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POSTER ABSTRACTS

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

Clinical Implications of Germline Predisposition Gene Variants in Patients with Refractory or Relapsed B Acute Lymphoblastic Leukemia

Zhao Defeng[1], *Tong Wu, MD*[2], *Chunrong Tong, MD*[3], *Lin Yuehui, MD*[4], *Qinlong Zheng, MD*[5,6]

[1]Beijing Gobroad Boren Hospital, Beijing,China, China
[2]Department of Bone Marrow Transplantation, Beijing Gobroad Boren Hospital, Beijing, China
[3]Department of Hematology, Beijing Gaobo Boren Hospital, Beijing, China
[4]Beijing Gobroad Boren Hospital, beijing,China, China
[5]Department of Medical Laboratory, Beijing Gaobo Boren Hospital, Beijing, China
[6]Laboratory of Molecular Diagnostics, Beijing GoBroad Boren Hospital, Beijing, China

Objectives: Gene variants are important factors in prognosis of the patients with hematological malignancies. In current study, our team investigate the relationship between blood and immune system germline predisposition variants and refractory/relapsed acute B lymphoblastic leukemia in patients.

Methods: The study included 75 patients with refractory/recurrent acute B-lymphoblastic leukemia between January 2020 and December 2022. The first group of 41 patients, median age 13.5 years (range: 2-66 years), had not had a bone marrow transplant. The second group of 34 patients with a median age of 28.5 (range: 4-51 years old, once had a bone marrow transplant. More than 700 genetic susceptibility genes related to blood and immune system diseases were detected in all patient samples using high-throughput DNA sequencing technology to detect the type and number of Class I and Class II gene variants. The average sequencing depth was 150×. Class I refers to the gene variants that are clearly significant in guidelines or authoritative research literature. Class II are genetic variants that software analysis suggests may be harmful.

Results: In the first group, 41 patients had an average number of Class I genetic susceptibility gene variants of 3.8 and Class II genetic susceptibility gene variants of 14.5 per patient. A total of 94 Class I genetic susceptibility gene variants were found, Thirty-two of them were recurrent more than 3 times that including HIF1A,SERPINE1,CFTR,CHEK2,ELANE,IFIH1,IRF7,JAK3,NCF2,PRF1,TGFBR2,TNFRSF13B,ATM,CYP3A4,ITGA2,NUDT15,THBD,BTLA,DNA The functions of these genes involve in combined immunodeficiency, autoinflammatory disease, complement deficiency, immune deficiency, T-cell dysfunction and antibody deficiency. After remission by CART cell therapy, twenty-three of the 41 patients underwent haploidentical hematopoietic stem cell transplantation, among which 5 patients relapsed after transplantation, three of the five donors of relapsed patients were also found HIF1A and SERPINE1 gene variants.

In the second group of 34 patients, the average number of Class I genetic susceptibility gene variants in each patient was 3, and the average number of class 2 genetic susceptibility gene variants was 14. A total of 53 class 1 genetic susceptibility gene variants were found, Eleven of them were recurrent more than 3 times that Including BTLA,MPEG1 ,KIT,SERPINE1,STK11,TP53,UGT1A1,EP300,FANCA,YARS2,F7,and four donors also carried the above gene variants, which were EP300. MPEG1, SERPINE1, YARS2 . After 34 patients achieved remission by CART cell therapy, 9 patients underwent the second hematopoietic stem cell transplantation (related half-matched), and 3 of them relapsed after the second transplantation (average 2.3 months). Two of the 3 donors of relapsed patients after second hematopoietic stem cell transplantation were also found BTLA and MPEG1 gene variants.

Conclusions: Our results have shown that genetic susceptibility gene variants related to blood and immune system diseases are associated with refractory or relapsed acute B lymphoblastic leukemia. The number of genetic susceptibility gene variants may be related to the relapse of leukemia. 32 Class I genetic susceptibility gene variants may be related to the relapse of leukemia during chemotherapy, and 11 class I genetic susceptibility gene variants may be associated with relapse after bone marrow transplantation. Donor carrying genetic susceptibility gene variants (HIF1A and SERPINE1, EP300, MPEG1, YARS2, BTLA) may be associated with relapse after transplantation. Genetic susceptibility gene variants may also be helpful in the selection of bone marrow transplant donors.

Keywords Acute lymphoblastic leukemia, germline predisposition gene, hematopoietic stem cell transplant, , relapse, hematological malignancy

Disclosures No relevant conflicts of interest to declare.

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