Editorial
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Seon Young Kim, M.D., Ph.D.
Department of Laboratory Medicine, Seoul National University Hospital, Seoul, Korea

Advances and Challenges in Fusion Gene Detection in Acute Leukemia

Fusion gene detection is essential for the accurate diagnosis, risk stratification, and targeted treatment of acute leukemia [1]. Laboratory technologies to detect fusion genes have continuously evolved, from conventional chromosome analysis following the landmark discovery of the Philadelphia chromosome to fluorescence *in situ* hybridization (FISH) and reverse transcription–polymerase chain reaction (RT-PCR) [2]. To further improve the diagnostic yield and sensitivity, clinical laboratories have increasingly adopted next-generation sequencing-based targeted RNA-sequencing panels. Compared with gene-by-gene approaches, these panels enable the detection of a broader spectrum of fusion genes and improve the identification of cryptic rearrangements frequently missed by conventional cytogenetics [3, 4].

More recent advancements have led to the development of comprehensive genomic platforms, including whole-transcriptome sequencing [5], whole-genome sequencing [6], optical genome mapping [7], and long-read sequencing [8]. These unbiased approaches have expanded the detectable spectrum of genomic rearrangements and enabled the identification of growing numbers of novel and rare fusion genes, thereby broadening our understanding of the genomic landscape of acute leukemia [9, 10]. While the continued evolution of these technologies will further enhance the detection and characterization of gene fusions, their effective implementation requires careful interpretation of results and a clear understanding of their analytical limitations.

In this issue of *Annals of Laboratory Medicine*, Kim *et al*. [11] evaluated the performance of whole-RNA sequencing for fusion gene detection in acute leukemia in comparison with conventional diagnostic methods, including karyotyping, FISH, and RT-PCR. The authors retrospectively analyzed 101 patients with acute leukemia who underwent both conventional diagnostic testing and whole-RNA sequencing. RNA sequencing identified at least one fusion gene in 50.5% of patients, compared with 46.5% detected by conventional methods, with an overall concordance rate of 80.8% and a sensitivity of 83.3%. Notably, RNA sequencing detected 12 additional fusion genes in cases that tested negative by conventional diagnostics, accounting for 21.4% of conventionally fusion-negative cases. These included several rare and previously unrecognized rearrangements, as well as four novel fusion genes. Furthermore, RNA sequencing clarified fusion partner genes in three cases where conventional methods had identified only incomplete rearrangements and enabled reclassification of five patients into more precisely defined molecular subtypes. The authors recognized that detection may remain challenging in cases involving low transcript abundance, low blast proportion, or genomic mechanisms that do not generate detectable fusion transcripts, such as enhancer hijacking.

As genomic technologies continue to advance, their effective integration into clinical practice holds immense promise for transforming leukemia care. As illustrated in this study, whole-RNA sequencing represents a powerful tool for fusion detection in acute leukemia and highlights the expanding potential of genomic technologies in leukemia diagnostics. In clinical practice,

whole-RNA sequencing may be implemented within existing diagnostic workflows, alongside karyotyping, FISH, RT-PCR, and targeted RNA-sequencing panels, as a complementary approach to maximize fusion detection, resolve ambiguous rearrangements, and characterize cases that test negative by conventional methods. Establishing appropriate validation strategies, quality control frameworks, and standardized analytical approaches will support the broader clinical implementation of these technologies. The integration of these emerging technologies into diagnostic workflows is expected to facilitate more precise molecular classification and improved clinical management of patients with acute leukemia.

AUTHOR CONTRIBUTIONS

The author confirms sole responsibility for manuscript conception and preparation.

CONFLICTS OF INTEREST

None declared.

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Corresponding author: Seon Young Kim, M.D., Ph.D.
Department of Laboratory Medicine, Seoul National University Hospital, 101 Daehak-ro, Jongno-gu, Seoul 03080, Korea
E-mail: ksuny55@gmail.com

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