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Integrative approaches through transcriptome profiling to identify subset-specific gene activity in myeloma

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Statement of the Problem: The heterogeneous subsets in hematological malignancy such as multiple myeloma may be better characterize when tumor profiling were performed in multiple different dimensions. An integrative approach is needed to predict cell subset with potentially higher clonogenic potential and this has been a long-standing question in myeloma. However when analyzing bone marrow (BM) aspirates for RNA studies, one major challenge is to properly exclude signatures of non-myelomatous populations from the actual signatures of myeloma subsets that coexist within the same BM niche. Although CD138 is constitutively expressed in aberrant plasma cells, several patients do not express CD138 at high levels. These cases warrant further investigation before they can be subjected for downstream gene expression studies. Additional markers such as CD319 or CD229 were found to be useful since they were highly expressed in myeloma but not in normal plasma cells.

Methodology & Theoretical Orientation: The tumor cells identified from primary $CD138^{hi}$ myeloma population were sorted into four subsets using fluorescence-activated cell sorting based on expression of CD19, CD20, CD27 and CD56 surface markers. The sorted cells were subjected to RNA-sequencing and low-input microarray workflows.

Findings: The overall proximity between myeloma subsets were assessed using eigengene modules and cluster analyses. For myeloma that lack CD19 surface marker density, several distinct cellular immunophenotypes were identified. Two of the subsets show large similarity in transcription profile. Since they also lack CD27 surface expression, these clones could actually escape apoptosis induced by CD27-CD70 ligand interactions, as compared to the rare $CD27^{hi}$ myeloma cells.

Conclusion & Significance: Together, high-dimensional data extracted using combination of clinically relevant markers along with sufficient set of exclusion markers will permit mining for functional differences or similarity between subsets that might not be previously manifested in the bulk primary tumor population.

Biography

Siti Sarah Daud has received her PhD in Leukemia Research from School of Medicine, Cardiff University, UK in 2014. Prior to that, she pursued Masters in Medical Science, focusing on childhood leukemia at University of Malaya, Malaysia. During her postgraduate years, she had served at Pediatric Oncology Research Unit and was involved in chimerism typing for post-hematopoietic stem cell transplant patients at University of Malaya. Presently, she holds a Research Fellow Position at Department of Pediatrics, National University of Singapore. Her current research focuses on understanding the relation of heterogeneity in multiple myeloma subpopulations towards natural killer-cell immune response. She also has experience to ascertain low-input transcriptome workflows for human and non-human primate's platforms.

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