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The pediatric Acute Myeloid Leukemia (AML) is a high-risk and hard-to-treat childhood cancer that originates in the bone marrow from immature white blood cells. Recently, more and more evidence indicates that aberrant splicing of genes is a common characteristic for AML.

Gene expression profiles have proved extremely useful for identifying genes that are associated with clinical characteristics and survival outcome of cancer patients. However, conventional gene expression profiles do not account for the differences observed in expressed isoforms when alternative RNA splicing is analyzed. Alternative RNA splicing can generate dozens of distinct transcripts from individual genes and the expressions of some transcript isoforms may correlate with the patients' characteristics and survival outcome.

Current statistical methods in detecting and analyzing differentially expressed and spliced isoforms are limited. Recently we developed a novel approach to identifying differentially expressed or spliced isoforms among different medical conditions. We used a linear mixed effects model-based approach for analyzing the complex alternative RNA sequencing regulation patterns detected by whole-transcriptome RNA-sequencing technologies. Here, we applied this approach to perform differential isoform expression/splicing analysis with 234 patients in which 153 patients who were relapsed or dead within 3 years (Cases) and 81 who achieved continuous complete remission for three or more years (Controls). As a result, we identified 1144 genes with differentially expressed or spliced isoforms and 740 genes whose isoforms are differentially spliced between pediatric AML patients with good and bad outcomes. Our analysis provided biological insight for the disease progression as well as the biomarkers and therapeutic targets for the pediatric AML.