ArRay of Hope: Mining the Expression Profiling in Childhood Acute Lymphoblastic Leukaemia

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Abstract

Childhood ALL is the most common form of childhood cancer, accounting for one-third of the childhood cancers diagnosed in Singapore. Currently we achieve about 70% cure for this disease in Singapore. This high cure rate makes it necessary for us to optimise the risk-benefit ratio of our treatment. This is achieved by careful stratification of children into different risk groups of relapse and tailoring the intensity of therapy to commensurate with the risk of relapse. To risk stratify patients, we currently require 4 different laboratory platforms of morphology, immunophenotyping, cytogenetic analysis and molecular screening for oncogene fusion transcripts. These platforms are both costly and technologically demanding which make it not available to most children in developing countries.

To determine whether the gene expression profile of diagnostic leukaemia blasts at diagnosis could allow us to risk-stratify patients according to current conventional criteria, we utilized the Affymetrix HG-U95Av2 platform, to study the expression profiles of 389 paediatric ALL diagnostic samples treated in SJCRH. 360 (93%) samples were successfully analysed.

For risk-stratification, we achieved exceedingly high apparent and true accuracy rates of $> 95\%$ in predicting subgroup of ALL that the patient belongs to, using the gene expression profiling platform alone. Specifically, we were able to identify the 6 important subgroups of childhood ALL: T-lineage, E2A-PBX1, TEL-AML1, MLL rearrangement, BCR-ABL and hyperdiploid subgroups using subgroup specific classifiers in a decision tree format. More remarkably, using the gene expression profiles of leukaemia blasts at diagnosis, we were able to separate the cases into 2 different groups with significantly different risk of relapse (80% vs 3%). In addition, the gene expression profile prognostic factor is independent of the NCI/Rome criteria currently in use for risk stratification ($p < 0.0001$).