

## **Title: A Practical Guideline for MicroRNA Sequencing Analysis in Chronic Lymphocytic Leukemia: Deciphering MicroRNA-Gene Interactions in CLL Pathogenesis and Therapy Response**

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### **Abstract**

MicroRNAs (miRNAs) are small non-coding RNAs that regulate gene expression. They have been associated with several diseases and cancers, including chronic lymphocytic leukemia (CLL). CLL is the most common form of adult leukemia, and its pathogenesis is driven by the deletion of miRNAs, such as the miR-15a/16-1 cluster. In addition to initiating the development of CLL, the function of miRNAs in regulating the progression and phenotype of this tumor remains to be investigated. Here, we present a computational pipeline, from the processing of miRNA sequencing files to functional analysis, including differential gene expression and gene set enrichment analysis. The analysis revealed dysregulated expression profiles of miRNAs in CLL. The target genes of these miRNAs are not only associated with the response of CLL patients to current therapies but also involved in several cancer hallmarks, including the avoidance of cell death, the deregulation of cellular energetics, the activation of invasion and metastasis, and genome instability. The identified miRNA-gene interactions offer valuable insights for developing potential targeted therapies for CLL. In addition, we underscored the importance of a practical and robust computational pipeline to ensure the reliability of miRNA sequencing data analysis and reproducibility of the results.