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Blood 142 (2023) 6060–6061

The 65th ASH Annual Meeting Abstracts

ONLINE PUBLICATION ONLY

618.ACUTE LYMPHOBLASTIC LEUKEMIAS: BIOMARKERS, MOLECULAR MARKERS AND MINIMAL RESIDUAL DISEASE IN DIAGNOSIS AND PROGNOSIS

A Study on Heterogeneity and Early Response to Chemotherapy in Pediatric ETV6-RUNX1 Positive Acute Lymphoblastic Leukemia By RNA-Seq Expression Profile

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Objective
ETV6-RUNX1 positive ALL is the most common type in childhood acute lymphoblastic leukemia(ALL), and it is also a type with good prognosis. However, there are still recurrent or refractory cases in this type, and there is still heterogeneity among individuals.In this research, we investigate the heterogeneity of ETV6-RUNX1 positive ALL in children by RNA-seq expression profile, and to explore the early response to chemotherapy and microenvironment characteristics of different clusters, so as to provide evidences for the exploration of genetic high-risk factors and clinical personalized diagnosis and treatment of such children.

Method
From September 2019 to June 2021, 72 children with newly diagnosed ETV6-RUNX1 positive ALL in standard risk group were enrolled and treated with CCLG-ALL-2018 chemotherapy protocol, which were all detected by RNA-seq technology. The sequencing results were analyzed by cluster analysis and bioinformatics analysis. We explored the early response to chemotherapy and microenvironment characteristics of the different clusters.

Result
ETV6-RUNX1 positive ALL were divided into three groups according to the RNA-seq expression profile including 16 cases (22.2%) in ER1 group, 35 cases (48.6%) in ER2 group and 21 cases (29.2%) in ER3 group. The number of patients with co-negative minimal residual disease (MRD) by flow cytometry (MRD-FCM) and next-generation sequencing (MRD-Gene) on the 15th day of chemotherapy in ER1 and ER3 groups was significantly different (3/16 vs. 13/21, P=0.0178), while there were 17 cases (17/35) with co-negative MRD in ER2 group after fifteen-day chemotherapy. It showed that the proportion of NK cells (P=0.056) and CD8 $^{+}$ T cells (P=0.047) in peripheral blood in ER1 group were both higher than those in ER3 group. Compared with ER3 group, ER1 group showed low expression of RPL41 and high expression of MRPS28 and SERPIND1, which were mainly involved in stress, proliferation and drug resistance of cells and the differentiation of hematopoietic stem cell. In addition, ER1 group showed lower expression of ribosome-related genes and higher activation of mTOR pathway than ER3 group.

Conclusion
The heterogeneity in gene expression profile were presented in children with ETV6-RUNX1 positive ALL. Compared with ER3 group, patients in ER1 group may have a poorer early response to chemotherapy with a relatively higher risk due to the stronger proliferation and drug resistance of leukemic cells probably. For patients in ER1 group, even if MRD is negative on the 15th day of themotherapy, it may be necessary to strengthen the observation of early response and consider the treatment for escalated risk in time.

Disclosures No relevant conflicts of interest to declare.

https://doi.org/10.1182/blood-2023-184389