



The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

617.ACUTE MYELOID LEUKEMIAS: BIOMARKERS, MOLECULAR MARKERS AND MINIMAL RESIDUAL DISEASE IN DIAGNOSIS AND PROGNOSIS**Identification of Novel Transcripts and Potential Therapeutic Targets for Acute Leukemia**

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Acute leukemia is a heterogeneous disease with many genomic scars. Recent advances in targeted therapy and immunotherapy have improved the prognosis of this disease. However, prognosis still remains poor, and the identification of novel leukemia-specific transcripts may provide new strategies for leukemia therapy. We developed a novel long-read transcriptome method for sequencing full-length RNAs by directly capturing the 5'-end cap structures and the 3'-end poly(A)-tails of individual RNA molecules. We applied this method to bone marrow samples with various acute leukemias, including acute myeloid leukemia, acute lymphoid leukemia, and other rare types of acute leukemia. We covered full-length poly(A)+ RNAs with an average length distribution of over 3,000 bp, a much longer size distribution than previously reported. This not only led to the discovery of a wide array of uncharacterized transcript isoforms of known genes, but also to the discovery of 1,903 novel genes that are not annotated in the current human gene database. We also found that more than 60% of these new human genes were single exon genes and that many of them emerged from primates. This implicates that these new genes may contribute to human-specific leukemia biology. In addition, among these new human genes, 485 genes were predicted to have the potential to encode putative proteins using a GeneMarkS-T program. A fraction of new genes identified in this study were highly leukemia specific as shown by bulk CAGE-seq analysis of over 100 blood tumor samples and by single-cell RNA sequencing analysis of more than 300,000 bone marrow cells from leukemia patients, highlighting their potential as useful biomarkers and novel therapeutic targets. In sum, we constructed a comprehensive atlas of full-length RNA molecules in acute leukemia and identified a large number of uncharacterized ones. Our study provides a versatile framework for exploring novel transcripts and future therapeutic strategies in human diseases.

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