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Prognosis Analysis and Validation of Fatty Acid Metabolism-Related Signature in Chronic lymphocytic leukemia

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INTRODUCTION

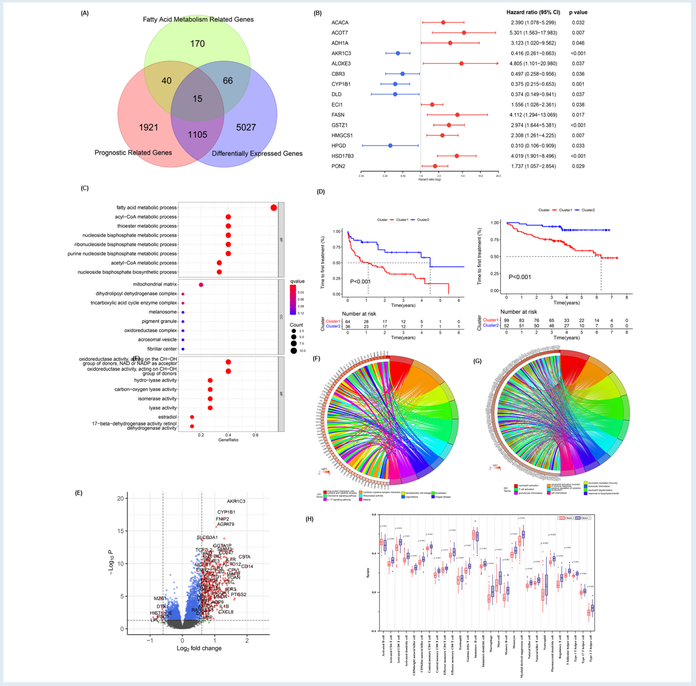
Chronic lymphocytic leukemia (CLL) is the most common leukemia in the western world. Although the treatment landscape for CLL is rapidly evolving, there are still part of patients develop disease refractory and relapse, which shows CLL's heterogeneity. Therefore, it is important to distinguish high-risk patients from CLL population during the early stage of the disease and apply a more suitable treatment strategy. Fatty acid (FA) metabolism contributes to tumorigenesis, progression, and therapy resistance through enhanced lipid synthesis, storage, and catabolism. In this study, we aimed to construct a prognostic model to improve the risk stratification of CLL and reveal the link between FA metabolism and CLL.

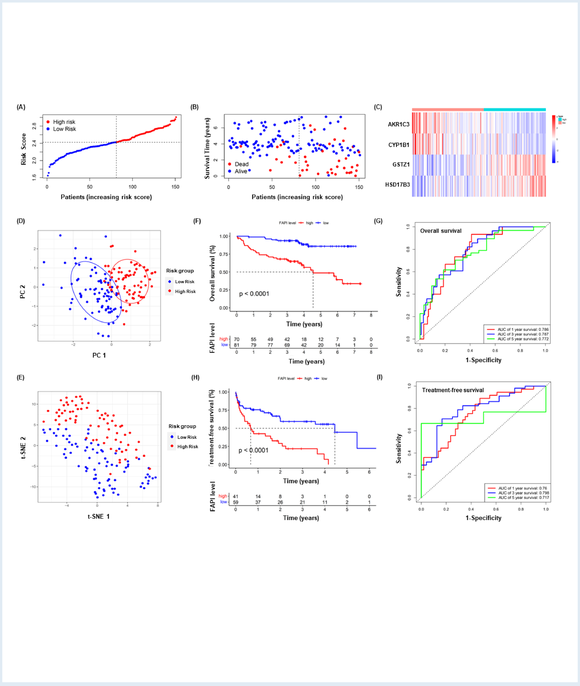
METHODS

The differentially expressed fatty acid metabolism-related genes (FMGs) in CLL were filtered through univariate Cox regression analysis based on public databases. Patients in the cohort are divided into 2 clusters. Enrichment analysis of prognostic fatty acid (FA) metabolism-related genes was performed to explore functional enrichment. CIBERSORT and single-sample gene set enrichment analysis (ssGSEA) were performed to estimate the immune infiltration score and immune-related pathways. Besides, the least absolute shrinkage and selection operator (LASSO) Cox algorithms were carried out to establish a novel prognostic model.

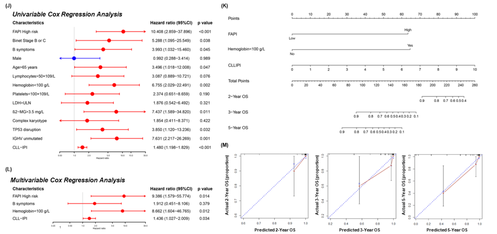
RESULTS

We obtained CLL RNA microarray profiles from public database and identified 15 prognostic-related FMGs. CLL patients were divided into two molecular clusters based on the expression of FMGs. The Kaplan–Meier analysis showed that patients in Cluster 1 had statistically significant worse TFS (P<0.001) and OS (P<0.001). KEGG functional analysis showed that several pathways, including the chemokine signaling pathway, IL-17 signaling pathway, NF-κB signaling pathway, PD-L1expression and PD-1 checkpoint pathway in cancer, and T cell receptor signaling pathway were enriched. Then, we conducted LASSO Cox regression analysis to establish the FA metabolism-related prognostic index (FAPI), exhibiting similar prognostic significance. Finally, a novel nomogram prognostic model including CLL-IPI was constructed, exhibiting reliable effectiveness and accuracy.





RESULTS



CONCLUSION

In conclusion, we established a reliable predictive signature based on FA metabolism-related genes and constructed a novel nomogram prognostic model, supporting the potential preclinical implications of FA metabolism in CLL research.