YLL SoM PhD student’s abstract selected for plenary presentation at the 14th International Myeloma Workshop

The 14th International Myeloma Workshop held from 3 – 7 April 2013 at Kyoto, Japan

The International Myeloma Workshop is the defining meeting in myeloma with a focus on both the basic and preclinical, and the clinical studies, conducted in Oral Presentations, Consensus Panels and Poster Presentations.

Mr BI Chonglei is our PhD student in the Department of Medicine under the main supervision of A/Prof Chng Wee Joo. His research focus is on the identification of tumor suppressor microRNAs abnormally silenced by epigenetic mechanisms in multiple myeloma. Using pharmacological compounds that reverse the epigenetic silencing process followed by global genomic methods, he has revealed novel, functionally relevant tumor suppressor microRNAs that provide insights into myeloma pathogenesis and biology, and serve as potential targets for therapy.
Abstract
Identification of Tumor Suppressive microRNAs in Multiple Myeloma by Pharmacologic Unmasking
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Deregulation of microRNAs (miRNAs) has been associated with pathogenesis and prognosis of multiple myeloma (MM). Although several causes may lead to miRNA deregulation, epigenetic alterations such as aberrant DNA methylation and/or histone modifications, have emerged as the main culprit. We conducted genome-wide screening for miRNAs induced by demethylating agent 5-azacytidine (5’aza), global histone methylation inhibitor DZNep and histone deacetylase inhibitor SAHA respectively in MM cells. Among the 1205 human miRNAs profiled, 32 were consistently upregulated by 5’aza. These miRNAs were closely associated with CpG islands and include miR-155, miR-198, miR-135a*, miR-200c, miR-125a-3p, miR-188-5p which were under-expressed in MM patients, miR-150*, miR-3141, miR-4257 and miR-1471 which were upregulated by all three compounds, as well as miR-483-5p, miR-663, and miR-630 with known tumor suppressor functions in other cancers. Among the predicted mRNA targets of these 13 miRNAs, 305 were upregulated in MM patients (UAMS dataset, GSE2658) and contained a 46-gene signature that was associated with patient survival. Ectopic restoration of miR-155, miR-198, miR-135a*, miR-200c, miR-663 and miR-483-5p significantly repressed MM cell proliferation, colony formation and migration. In summary, we have revealed important, epigenetically silenced tumor suppressor miRNAs by pharmacologic reversal of epigenetic silencing. These miRNAs are of functional relevance and affect genes that are associated with survival in myeloma.