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METABOLIC ALTERATIONS INDUCED BY EPIGALLOCATECHIN-3-GALLATE IN A MYELODYSPLASTIC SYNDROME MOUSE MODEL: A METABOLOMIC APPROACH

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Introduction: Myelodysplastic syndromes (MDS) are hematologic malignancies characterized by ineffective hematopoiesis and high risk of progression to acute myeloid leukemia (AML). Epigallocatechin-3-gallate (EGCG), a green tea polyphenol, exhibits anti-cancer effects through diverse mechanisms, including metabolic modulation. **Objectives:** This study assessed EGCG-induced metabolic alterations in a transgenic MDS mouse model using untargeted metabolomics. **Material and methods:** C57BL/6-Tg(Vav1-NUP98/HOXD13) mice were treated for 30 days with EGCG (50 mg/kg/day, intraperitoneally) or saline (control). Serum samples were analyzed by LC-ESI-QToF-MS in positive and negative ionization modes. Data processing (Progenesis^{TM} QI) and statistical analysis (MetaboAnalyst^{TM} 5.0) included PCA, VIP score ranking, and KEGG-based pathway enrichment. **Results:** From 3,910 detected features, 72 metabolites were identified—predominantly glycerophospholipids, fatty acids, and steroids. PCA revealed distinct metabolic profiles between groups. Seven significantly altered pathways were identified, including unsaturated fatty acid biosynthesis, amino acid metabolism (alanine, aspartate, glutamate, glycine, serine, and threonine), and ketone body synthesis/degradation. Elevated β-hydroxybutyrate suggested enhanced fatty acid β-oxidation and a metabolic shift from glycolysis toward lipid-based energy production. **Discussion and conclusion:** EGCG treatment in MDS mice induced broad metabolic reprogramming, reducing unsaturated fatty acid synthesis while enhancing β-oxidation and ketogenesis—conditions less favorable to glycolysis-dependent neoplastic cells (Warburg effect). These changes may lower membrane fluidity, disrupt signaling pathways, restrict nucleotide biosynthesis, and modulate epigenetic regulation via one-carbon metabolism. Such metabolic stress could contribute to EGCG's anti-cancer activity by impairing tumor cell proliferation and survival. Further preclinical and translational studies are warranted to confirm these mechanisms and explore EGCG's potential as a metabolic modulator and adjuvant therapy in MDS and related hematologic malignancies.

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MICALL2 IN ACUTE MYELOID LEUKEMIA: AN INTEGRATIVE APPROACH USING BIOINFORMATICS AND ARTIFICIAL INTELLIGENCE

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Introduction: Acute Myeloid Leukemia (AML) is a hematological malignancy of well-recognized clinical and epidemiological relevance, due to its high incidence and mortality rates worldwide. Its pathogenesis involves the uncontrolled proliferation of immature myeloid precursors in the bone marrow, impairing normal hematopoiesis. Recent bioinformatics studies supported by artificial intelligence tools have identified the MICALL2 protein as a promising prognostic marker, given its involvement in cytoskeletal regulation and in cellular processes such as adhesion, migration, metabolism, and intracellular signaling. Although MICALL2 has already been implicated in solid tumor development, its role remains unexplored in hematological malignancies. **Objectives:** In this context, the present study aimed to investigate the functional and prognostic role of the MICALL2 protein in Acute Myeloid Leukemia through bioinformatic analyses applied to transcriptomic data from public databases. **Material and methods:** Data from AML patients in the TCGA cohort were analyzed. Samples were dichotomized based on MICALL2 expression levels, with the cut-off defined by ROC curve analysis. Overall survival and disease-free survival were assessed using Kaplan–Meier analysis, and the same stratification was used for gene ontology and enrichment analyses. MICALL2 expression in normal hematopoiesis was investigated using NCBI data and visualized through hierarchical plots generated via

the BloodSpot platform. **Results:** A correlation was identified between high MICALL2 gene expression and improved overall survival (p = 0.005; HR = 1.90), as well as a higher prevalence of patients classified in the intermediate molecular risk group (p = 0.005; HR = 0.277). Functional analyses revealed that elevated MICALL2 expression is associated with increased activation of pathways related to cell proliferation, energy metabolism, and DNA repair, while repressing signaling and differentiation processes. Significant positive correlations were observed between MICALL2 and genes involved in metabolism and inflammatory response, along with negative correlations with genes related to cellular differentiation, apoptosis, and stress response. Regarding its expression during hematopoiesis, MICALL2 levels were higher in erythroid cells compared to hematopoietic stem cells, while other lineages displayed homogeneous expression profiles. **Discussion and conclusion:** The association between high MICALL2 expression and favorable prognostic variables in AML suggests a relevant regulatory role within the biological heterogeneity of the disease. Although functionally linked to proliferation, metabolism, and repair pathways, its expression pattern correlates with less aggressive clinical profiles, possibly reflecting cellular states with higher degrees of differentiation or reduced functional plasticity. The increased expression in the erythroid lineage during physiological hematopoiesis reinforces its involvement in specific transcriptional programs, potentially influencing the behavior of distinct leukemic subgroups. These findings support the hypothesis that MICALL2 may serve as a potential prognostic biomarker and underscore the importance of its functional investigation in experimental models to validate its clinical and therapeutic applicability.

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MIRNA-RELATED COPY NUMBER VARIATIONS IN PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA

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Introduction: MicroRNAs (miRNAs) are a class of non-coding RNAs that act post-transcriptionally to regulate gene expression, playing an essential role in hematopoiesis and carcinogenesis. In acute lymphoblastic leukemia (ALL), chromosomal alterations in regions involving miRNA genes can modify their expression, affecting tumor suppressor miRNAs and oncomiRs, and impacting pathways related to proliferation, apoptosis, and cellular differentiation. Specific miRNA profiles can be associated with molecular subtypes of ALL, serving as a means of classification, as well as potential biomarkers for diagnosis and prognosis. **Objetivos:** This study aimed to investigate the copy number variation (CNV) profile of patients with ALL from a reference cancer hospital diagnosed, with the goal of identifying alterations in chromosomal regions involving miRNAs and their possible impacts. **Material and methods:** A total of 16 pediatric ALL patients (5 ± 3 years) were selected for analysis by array comparative genomic hybridization (aCGH). Samples were processed using the PureLink Genomic DNA Mini Kit. The aCGH was performed on an Agilent 4x180k CGH + SNP microarray. Subsequently, the patients' DNA underwent enzymatic digestion, and labeling with the fluorochrome cyanine 5 was carried out using random primers and the exo-Klenow fragment DNA polymerase. The control DNA was labeled with the fluorochrome cyanine 3. Patient and control DNA samples were combined and hybridized on the microarray. Data were analyzed using Agilent's CytoGenomics v5.0 software. **Results:** Fifty-eight different miRNAs were identified in a total of 72 alterations involving these genes. These alterations were observed in 15 of the 16 patients analyzed, with an average of 4.8 alterations per patient, and were present in all 22 autosomal chromosomes as well as both sex chromosomes. The detected chromosomal alterations consisted of 34 losses, 28 gains, 8 amplifications, and 2 deletions. The distribution of alterations by chromosome showed the highest frequency on chromosome 1, with 11 alterations, followed by chromosome 22 with 9 alterations, all located in band q11.22, chromosome 9 with 7 alterations, and chromosome 11 with 5 alterations. The most frequent miRNAs were miR650, present in 9 patients, followed by miR3156-3 in 5 patients, and miR491 in 3 patients. The 8 amplifications detected were on chromosome 22 in band q11.22, where the miR650 gene is located. **Discussion and conclusion:** This study reveals that a high heterogeneity of miRNAs among patients was evidenced. The presence of alterations in these genes in 15 out of 16 patients indicates that these events are recurrent and possibly relevant for ALL. The higher concentration of alterations in chromosomes 1, 9, 11, and 22 points to potential regions harboring important elements for carcinogenesis. Additionally, the presence of various types of alterations demonstrates the complexity of how miRNA expression and post-transcriptional regulation can be affected. The most frequent miRNAs identified have been described in other hematological pathologies, involved in processes such as cell proliferation, apoptosis, and stress response. Finally, it is important to highlight the amplification of miR650, present in 8 of the 16 patients, increasing its expression, which can lead to the repression of tumor suppressor genes, promoting evasion of apoptosis, tumor progression, potential resistance to treatments and survival and aggressiveness of malignant cells, being correlated with a worse prognosis.

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