Prognostic and Therapeutic Role of Hypoxia-Inducible Factor-1 Alpha (HIF-1α) in Acute Myeloid Leukemia: A Systematic Review

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Introduction

Acute myeloid leukemia (AML) is a heterogeneous hematologic malignancy characterized by clonal proliferation of myeloid precursors in the bone marrow. The hypoxic microenvironment of the bone marrow niche plays a crucial role in leukemogenesis by stabilizing hypoxia-inducible factor-1 alpha (HIF-1α), a transcription factor involved in angiogenesis, metabolism, and cell survival. Overexpression of HIF-1α has been increasingly recognized as a contributor to chemotherapy resistance and poor clinical outcomes in AML. Despite its biological significance, the prognostic and therapeutic implications of HIF-1α remain incompletely defined.

Aim

To systematically evaluate the prognostic significance and therapeutic potential of hypoxia-inducible factor-1 alpha (HIF-1α) in acute myeloid leukemia (AML).

Objectives

- To assess the correlation between HIF-1α expression and clinical outcomes in AML, including overall and event-free survival.
- To examine the association of HIF-1α with chemotherapy resistance and disease progression.
- To explore the role of HIF-1α as a prognostic biomarker in cytogenetically and molecularly defined AML subtypes.
- To evaluate the therapeutic implications of targeting HIF-1α in AML management.

Methods

A systematic review was conducted in accordance with PRISMA guidelines. Databases including PubMed, Scopus, and Google Scholar were searched for relevant literature published between 2010 and 2025. Inclusion criteria were clinical studies evaluating HIF-1α expression in AML patients and its relationship with prognosis, treatment resistance, or therapeutic targeting. Studies were screened, selected, and qualitatively synthesized due to clinical heterogeneity among methodologies and reported outcomes.

Results

Five eligible studies were included. All studies reported significant overexpression of HIF-1α in AML patients compared to controls. Elevated HIF-1α expression was associated with increased relapse rates, lower complete remission rates, and inferior overall and event-free survival. In cytogenetically normal AML, cytoplasmic HIF-1α (cytoHIF-1α) independently predicted poor outcomes (OS: P=0.0058, HR=0.38; EFS: P=0.0151, HR=0.43). Co-expression of HIF-1α with Beclin-1 or VEGF-A further correlated with aggressive disease. Mechanistic insights revealed HIF-1α's interaction with YAP enhances adriamycin resistance and leukemic cell survival under hypoxia

Summary

HIF-1α overexpression is a consistent indicator of poor prognosis and therapeutic resistance in AML. Its expression profile in genetically diverse AML subtypes underscores its utility as a biomarker and treatment target.

Discussion

This review highlights the central role of HIF-1α in AML pathogenesis, prognosis, and therapy resistance. Targeting HIF-1α or its downstream pathways holds promise for improving outcomes, particularly in high-risk AML. Further large-scale, prospective studies and clinical trials are warranted to validate these findings and develop HIF-1α-based therapeutic strategies.

References

Key Studies on HIF-1α in Acute Myeloid Leukemia

1. Chanswangphuwana C et al. studied HIF-1α impact in Nucleophosmin1 mutated AML
2. Deeb G et al. linked HIF-1α expression with poor survival in normal karyotype AML
3. Jabari M et al. analyzed HIF1α and VEGF-A expression in de novo AML patients
4. Radwan SM et al. explored Beclin-1 and HIF-1α gene expression as biomarkers
5. Ali T et al. found aberrant HIF1-α and SIX-1 expression predicts poor prognosis

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