Endocrinología, Diabetes y Nutrición

2 - MULTI-OMIC INTEGRATIVE APPROACH OF M6A-EPITRANSCRIPTOMIC, TRANSCRIPTOMIC AND SPLICING ALTERNATIVE EVENTS, REVEALED POTENTIAL CANDIDATE FOR THE DIAGNOSIS OF COLORECTAL CANCER

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Resumen

A few studies that focus on N6-methyladenosine (m6A, an epigenetic mark in mRNA) in circulating leukocytes and their contribution to colorectal cancer (CRC). Methods. High-throughput sequencing to investigate the m6A epitranscriptome, transcriptome, and alternative splicing events in leukocytes obtained from both healthy participants (n = 16) and patients with CRC (N = 16). For the m6A-methylome analysis, we employed MeRIP-seq (Methyl RNA immunoprecipitation) to selectively isolate m6A marks. Subsequently, we performed an integrative analysis to combine these datasets, aiming to identify potential diagnostic biomarkers. Results. Analysis of m6A epitranscriptomic profiles revealed an overall hypomethylation of RNA in patients with CRC,suggesting dysregulation of collagen organization and focal adhesion. Transcriptomic analysis identified significant downregulation of genes in patients with CRC (1,194 upregulated and 2,663 downregulated genes, p 0.05) associated with extracellular processes, protein metabolism, and immune function in CRC. Furthermore, alternative splicing events were significantly increased in CRC (14,213 alternative events were significantly increased, whereas 6,954 alternative events were significantly decreased, p 0.05), affecting genes involved in protein metabolism and metabolic pathways. Integrative analysis highlighted strong correlations between m6A-epitranscriptome, transcriptome, and alternative splicing datasets, with alternative splicing events demonstrating the highest discriminatory capacity for CRC detection, with a high AUC value. We propose several gene candidates using Random Forest Analysis, such as ENOX2, UBE3A, and RUBCNL genes, with high predictive capacity. Conclusion. This multi-omics approach provides insights into the molecular signatures underlying CRC pathogenesis, particularly regarding the epigenetics of RNA and RNA metabolism in circulating leukocytes. Our findings offer potential biomarkers for the diagnosis of CRC.