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ORIGINAL RESEARCH

AKAP9 Upregulation Predicts Unfavorable Prognosis in Pediatric Acute Myeloid Leukemia and Promotes Stemness Properties via the Wnt/β-Catenin Pathway

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Background: PRKA kinase anchor protein 9 (AKAP9) is a scaffold protein involved in various cellular processes, including cell adhesion, proliferation, differentiation, and apoptosis. Although the oncogenic role of AKAP9 in solid tumors is well elucidated, the functions and mechanisms of AKAP9 in acute myeloid leukemia (AML) are still not understood.

Methods: We used the gene expression omnibus (GEO) database (GSE2191) to determine the mRNA expression of AKAP9 in the bone marrow of pediatric AML and healthy patients. We further used the therapeutically available research to generate effective treatments (TARGET) database to elucidate the relationship between AKAP9 expression and clinical outcomes in pediatric patients with AML. In addition, cell proliferation, cell cycle, apoptosis, RT-PCR, and Western blotting assays were applied to reveal the functions of AKAP9 and the underlying mechanisms of AKAP9 silencing in THP1 and HL60 cell lines.

Results: AKAP9 is overexpressed in the bone marrow of pediatric AML patients as compared with that of healthy patients. High expression of AKAP9 was found to be a predictor of poor overall survival (OS) and event-free survival (EFS). Using univariate and multivariate survival analyses, we found that high AKAP9 expression is an independent predictor of a worse OS and EFS. Functionally, AKAP9 silencing significantly inhibited AML cell proliferation, and cell cycle progression and promoted apoptosis. Moreover, AKAP9 silencing significantly downregulated the expression of stemness markers and β-catenin.

Conclusion: AKAP9 upregulation is a predictor of unfavorable prognosis, promotes stemness, and activates the Wnt/β-catenin pathway in AML patients. AKAP9 may act as a prognostic biomarker of AML in pediatric patients and a future therapeutic target.

Keywords: PRKA kinase anchor protein 9, acute myeloid leukemia, prognosis, leukemic stem cells, pediatric

Introduction

Acute myeloid leukemia (AML) is a common hematological malignancy characterized by a clonal malignant proliferation of myeloid primordial cells.[1] AML has a poor prognosis and is the main cause of death in children and adults under 35 years of age in China.[2] Chemotherapy remains the primary treatment option for patients with AML. Despite the improvement in AML research and therapies,

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