Decoding Hedgehog Signaling in Acute Myeloid Leukemia: Expression, Methylation, and Prognostic Implications

A. Goel[1], S.K. Pradhan[2], S. Govekar[3], T. Jha[4], G. Kapatia[1], P.S. Dhoat[1], A. Pathak[1], S. Ganguly[5]

1. All India Institute of Medical Sciences, Bathinda, India
2. NIT, Rourkela, India
3. All India Institute of Medical Sciences, Rishikesh, India
4. Medical College Kolkata, Kolkata, India
5. JIPMER, Puducherry, India

Introduction

- The Hedgehog (Hh) signaling pathway plays a critical role in embryonic development, stem cell maintenance, and tissue homeostasis. Dysregulation of this pathway has been implicated in various cancers, including acute myeloid leukemia (AML).
- However, the roles of specific Hh pathway genes in AML, such as *WNT6*, *BMP8B*, *HHIP*, *SUFU*, *CSNK1G3*, and *CSNK1A1*, remain unclear.
- This study investigates the expression, methylation status, survival correlation, and functional enrichment of these genes to elucidate their roles in AML pathogenesis and prognosis.

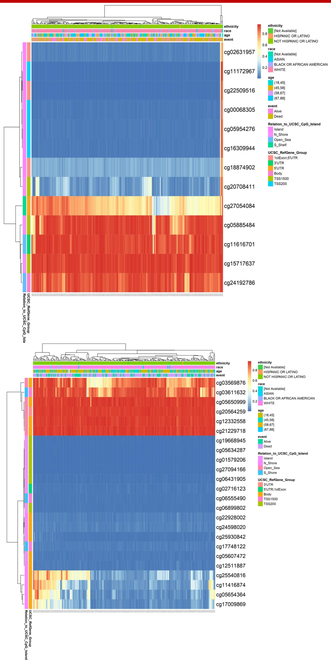
Aim & Objectives

- Assess expression and methylation status of six Hh pathway genes (WNT6, BMP8B, HHIP, SUFU, CSNK1G3, CSNK1A1) in AML.
- Evaluate association with survival and functional pathways.

Methods

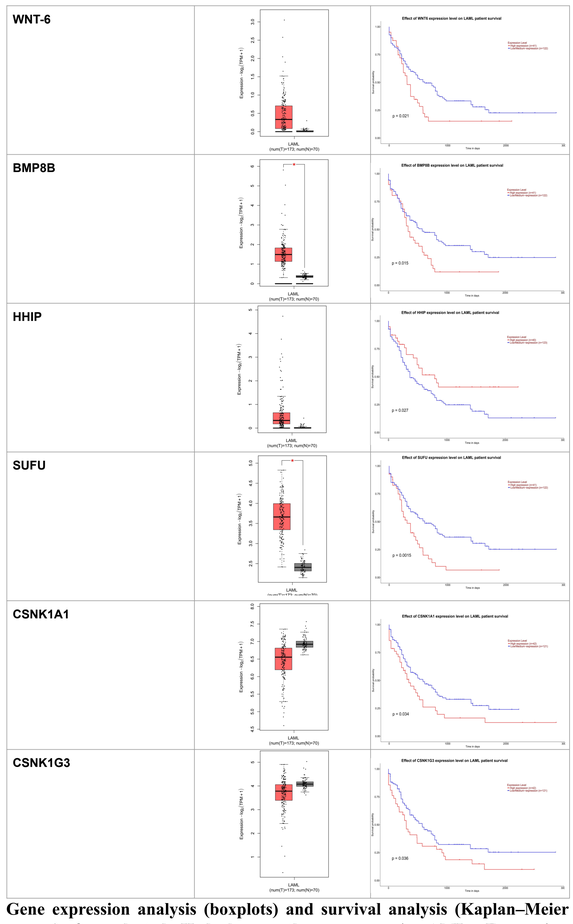
- In this retrospective bioinformatics study, we analyzed the Cancer Genome Atlas–LAML dataset using 220 AML cases for differential expression and promoter methylation of the selected genes compared to normal controls.
- Analyses in this study included differential expression and promoter methylation assessment to identify transcriptional and epigenetic alterations in Hedgehog pathway genes. Survival analysis using Kaplan–Meier curves evaluated the prognostic significance of gene expression levels. Functional enrichment analyses were performed using Gene Ontology and KEGG pathway annotations to explore the biological processes and signaling cascades associated with these genes. Additionally, correlation and interaction network analyses were conducted to identify potential relationships and functional linkages among the selected genes and related pathways

Results



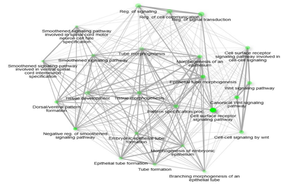
Differential gene expression and promoter methylation for Hedgehog pathway genes in AML. WNT6, BMP8B, HHIP, and SUFU are upregulated; CSNK1G3 and CSNK1A1 are downregulated and hypermethylated.

Results



Gene expression analysis (boxplots) and survival analysis (Kaplan–Meier curves) for selected Hedgehog pathway genes in AML. Expression differences are shown between AML cases and controls, with corresponding survival curves indicating the prognostic impact of high versus low/medium expression levels. p-values from log-rank tests are shown.





Network shows interconnections among enriched biological processes (node size: gene-set significance), highlighting extensive pathway crosstalk relevant to AML pathogenesis.

Conclusion

- This study highlights the dysregulation of Hh pathway genes in AML and their roles in leukemogenesis. The association of *CSNK1G3* and *CSNK1A1* downregulation with hypermethylation emphasizes the impact of epigenetic modifications on the Hh pathway.
- These genes show promise as potential biomarkers and therapeutic targets in AML. Future research should explore strategies to modulate the Hh signaling pathway for improved treatment outcomes.

References

- Lainez-González D, Serrano-López J, Alonso-Domínguez JM. Understanding the Hedgehog Signaling Pathway in Acute Myeloid Leukemia Stem Cells: A Necessary Step toward a Cure. Biology (Basel). 2021 Mar 24;10(4):255. doi: 10.3390/biology10040255. PMID: 33804919; PMCID: PMC8063837.
- Kobune, M., Iyama, S., Kikuchi, S. et al. Stromal cells expressing hedgehog-interacting protein regulate the proliferation of myeloid neoplasms. Blood Cancer Journal 2, e87 (2012). https://doi.org/10.1038/bcj.2012.36



Archit Goel, MBBS
All India Institute of Medical Sciences, Bathinda, India
Oncoarchit@gmail.com

SOHO ANNUAL MEETING 2025