Fatty Acid Metabolism Fingerprints Predict Prognosis and Regulate Immunophenotype in Chronic Lymphocytic Leukemia

Yang Zhang[1], Xinting Hu[2], Zheng Tian[2], Hua Wang[1], Xin Zhang[2], Xin Wang[1,2] and Ya Zhang[1,2*]

Correspondence to Prof. Ya Zhang: maryzhangya@gmail.com

1.Department of Hematology, Shandong Provincial Hospital Affiliated to Shandong First Medical University, Jinan, Shandong, 250021, China.
2.Department of Hematology, Shandong Provincial Hospital, Shandong University, Jinan, Shandong, 250021, China.

Introduction

● Chronic lymphocytic leukemia (CLL) is characterized by immune dysfunction and potentially reprogrammed in fatty acid metabolism (FAM).

● However, it is currently unclear how FAM regulates immune function in CLL.

Methods

● Differential expression analysis was performed on RNA sequencing data from 180 CLL patients and 32 healthy controls, and FAM-related genes were identified.

● The *FAM-score* was constructed in the training cohort of 487 CLL patients by Cox-LASSO regression analyses and validated in the independent cohort of 195 CLL patients.

Results

Figure 1

● The present study identified 864 DEGs between CLL patients and healthy donors, of which 34 genes were related to FAM (|logFC| < 1.2, $p < 0.05$; Figure 1A, B).

Figure 2

● Through Cox-LASSO regression analysis, 3 genes(LPL, SOCS3, CNR1) with independent prognostic significance were selected to construct the FAM associated risk score named *FAM-Score* (Figure 2A).

● The ROC analysis showed better specificity and sensitivity of FAM-Score (AUC = 0.738, $p < 0.001$) than Binet stage (AUC = 0.527, $p = 0.487$; Figure 2B).

● The Kaplan–Meier curves suggested a significant association between high-risk subgroup and undesirable overall survival in both the training set and the independent validation set ($p < 0.001$, Figure 2C; $p = 0.006$, Figure 2D).

Figure 3

● The immune infiltrates between two subgroups showed significant differences in T cells, NK cells, and macrophages, suggesting the impact of FAM on CLL immunophenotype (Figure 3).

Conclusions

● The *FAM-score* predicts the survival outcomes of CLL patients and distinguishes CLL patients with different immunophenotypes effectively.

● The FAM reprogramming is an integral part of shaping individual immune characteristics in CLL.