies, including droplet digital PCR (ddPCR), multiparametric flow cytometry, and next-generation sequencing (NGS), enable sensitive detection of MRD (up to 10^{-3}–10^{-6} leukemic cell burden) [1, 4-6].

NGS is widely used in the diagnosis and risk stratification of AML [7, 8]. With improving methodology and decreasing costs, the application of NGS for detecting MRD in AML has become promising [4]. MRD monitoring in AML is more challenging given the heterogeneity of the disease with diverse genetic abnormalities, especially when recurrent gene fusions are absent, as against other acute leukemias with well-defined targets, such as immunoglobulin rearrangements in ALL [4]. Using NGS, targets encompassing fusion genes and recurrently mutated genes, such as *NPM1* and *FLT3*-ITD, can be identified [9, 10], and multiple gene mutations specific to each patient can be considered for MRD monitoring. Approximately 96% of AML patients have more than one driver mutations [11]. Unlike other methods that detect a single or few focused targets, NGS offers the detection of numerous targets in a single assay. The advantages of NGS may be particularly useful for MRD testing in patients with AML.

In their study in this issue, Kim, *et al.* [12] provide the results of a newly developed targeted NGS panel for MRD that can be used for routine testing of AML patients. The error-corrected targeted NGS panel for MRD, which includes 24 genes, can be applied to approximately 78% of patients with AML. The panel's accuracy was validated by comparing it with that of the ddPCR assay, and a sensitivity of 0.25% was achieved using serially diluted samples. More than half the samples from patients with morphological remission who underwent one month of chemotherapy presented with MRD by NGS. Conclusively, Kim, *et al.* [12] suggested a broad NGS panel that can enable MRD monitoring of most AML patients without gene rearrangements.

The application of NGS technology in the diagnosis and risk stratification of AML is providing novel insights for clinical decisions. Further development and application of NGS technology to detect MRD in future studies and in clinical practice will highlight the usefulness of the test. While some challenges hinder the application and interpretation of the NGS MRD test, such as the presence of clonal hematopoiesis of indeterminate potential mutations, the data presented in this issue provide insights use-

ful for clinical laboratory professionals and hematologists. We expect highly accurate and sensitive MRD detection methods to become widely available and actively used in clinical laboratories in the near future, thereby contributing significantly to improved patient outcomes.

AUTHOR CONTRIBUTIONS

Kim SY and Huh HJ contributed to writing the manuscript and approved the submission of the final manuscript.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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