CDKN2A/B, PAX5 Deletion in Paediatric B-ALL Patients in Malaysia

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In B-cell precursor acute lymphoblastic leukaemia (BCP-ALL), B-cell development is arrested at the precursor B cell receptor (pre-BCR) checkpoint and malignant blasts avoid clonal extinction by hijacking pre-BCR signalling in favour of the development of BCP-ALL. These genetic changes found in key BCP-ALL signalling pathways have been utilised in risk stratification for treatment in a large number of protocols worldwide. The most common secondary alterations in genes involved in B-cell differentiation (*PAX5, IKZF1, EBF1*), RAS signalling, JAK/STAT signalling, cell cycle regulation and tumour suppression (*RB1*, *CDKN2A/B, TP53*) can contribute to the leukemogenesis and linked to BCP-ALL stratification. In addition, few recent meta-analyses studies indicate adverse impact of *CDKN2A/B* deletions possibly being more prominent in Asian patients. Here, we studied the prevalence of *CDKN2A/B* and *PAX5* deletions and their implications with co-operating genetic abnormalities in paediatric BCP-ALL patients using SNP6 copy number array and multiplex ligation-dependent probe amplification. Deletions in the genes *CDKN2A/B* and *PAX5* were the most common focal changes observed in this Malaysian BCP-ALL cohort. There are a total of 25 patients (45%) detected with *CDKN2A/B* or *PAX5* focal deletion; their primary abnormalities are *BCR-ABL1*, *ETV6-RUNX1*, *FUS-ERG*, *TCF3-PBX1*, high hyperdiploidy and B-other ALL. Eighteen patients (32%) harboured the *CDKN2A/B* and/or *PAX5* focal deletions. Further correlation with the BCP-ALL treatment outcome data for these patients will reveal the prognostic implications of these markers in this cohort. Overall, our data agree with the previous studies and conform *CDKN2A/B* and/or *PAX5* deletion as the highly prevalent copy number alteration in Malaysian pilot childhood BCP-ALL cohort.

Keywords: single-cell, mRNA-seq, functional studies, Fluidigm, Polaris

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