SOHO ANNUAL MEETING 2024

A Prospective Study to Evaluate the Prognostic Implications and Molecular Mechanism of *SLC40A1* Gene in Primary Acute Myeloid Leukemia

H. GOEL[1], A. CHOPRA[1], A. RANJAN[1], J.P. MEENA[1], A.K GUPTA[1], G.K. VISHWANATHAN[1], S. BAKHSHI[1], M.A. KHAN[1] and P. TANWAR[1]

1. All India Institute of Medical Sciences, New Delhi, India

INTRODUCTION

Acute myeloid leukemia (AML) is a genetically heterogeneous hematologic disorder characterized by abnormal myeloid progenitor cell proliferation and differentiation, often accompanied by genetic and epigenetic alterations. Iron metabolism is implicated in various cancers, yet its role in AML remains poorly understood. Ferroportin, encoded by the *SLC40A1* gene, is vital for cellular iron export, but its significance and interactions in AML are unclear.

AIM

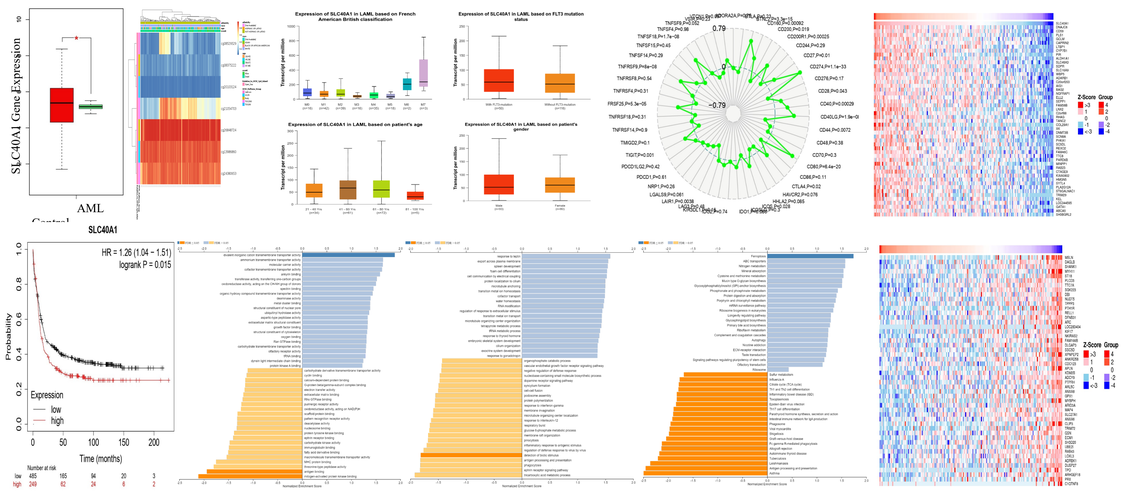
This study aimed to characterize the molecular functions, clinical relevance, and prognostic value of the *SLC40A1* gene in AML.

METHOD

We investigated *SLC40A1* gene expression in AML (n=173) and control (n=70) cases, followed by correlation analysis to identify associated genes using the Linked Omics database. Prognostic significance was evaluated using Kaplan–Meier survival estimation. DNA methylation status was assessed using the MEXPRESS database. Molecular mechanisms were explored via gene set enrichment analysis (GSEA), and the relationship with immune checkpoints was studied using the SANGER Box 3.0 database.

RESULTS

SLC40A1 mRNA was significantly overexpressed in AML cohorts and correlated with poor overall survival ($P<0.05$). Positive correlations were found with *DNAJC6, CD59, PLS1, GCLM*, and *CAPRIN2* genes, while negative correlations were observed with *MSLN, MYH11, DAGLB, ST18*, and *PLCD3* (PCC <0.80). Lower methylation levels of *SLC40A1* were observed in AML, inversely associated with gene expression. Gene enrichment analysis revealed enrichment in biologic processes such as lymphocyte homeostasis, endothelium development, spleen development, cell communication, and cell differentiation, while in molecular function *SLC40A1* gene was enriched in iron ion transmembrane transporter, metal cluster binding, growth factor binding, and catalytic activity. KEGG pathway analysis implicated *SLC40A1* in critical pathways like hematopoietic stem cell differentiation, ferroptosis, mRNA surveillance pathway, autophagy, TGF-beta signaling pathway, and signaling pathways regulating pluripotency of stem cells. Additionally, SLC40A1 positively correlated with immune checkpoints including CD160, CD274, CD40, CD44, and CD80.



CONCLUSIONS

SLC40A1 plays a significant role in AML progression and may serve as a potential prognostic biomarker and therapeutic target. This study provides insights into the molecular mechanisms underlying *SLC40A1* involvement in AML pathogenesis, offering avenues for novel therapeutic interventions.

REFERENCES

1. **De R, Prakash KU, Edison ES.** Complex Interactions in Regulation of Haematopoiesis-An Unexplored Iron Mine. *Genes (Basel)*. 2021;12(8):1270.

2. **Bogdan AR, Miyazawa M, Hashimoto K, Tsuji Y.** Regulators of Iron Homeostasis: New Players in Metabolism, Cell Death, and Disease. *Trends Biochem Sci*. 2016;41(3):274-286.

3. **Brissot E, Bernard DG, Loréal O, Brissot P, Troadec MB.** Too much iron: A masked foe for leukemias. *Blood Rev*. 2020;39:100617.

ACKNOWLEDGEMENTS

"We deeply appreciate the support provided by AIIMS, CSIR, and SOHO, whose contributions have been instrumental in the success of our endeavors."

CONTACT INFORMATION

Presenting Author : goel.harsh271@gmail.com