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Opinion Article

Identification of Prognosis in Acute Myeloid Leukemia by using Cuproptosis-Related Molecular Technique

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DESCRIPTION

AML is a type of blood cancer that develops when hematopoietic progenitors in the bone marrow proliferate uncontrollably. The most prevalent kind of adult leukemia is AML. Over the past few decades, there hasn't been much advancement in AML treatment strategies. Overall Survival (OS) for AML patients is less than 40%, which is still an unacceptable result. Investigating the molecular causes of AML and finding new prognostic biomarkers is therefore crucial since they could improve both the course of treatment and the prognosis of AML patients. All forms of life depend on transition metals like Fe, Mn, Cu, and Zn as trace elements. These metal ions have a role in electron transfer and signaling pathways within cells, as well as being essential enzyme cofactors. When present in excess, certain transition metals can be hazardous. Numerous regulatory circuits work together to strictly regulate appropriate amounts of metal ions in organisms. This Tricarboxylic Acid Cycle (TCA)-dependent programmed cell death is typified by protein lipoylation. It is a unique type of cell death mechanism that is not the same as autophagy, necrosis, apoptosis, or ferroptosis. *FDX1* is a crucial regulator that controls protein lipoylation and cuproptosis. After entering mitochondria, copper directly binds the lipoylated TCA enzymes. Thus, loss of Fe-S cluster-containing proteins and lipoylated protein aggregation caused acute proteotoxic stress. According to this study, cells that rely on mitochondrial respiration might be more susceptible to cuproptosis. A new type of cell death that is programmed is called cuproptosis. Regarding its role in leukemia, less is known. We compared the mRNA levels of 14 CRGs in this investigation. The majority of them displayed distinct expressions in AML patients compared to healthy controls. Separately, three genes—*DLAT*, *LIPT1*, and *GCSH*—were found to have considerable predictive value. LASSO Cox regression analysis based on the expression of three genes: *GCSH*, *LIPT1*, and *PDHA1* in order to investigate the function of cuproptosis in AML in more detail. In the TCGA cohort, the 3-gene signature performed well in predicting the diagnosis and prognosis of AML. Specifically, a negative outcome was associated with a high risk-score. An additional cohort from the GEO database was used to confirm the results. An enzyme that *GCSH* encodes may be lipoylated and activated by FDX1. AML and soft tissue sarcoma showed decreased *GCSH* levels, whereas breast cancer tissues showed higher levels of this protein. *LIPT1* is involved in the route of lipoic acid metabolism. It has been shown recently that *LIPT1* is effective in moving lipoic acid moieties from one protein to another. The pyruvate dehydrogenase complex, which controls pyruvate entry into the TCA cycle, includes PDHA1. Two genes that decrease tumor growth were *LIPT1* and *GCSH*. A higher prognosis was associated with higher expression of these two genes. Further research is required to understand how these genes function during cuproptosis. Based on risk score analysis, we examined DEGs in AML subgroups and discovered that cuproptosis might interact with inflammatory responses. The DEGs were primarily enriched in immune response-related inflammation, according to GO and KEGG analysis. Furthermore, there was enrichment in the B cell receptor signaling pathway. The PPI network revealed that the top 3 genes were all involved in immune response. LILRB2 is a leukocyte immunoglobulin-like receptor family member that is expressed on myeloid lineage cells. Myeloid cells include dendritic cells, which include pDCs and aDCs. They were enriched using immune cell infiltration analysis in the high-risk group.

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