High resolution single nucleotide polymorphism analysis of genomic aberrations in childhood acute lymphoblastic leukaemia

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Abstract

Leukaemia is the sixth most frequent cancer in Malaysia and the commonest cancer in children. Acute Lymphoblastic Leukaemia (ALL) is one of the major causes of death in children. Acquired chromosomal abnormalities are the hallmark of ALL, which define biologically distinct subtypes of the disease. The strong association of many chromosomal abnormalities and prognosis has been utilized in risk stratification for treatment in a large number of protocols worldwide. High-resolution single nucleotide polymorphism (SNP) 6.0 array analysis was carried out on 55 Malaysian childhood precursor B-ALL (BCP-ALL) patients diagnosed between 2016 and 2017. The raw data was analyzed using Genotyping Console Software v4.2.0.26. SNP array results were validated using Multiplex Ligation-dependent Probe Amplification (MLPA) and Fluorescence in situ Hybridization (FISH). Our objective was systematically characterize genomic aberrations in childhood BCP-ALL among Malaysian populations. SNP array analysis revealed 31 copy number variant regions within the 55 samples. The most frequent copy number gains were on chromosome regions 22q11.22 (91%), 2p11.2 (64%), 15q11.2 (64%), 14q11.2 (51%) and Xq21.31 (44%) and the most frequent copy number losses were 4q13.2 (51%), 8p11.2 (33%) and 3q26.1 (31%). Gain of 22q11.22 and loss of 4q13.2 were the most frequent alterations found in this study. The recurrently targeted copy number abnormalities involved several leukaemia-related genes-CDKN2A/B, MLL, IKZF1, PAX5, RUNX1, ERG, CRLF2, SHOX, CSFR2A, BTG3 and ETV6. We identified several new recurrent aberrations with possible new target genes: Gain of 22q11.22 and loss of 4q13.2 were the most frequent alterations found in this study. These chromosomal regions contain genes such as POM121L1P, IGLL5 and UGT2B17. These potential genes may contribute to the leukaemogenesis in childhood BCP-ALL. Integrating the findings of this study with the clinical, cytogenetic and molecular biology data would allow us to propose new strategies that would improve the diagnosis, prognostication and treatment of Malaysian childhood BCP-ALL patients.

Keywords: BCP-ALL; SNP; MLPA; FISH.

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