

## **"MicroRNAs: Findings in Plasma Cell Disorders and their significance to predisposition".**

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Human genome plays a critical role in modulating cells' behavior. However there are number of layers of controls that affect how a cell will function. Dysfunction of these mechanisms also end up playing an important role in development and progression of cancer. With the newer high throughput technologies and better understanding of the genetics we have begun to analyze genomic changes in plasma cell disorder, especially multiple myeloma (MM) and Waldenstrom's Macroglobulinemia (WM) to understand the disease biology as well as to identify new targets and therapies. Global expression profile in WM has provided insight into pathobiology of the disease. However, effective expression is modulated by additional mechanisms such as alternate splicing and microRNAs. MicroRNAs are the small noncoding RNAs regulating expression of protein-coding genes by inducing cleavage of targeted transcripts or inhibiting translation. To better understand distinct mechanism involved in development of WM and to identify markers for diagnosis and/or novel targets for treatment we have evaluated expression of 384 microRNAs in 13 WM and 79 MM patients, and 13 healthy donors using miRNA array. Analysis of bone marrow derived CD138+ cells of WM patients as compared to CD138+ cells from HDs demonstrated modulated expression of 40 microRNAs. miRNA profiling demonstrated significant ( $p=0.001$ ) upregulation of miRs -192, -125b, -21, -155 and downregulation of miRs-181c, -572, and -650 in CD19+WM cells from patients compared to their counterpart from HDs. Comparison analysis of WM CD138+ cells to MM CD138+ cells identified 17 miRNA that are upregulated and 4 that are downregulated. In MM we have identified 2 groups with distinct microRNA expression pattern that differentiates survival groups. The genes targeted by these microRNAs have significant functional role in disease behavior with modulation of critical signaling pathways including apoptosis, hematopoietic cell differentiation and proliferation and survival through modulation functions of HOX, c-myc, and Bcl-2. Thus microRNAs plays a significant role in development and progression of plasma cell disorders and provides insight into possible therapeutic targets.