

Emerging Applications of Liquid Biopsy in Pediatric and Adult Leukemia Populations

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DESCRIPTION

The management of leukemia has traditionally relied on invasive bone marrow biopsies and peripheral blood analyses to detect malignant cells, assess treatment response, and monitor disease progression. While these conventional approaches have proven effective in diagnosing and stratifying patients, they are limited by their invasiveness, the risk of complications, and the potential for sampling errors due to the patchy distribution of leukemic cells. In leukemia, liquid biopsy presents an exciting opportunity to redefine monitoring strategies, improve patient comfort, and enable more dynamic, precise, and personalized disease management.

Leukemia is a heterogeneous hematologic malignancy characterized by the clonal proliferation of abnormal white blood cells, with subtypes ranging from Acute Myeloid Leukemia (AML) and Acute Lymphoblastic Leukemia (ALL) to Chronic Myeloid Leukemia (CML) and Chronic Lymphocytic Leukemia (CLL). Each subtype exhibits distinct genetic, epigenetic, and immunophenotypic features that influence disease course and therapeutic response. Conventional monitoring relies heavily on serial bone marrow aspirates, which, although informative, are invasive and may be challenging to perform frequently. Moreover, peripheral blood assessments often fail to capture Minimal Residual Disease (MRD) or early relapse, particularly when leukemic cells are present at very low levels or sequestered in extramedullary sites. Liquid biopsy overcomes many of these limitations by detecting tumor-derived nucleic acids and cellular components in plasma, serum, or other body fluids, allowing continuous, real-time surveillance of disease dynamics.

MRD refers to the small number of leukemic cells that remain in the patient's body after treatment and are often undetectable by conventional morphology-based methods. MRD is a critical prognostic factor, as its presence is strongly associated with

relapse and poor overall survival. Liquid biopsy techniques, including the analysis of cfDNA and circulating tumor RNA, can detect MRD at levels far below the threshold of traditional methods. High-sensitivity assays, such as digital droplet PCR and Next-Generation Sequencing (NGS), enable the identification of specific genetic mutations, chromosomal rearrangements, and clonal immunoglobulin or T-cell receptor gene sequences in circulating nucleic acids. By providing an early indication of residual disease, liquid biopsy allows clinicians to intervene promptly, adjusting therapy intensity or considering experimental treatments before overt relapse occurs.

Liquid biopsy also offers the potential to capture spatial heterogeneity in leukemia. While bone marrow aspirates sample a specific site, leukemic clones may reside in multiple niches, including the peripheral blood, spleen, liver, lymph nodes, or central nervous system. This heterogeneity can result in underestimation of disease burden or misidentification of dominant clones. Circulating nucleic acids and CTCs provide a systemic snapshot of the disease, reflecting contributions from multiple sites simultaneously. By capturing this heterogeneity, liquid biopsy facilitates a more comprehensive understanding of clonal architecture and disease evolution, which is essential for designing personalized treatment strategies and predicting therapeutic response.

The use of liquid biopsy in leukemia is not limited to monitoring established disease. It holds promise for early detection and risk stratification in high-risk populations. Individuals with pre-leukemic conditions such as myelodysplastic syndromes or clonal hematopoiesis of indeterminate potential can be monitored for the emergence of driver mutations using cfDNA analysis. Identifying molecular aberrations before the onset of overt leukemia may allow for early interventions or enrollment in preventive clinical trials, potentially altering disease trajectories and improving long-term outcomes.

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