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Dysregulation of microRNA in Waldenström macroglobulinemia

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Waldenström macroglobulinemia (WM) and multiple myeloma (MM) are both B-cell malignancies with distinct clinical and biological characteristics. Our study aimed to identify differentially expressed microRNAs (miRNAs) between CD19+ bone marrow cells from WM patients and CD138+ bone marrow cells from MM patients and explore their potential clinical implications. Next-generation sequencing (NGS) was employed to profile miRNA expression in WM and MM patient samples. Differentially expressed miRNAs identified through NGS were further validated using reverse transcription-quantitative polymerase chain reaction (RT-qPCR). Correlation analyses were performed to examine associations between miRNA expression levels and various clinical parameters in WM and MM patients. Additionally, bone marrow cells from WM patients were analyzed for gene mutations, CNVs, cnLOH, deletions, translocations, and rearrangements using the custom LYmphoid neXt-Generation Sequencing (LYNX) panel (Fig. 1).

NGS identified eight differentially expressed miRNAs ($p < 0,01$) between WM and MM bone marrow samples. RT-qPCR validation was performed on a new dataset of patients. Three out of the eight differentially expressed miRNAs were chosen for validation. RT-qPCR confirmed significant differential expression of two out of three miRNAs between the two groups. Certain miRNA expression levels showed significant correlations with clinical parameters, suggesting their potential roles in disease severity and progression.

Furthermore, analysis of bone marrow samples from WM patients revealed the presence of the *MYD88* mutation in a high proportion of samples, confirming its potential role in disease pathogenesis.

This study highlights the distinct miRNA expression profiles in WM compared to MM, with specific miRNAs correlating with clinical parameters indicative of disease severity and progression. The differential expression of certain miRNAs, alongside their correlations with serum biomarkers and patient demographics, underscores their potential as diagnostic or prognostic biomarkers. Additionally, the frequent occurrence of the *MYD88* mutation in WM patients further differentiates WM from MM at the molecular level and may offer insights into targeted therapeutic strategies. The findings suggest that miRNA profiling, in conjunction with genetic mutation analysis, can enhance the understanding of the molecular mechanisms underlying WM and MM. This could lead to improved

diagnostic accuracy and personalized treatment approaches for patients with these B-cell malignancies.

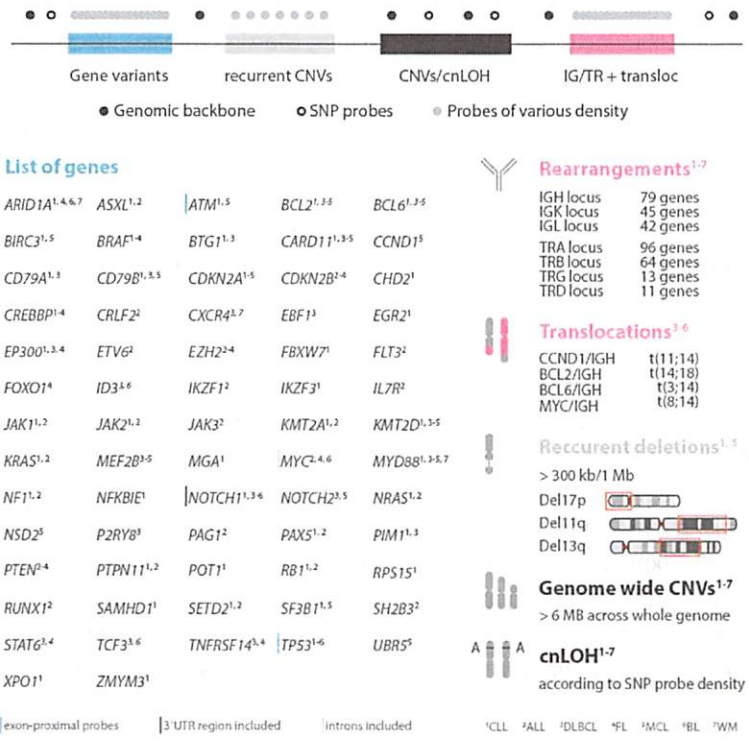

Figure 1: Schematic of the molecular markers targeted by the LYNX sequencing panel.

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