Genetic Landscape of Childhood B-Cell Precursor Acute Lymphoblastic Leukaemia in Malaysia

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Acute lymphoblastic leukaemia (ALL) is the major causes of death in children. In Malaysia, precursor B-cell leukaemia (BCP-ALL) is the commonest cancer in children and the sixth most frequent cancer. Acquired chromosomal abnormalities are the hallmark of ALL, which define biologically distinct subtypes of the disease. The strong association of many chromosomal abnormalities with prognosis has been utilised in risk stratification for treatment in a large number of protocols worldwide. Here, genetic characterisation of the Malaysian BCP-ALL cohort was performed to understand the prevalence of treatment stratification markers and contribute to the risk stratification model development. In a cohort of 56 BCP-ALL patients, chromosomal translocations and copy number variations (CNVs) were determined using various techniques, including a multiplex reverse transcriptase-polymerase chain reaction assay (HemaVision), high-resolution SNP6.0 microarray, and multiplex ligation-dependent probe amplification (MLPA). Primary abnormalities detected in this cohort included *BCR-ABL1* (5%), *ETV6-RUNX1* (9%), *FUS-ERG* (4%), *TCF3-PBX1* (9%), and high hyperdiploid (7%). SNP6.0 microarray data analysis revealed gene focal deletions in *EBF1*, *CDKN2A/B*, *PAX5*, *ETV6* and *RB1*, whereas focal amplifications were seen in *BTG1*, *SHOX-AREA-DOWN*, *CRLF2*, *CSF2RA*, *IL3RA*, *P2RY8*, *POR* and *COL5A1*. Most CNVs were further validated using MLPA, however several discrepancies were observed between the two techniques due to differences in probe coverage and the sensitivity. In summary, the data is the first to genetically characterise the primary and secondary copy number abnormalities in a cohort of Malaysian paediatric BCP-ALL indicating the necessity for further refinement of the national diagnostic protocol.

Keywords: Acute lymphoblastic leukaemia, Microarray, Multiplex ligation-dependent probe amplification, Genomics

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