A Novel 10-genes Ferroptosis-Related Prognostic Signature in Acute Myeloid Leukemia

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Abstract

Acute myeloid leukemia (AML) is one of the most common hematopoietic malignancies and exhibits a high rate of relapse and unfavorable outcomes. Ferroptosis, a relatively recently described type of cell death, has been reported to be involved in cancer development. However, the prognostic value of ferroptosis-related genes (FRGs) in AML remains unclear. In this study, we found 54 differentially expressed ferroptosis-related genes (DEFRGs) between AML and normal marrow tissues. Eighteen of these 54 DEFGRs were correlated with overall survival (OS) ($P < 0.05$). Using the least absolute shrinkage and selection operator (LASSO) Cox regression analysis, we selected 10 DEFGRs that were associated with OS to build a prognostic signature. Data from AML patients from the International Cancer Genome Consortium (ICGC) cohort were used for validation. Notably, the prognostic survival analyses of this signature passed with a significant margin, and the risk score was identified as an independent prognostic marker using Cox regression analyses. Further studies showed that AML was significantly associated with immune cell infiltration. In addition, drug-sensitive analysis showed that 8 drugs may be beneficial for treatment of AML and we used our own data (FAHWMU cohort) as a clinical validation. In conclusion, our study establishes a novel 10-gene prognostic risk signature based on ferroptosis related genes for AML patients and additionally we provide evidence that FRGs may be novel therapeutic targets for AML.

Introduction

Acute myeloid leukemia (AML) is characterized by a heterogeneity of molecular abnormalities and the accumulation of immature myeloid progenitors in the bone marrow and peripheral blood and represents the most common type of acute leukemia in adults (1, 2). Despite novel treatment options over the last years, the 5-year survival rate of AML patient remains unsatisfactory (3). Between 40 and 70% of AML patients relapse and become treatment-refractory, ultimately leading to treatment failure and even death. Therefore, there is an urgent need to develop novel prognostic biomarkers to monitor the prognosis of AML patients.

Ferroptosis is an iron-dependent form of regulated cell death driven by a lethal increase of lipid peroxidation (4, 5). It has been shown to play a key role for the suppression of tumorigenesis by removing the cells deficient in key nutrients in the environment or damaged by infection or ambient stress (6). Targeting ferroptosis is considered as a promising way for cancer patients, especially for malignancies that are resistant to traditional treatments (7, 8). However, the role of ferroptosis-related genes (FRGs) in the prognosis of AML remains unclear.

In this study, we constructed a ten ferroptosis-related differentially expressed genes (FRDEGs) prognostic signature based on the transcriptomic and clinical data of AML patients from The Cancer Genome Atlas

(TCGA) and Genotype-Tissue Expression Project (GTEx). Then the 10 FRDEGs prognostic signature was validated with the transcriptomic and clinical data of AML patients from International Cancer Genome Consortium (ICGC). Using functional enrichment analysis and correlation analysis, we further explored the potential molecular mechanisms involved in our signature. Finally, we performed a drug sensitivity analysis to explore potential gene targets.

Materials And Methods

Data collection

The RNA sequencing (RNA-seq) and clinical data of two AML cohorts were downloaded from public database, including 151 tumor samples of AML patients from TCGA (<https://portal.gdc.cancer.gov>) and 92 tumor samples of AML patients from ICGC (<https://dcc.icgc.org/projects/LIRI-JP>). Besides, RNA-seq data of 70 normal marrow samples were obtained from GTEx (<https://www.genome.gov/>). All the expression data from the three databases were normalized using the perl, respectively. The current research follows the TCGA and ICGC data access policies and publication guidelines. A total of 60 FRGs utilized in this study were obtained from the previous literature (Supplementary Table 1) (7).

In addition, we collected 57 tumor sample of AML patients from the First Affiliated Hospital of Wenzhou Medical University (FAHWMU) as validation data.

Construction of a prognostic 10-gene signature

The "limma" R package was used to identify the DEGs between tumor samples from TCGA and normal samples from GTEx with a false discovery rate (FDR) < 0.05. Moreover, with the help of the "limma" R package, we identified 60 FRGs of prognostic value and calculated their FDR using the Benjamin-Hochberg (BH) method. Protein-Protein Interaction Networks (PPI) and correlation networks of the intersecting 18 genes were generated using the STRING database ([STRING: functional protein association networks \(string-db.org\)](https://string-db.org)). Least absolute shrinkage and selection operator (LASSO) Cox regression was performed using the "glmnet" R package. The independent variable in the regression was the normalized expression matrix of candidate prognostic differentially expressed genes, and the response variables were overall survival (OS) and status of patients in the TCGA cohort. The optimum penalty parameter (λ) for the model was determined by tenfold cross-validation following the minimum criteria (i.e. the value of λ corresponding to the lowest partial likelihood deviance). The risk scores of the patients were calculated according to the normalized expression level of each gene and its corresponding regression coefficients. The formula was established as follows:

$$\text{score} = e^{\sum (\text{expression level of each gene} \times \text{corresponding coefficient})}$$

Patients were stratified into high- or low-risk groups based on the median value of their risk score. Patients in the ICGC were also stratified into a high- and low-risk group based on values derived from this formula.

Validation of a prognostic 10-gene signature

Based on the expression levels of genes in the signature, we carried out Principal Component Analysis (PCA) using the "prcomp" function of the "stats" R package. Besides, t-distributed Stochastic Neighbor Embedding (t-SNE) was performed to explore the clustering of different groups using the "Rtsne" R package. Univariate and multivariate Cox regression analyses were used to identify independent prognostic factors. Receiver Operating Characteristic (ROC) curve analysis was used to predict overall survival with the R package "pROC". All statistical analyses were carried out using the R software, with $P \leq 0.05$ being considered statistically significant.

Functional enrichment, correlation, and drug-fast analysis

The "clusterProfiler" R package was utilized to conduct Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) analyses based on DEGs ($|\log_2FC| \geq 1$, $FDR < 0.05$) between the high- and low- group from TCGA cohort. P values were adjusted using the BH method. Moreover, we estimated the infiltration score of 16 immune cell types and the activity of 13 immune-related pathways using single-sample gene set enrichment analysis (ssGSEA) in the "gsva" R package. Besides, based on the Expression data (ESTIMATE) algorithm, we estimated the proportion of infiltrating immune cells and stromal cells to get immune, stromal and ESTIMATE score for every AML patient. Using CIBERSOFT algorithm, the relative content score of 22 TICs in every AML patient was calculated. CIBERSOFT is a gene-based deconvolution algorithm that infers 22 human tumor immune infiltrating cell types and quantifies (9). the Cancer Stem Cell (CSC) correlation analysis and tumor microenvironment correlation analysis were conducted using the "limma" and "estimate" R packages. We obtained candidate drugs from the TCGA database and calculated drug sensitivity using the "limma" and "impute" R packages.

Results

Flow chart and clinical data

The flow chart of this study is shown in **Figure 1**. Data from a total of 151 AML tumor samples from the TCGA cohort and 92 ICGC tumor samples derived from AML patients were used. Detailed clinical characteristics of patients are summarized in Table 1.

Identification of prognostic 18 FRDEGs in the TCGA cohort

We found that the majority of FRGs were differentially expressed between TCGA tumor samples and GTEx normal samples (54/60, 90%). Eighteen of these FRDEGs (presented in the Venn diagram in **Figure 2B, C**) were associated with OS in univariate Cox regression analysis ($p < 0.05$, **Figure 2A**). Using PPI network construction, we identified that SLC7A11, G6PD, GPX4, HMOX1, and FTH1 represented be the hub genes (**Figure 2D**). A correlation analysis is shown in **Figure 2E**.

Ten FRDEGs were selected and 10-gene signature was constructed in the TCGA cohort

The above mentioned 18 prognostic FRDEGs were further filtered using *LASSO Cox regression analysis*, which resulted in 10 genes for further analysis (**Supplementary Figure A, B**). A risk score was calculated using mRNA expression levels and relevant coefficients of these 10 genes with the following formula:

$$\text{Risk score} = (-0.548 * CD44) + (0.371 * CHAC1) + (0.629 * CISD1) + (0.399 * DPP4) + (-0.849 * NCOA4) + (0.299 * SAT1) + (0.485 * SLC7A11) + (0.280 * AIFM2) + (1.391 * G6PD) + (0.955 * ACSF2).$$

Survival analyses of the 10-gene signature in TCGA, ICGC and FAHWMU cohort

Patients in the TCGA, ICGC or FAHWMU cohort were then divided into a high- or low-risk group according to the median cut-off value. The results of Kaplan-Meier curve indicated that patients in the low-risk group exhibited a significantly better OS than those in the high-risk group in TCGA (**Figure 3A**, $P < 0.001$), ICGC (**Figure 3C**, $p < 0.001$) and FAHWMU cohort (**Figure 3E**, $P < 0.05$). The predictive performance of the risk score for OS was evaluated by time-dependent ROC curves. In the TCGA cohort, the area under the curve (AUC) reached 0.841 in year 1, 0.811 in year 2, and 0.849 in year 3 (**Figure 3B**). In the ICGC cohort, the AUC was 0.634 in year 1, 0.680 in year 2, and 0.678 in year 3 (**Figure 3D**). However, the survival time of patients in FAHWMU cohort did not reached 3 years, and only one patient's survival time reached 2 years, so the AUC of 10-genes signature in FAHWMU cohort was 0.772 in one year and 1.0 in two years (**Figure 3F**). The t-SNE and PCA plots, mapped based on the risk score of each patient, was showed in **Figure 4A, B** of TCGA cohort, **Figure 4C, D** of ICGC cohort and **Figure 4E, F** of FAHWMU cohort. The red point in Figure 4A, B, C, D means patient in high-risk group, while blue point means patient in low-risk group. It can be found that the red points clustered in one part, while the blue points clustered in another part. This outcome suggested that our 10-genes signature may help get better prognosis prediction of AML patients, which could be all found in TCGA, ICGC and FAHWMU cohort.

Identification of independent prognostic value

Univariate and multivariate Cox regression analyses were carried out among the available variables to determine whether the risk score was an independent prognostic predictor for OS. In TCGA cohort, the risk score was significantly associated with OS in both the univariate Cox regression analyses (HR = 3.563, 95% CI = 2.513-5.051, $P < 0.001$) (**Figure 5A**) and multivariate Cox regression analyses (HR = 3.517, 95% CI = 2.420-5.112, $P < 0.001$) (**Figure 5B**). Similar results including both univariate Cox regression analyses (HR = 2.136, 95% CI = 1.370-3.330, $P < 0.001$) (**Figure 5C**) and multivariate Cox regression analyses (HR = 1.969, 95% CI = 1.250-3.100, $P = 0.003$) (**Figure 5D**) were also found in the ICGC cohort. Except for the risk score, age is another character that was identified as the independent prognostic factors ($P < 0.05$)

GO and KEGG analysis of DEGs in high- and low-risk group

GO analysis (**Figure 6B**) showed that DEGs were significantly involved in the biological processes of extracellular structure (matrix, external side of plasma membrane collagen, cell-cell adhesion), the cellular components that occur in cytoplasmic lumen and some immune-related function (leukocyte chemotaxis, leukocyte chemotaxis, immune receptor, cytokine). The pathways of the KEGG database (**Figure 6C**) indicated that DEGs highly expressed in high-risk group were significantly involved in the immune and stromal related-pathway (phagosome, chemokine, viral protein interaction with cytokine and cytokine receptor, ECM-receptor interaction), whereas the DEGs down-regulated in the low-risk group were significantly involved in signaling pathways like hematopoietic cell lineage and B cell receptor. This outcome of GO and KEGG revealed that the DEGs may play a significant role in the prognosis and immune-related response in AML patients.

Immune infiltration was significant related with the risk score of 10-genes signature

The scatter plots are used to explore the association between the tumor microenvironment and the risk score. As showed in **Supplementary Figure C**, the immune score is significantly positive correlated with risk score ($p < 0.0001$; $R = 0.43$, $R > 0$ means positive correlation. The closer is R to 1.0, the more significant the correlation is), and in **Supplementary Figure D**, the scatter plot showed that the stromal score and risk score are also positive correlated, but the correlation is not such remarkable compared to the immune score ($p = 0.03$; $R = 0.19$). Besides, the outcome of GSEA analysis (**Figure 6A**) indicated that the top 10 most significant pathways of EDGs between high- and low-risk group are largely involved in the biological processes of immune response (antigen processing and presentation, B cell receptor signaling pathway, chemokine signaling pathway, cytokine-cytokine receptor interaction, Fc gamma r mediated phagocytosis, natural killer cell mediated cytotoxicity, NOD-like receptor signaling pathway, T cell receptor signaling pathway, Toll like receptor signaling pathway). Therefore, we further explored the correlation of 18 immune-related cell and the risk score in 10-genes signature with CIBERSOFT algorithm. In **Figure 7A**, 8 types of immune-related cells (naive B cells, Plasma cells, T cells CD4 memory, NK cells, Monocytes, Dendritic cells, Mast cells and Eosinophils) are correlated with immune score ($p < 0.05$). Among the 8 types

of immune-related cells, only 3 types of cells (T cells CD4 memory, Monocytes and Mast cells) have the positive correlation of cell level or cell activity with high score of immune score, while the other 5 types of cells are negatively correlated. Then 4 types of cells (B cells memory, Monocytes, T cells CD4 memory, Mast cells, $p < 0.05$) were selected with the correlation analysis between high- and low-risk group (Figure 7B-E). The expression of Monocytes in the high-risk group is higher than the low-risk group, and the expression level of B cell memory has no significant difference in the high- and low-risk group, while the expression of T cells CD4 memory and Mast cells are lower than low-risk group. This data indicated that the immune infiltration is significantly related with the risk score of 10-genes signature

AML patients with high risk-score may be sensitive to 8 drugs

Drug sensitivity analysis is used to identify potential drugs that AML patients may be sensitive or resistant when the expression of genes in 10-genes signature are upregulated. As showed in **Figure 8**, the top 16 drugs are ranked by p-value ($p < 0.05$), only ARRY-162, Cobimetinib, Mitomycin and Irofulven have a positive correlation with the expression level of genes (SAT1, G6PD; the calculation coefficient of them in 10-genes signature is positive) in 10-genes signature. Although 4 drugs (Tamoxifen, Oxaliplatin, Fulvestrant and Imatinib) are negatively correlated with the expression level of CD44, the calculation coefficient of CD44 in 10-genes signature is negative, so the patients in the high-risk group may be sensitive to the 4 drugs. Thus, 8 drugs (ARRY-162, Cobimetinib, Mitomycin, Irofulven, Tamoxifen, Oxaliplatin, Fulvestrant and Imatinib) were selected and AML patients with high risk-score may be sensitive to them.

Discussion

AML patients have benefited from advances in targeted molecular and immunotherapy (10, 11), but the 5-year survival rate of AML patients remains unsatisfactory due to high relapse rates. Stratification of patients into high- and low-risk groups based on reliable molecular signatures may aid in selecting appropriate treatment strategies in line with precision medicine. Many studies have reported a vital role of FRGs in tumorigenesis (12-14). However, the relationship between AML prognosis and FRGs remains unclear. In this study, we established a novel ferroptosis-related prognostic gene signature for AML patients. We assessed the relationship of 60 FRGs in AML tumor samples with OS and identified 18 FRDEGs which were differentially expressed in AML tissue compared with normal controls. Using LASSO Cox regression, we selected ten of these 18 FRDEGs for construction of a prognostic gene signature. We also compared enrichment score of infiltration of immune cells and immune pathways between high- and low-risk patients, investigated functional mechanisms using GSEA, and assessed potentially suitable drugs. This novel 10-gene signature may contribute to the improvement in the prediction of AML prognosis and patient stratification for therapeutic strategies.

The FRGs (CD44, CHAC1, CISD1, DPP4, NCOA4, SAT1, SLC7A11, AIFM2, G6PD, and ACSF2) are included in our 10-gene signature. CD44 is a cell-surface glycoprotein involved in cell-cell interactions, cell adhesion, and migration (15). Previously, it has been demonstrated that CD44 expression is closely related with the occurrence of tumors, including AML (16-18). Stevens et al. found that CHAC1 contributes to the inhibition of AML via atovaquone (19). Genetic inhibition of CISD1 results in iron accumulation and subsequent oxidative injury in mitochondria, thus contributing to erastin-induced ferroptosis in HCC cells (20). In B-cell acute lymphoblastic leukemia, CHAC1 can overcome drug resistance and exert anti-leukemic activity (21). Loss of TP53 prevents nuclear accumulation of DPP4 and thus facilitates plasma-membrane-associated DPP4-dependent lipid peroxidation, resulting in ferroptosis (22). CARS1 has been included in a novel prognostic signature by Chen et al., which effectively predicts the prognosis of Clear Cell Renal Cell Carcinoma (23). Activation of SAT1 induces lipid peroxidation and sensitizes cells to undergo ferroptosis upon reactive oxygen species (ROS)-induced stress (24). Genetic inactivation of SLC7A11 has a synergistic effect with APR-246 for the promotion of cell death. G6PD has previously been proposed as a biomarker for AML (25). EBF3 acts as a tumor suppressor gene in AML, and AIFM2 is related to it (26). ACSF2 participates in the regulation of the lipid metabolism via peroxisome proliferator-activated receptor alpha. Recently, Wang et al. constructed a FRG signature for breast cancer patients, which included ACSF2 (27). All the 10 genes are significantly related to ferroptosis process and the prognosis of tumor, especially AML. Over a half of the genes included in our signature (CD44, CHAC1, SLC7A11, AIFM2, G6PD, CISD1) were previously investigated in AML, whereas the other four FRGs have not previously studied in this context.

Recently, immune infiltration has been reported to be involved in the progression of AML. For example, Luca et al. found that the bone marrow immune environment of AML patients is profoundly altered (28). Jian et al. also found a higher level of B and T cell activation in AML samples than non-tumor samples (29). NK cell can trigger the anti-leukemia responses (30) and ferroptosis has been shown to exert anti-tumor immune effects by triggering dendritic cell maturation (31). Therefore, we explored the association between immune cell infiltration and the risk score in this study. Our data revealed that the high-risk group is related to a larger expression of Monocytes. And Mika T et al found that the high expression of Monocytes is related to the failure of the first induction therapy in AML (32), which indicated that AML patients in the high-risk group with larger expression of Monocytes may be related to the decreased overall survival. Besides, it has been found that differentiated monocyte-like AML cells expressed diverse immunomodulatory genes and suppressed T cell activity in vitro (33). In this case, the high-risk group with lower level of T cells CD4 memory might associated with the higher counting of differentiated monocyte-like AML cells, which may be the one of reasons involved in the bad prognosis of high-risk group. In addition, the high-risk group showed enrichment in many pathways including immune-related biological processes, such as antigen processing and presentation, B and T cell receptor signaling pathway, and NK cell mediated phagocytosis. Besides, in our tumor microenvironment correlation analysis, the risk score was positively associated with the immune score. Our findings revealed an association between the 10-gene signature and immune cell infiltration.

In the past few decades, targeted cancer therapies have advanced rapidly. However, treatment of AML remains unsatisfactory (34). In this study, we performed a drug sensitivity analysis to find AML drugs that may have clinical benefits. We selected 8 drugs (ARRY-162, Cobimetinib, Mitomycin, Irofulven, Tamoxifen, Oxaliplatin, Fulvestrant and Imatinib) that AML patients with high risk-score may be sensitive to. Among them, ARRY-162, Cobimetinib, Mitomycin, Irofulven, Tamoxifen and Oxaliplatin have already been reported to have some studies in AML like clinical trials or just researches in cell (35-40). Imatinib has been authorized to treat chronic myeloid leukemia (CML) since 2001 (41). Only Fulvestrant has no reported study in AML. Though some of the above drugs are still under study or not investigated, our study of association between drug sensitivity and risk-score of 10-gene signature might indicate some therapeutic markers for further validation.

Recently, several studies of risk signature of AML have been established based on FRGs (42-44). However, our study still has many advantages. Firstly, we first report a novel ten FRGs prognostic risk signature for AML based on the data from TCGA and ICGC cohort. Secondly, we validated this 10-gene signature with clinical data (FAHWMU cohort). Thirdly, this signature revealed an association between FRGs and immune cell infiltration in AML. Finally, we found 8 drugs with potential have clinical advantages for AML treatment in the future. However, there are many limitations in our research. A single hallmark (ferroptosis) was used to construct a prognostic model, which may lead to the loss of many key prognostic genes of AML. In addition, the detailed roles of FRGs in AML should be further explored in the future.

Conclusion

In summary, our study establishes a novel prognostic risk signature of ten ferroptosis-related genes for AML patients. The prognostic risk signature proved superior compared to the other common prognostic factors. In addition, FRGs may represent novel therapeutic targets in AML.

Declarations

Data Availability

The source data of this study were derived from the public repositories, as indicated in the section of “Materials and Methods” of the manuscript. And all data that support the

findings of this study are available from the corresponding author upon reasonable request.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Author contributions

KZ, ZL and YZ conceived the project and wrote the manuscript. QT, ZY, BZ, YG, CW, and KY participated in data analysis. SJ and YS participated in discussion and language editing. All authors contributed to the article and approved the submitted version.

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Ethics statement

The studies involving human participants were reviewed and approved by the Human Research Ethics Committee in The First Affiliated Hospital of Wenzhou Medical University. The patients/participants provided their written informed consent to participate in this study. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Supplementary Materials

Table S1: 60 FRGs utilized in this study that were obtained from the previous literature.

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Tables

	TCGA cohort	ICGC cohort
No.of patients	130	92
Age (median,range)	56(21-88)	62(18-88)
Gender (%)		
male	70	49
Female	60	43
Stage (%)		
M0	12(9.2%)	NA
M1	30(23%)	NA
M2	32(24.6)	NA
M3	14(10.8%)	NA
M4	27(20.8)	NA
M5	12(9.2%)	NA
M6	2	NA
M7	1	NA
Survival status (%)		
Alive	52(40%)	0
Dead	78(60%)	93(100%)
Survival time (median)	364 days	303 days

Table 1. Clinical characteristics of AML patients used in this study

Figures

Figure 1

Flow chart of the data collection and analysis.

Figure 2

Identification of prognostic ferroptosis-related DEGs in the TCGA cohort. (A) Heat map of the 54 DEGs (T: tumor sample; N: normal sample). **(B)** Forest plots showing the results of the univariate cox regression analysis between gene expression and OS ($p < 0.05$). **(C)** Venn diagram to identify DEGs between tumor

and normal tissue that were correlated with OS. **(D)** The PPI network constructed using the STRING database illustrated interactions among the 18 DEFRGs genes. **(E)** The correlation network of the 18 DEFRGs genes. Different colors represent the correlation coefficients

Figure 3

Identification of ten optimal FRGs. **(A)** Kaplan-Meier curves for the OS of patients in the high-risk group and low-risk group in the TCGA cohort. **(B)** AUC of time-dependent ROC curves verified the prognostic performance of the risk score in the TCGA cohort **(C)** Kaplan-Meier curves in the ICGC cohort. **(D)** AUC of time-dependent ROC curves in the ICGC cohort. **(E)** Kaplan-Meier curves in the FAHWMU cohort. **(F)** AUC of time-dependent ROC curves in the FAHWMU cohort.

Figure 4

PCA and t-SNE analysis. **(A, B)** tSNE (A) and PCA (B) dimension reduction analysis of the high- and low-risk group based on the riskscore in TCGA cohort. **(C, D)** tSNE (C) and PCA (D) dimension reduction analysis of the high- and low-risk group based on the riskscore in ICGA cohort. **(E, F)** tSNE (E) and PCA (F) dimension reduction analysis of the high- and low-risk group based on the riskscore in FAHWMU cohort. (high: high-risk group; low: low-risk group)

Figure 5

Independent prognostic value of the 10-gene signature. Forest plots of univariate cox regression analyses **(A)** and multivariate cox regression analyses **(B)** containing clinical feature and riskscore in TCGA cohort. Forest plots of univariate cox regression analyses **(C)** and multivariate cox regression analyses **(D)** containing clinical feature and riskscore in the ICGC cohort.

Figure 6

Functional analysis of the 10-gene signature. **(A)** The GSEA plot of top ten enriched pathways of DEGs between high- and low-risk groups. **(B)** Gene Ontology (GO) enrichment analysis of DEGs between high- and low- groups ($p < 0.05$, $q < 0.05$; BP: biological process; CC: cellular component; MF: molecular function). **(C)** Kyoto Encyclopedia of Genes and Genomes (KEGG) enrichment analysis of DEGs between high- and low- groups ($p < 0.05$, $q < 0.05$).

Figure 7

Analysis of tumor microenvironment in 10-gene signature.

(A) Correlation plots of 18 immune-related cells (derived from CIBERSOFT algorithms), stromal scores and immune score (derived from ESTIMATE algorithms) in AML (red: positive correlation; blue: negative correlation; $p < 0.05$). (B-E) violin diagram of 4 immune-related cells (B cells memory, Monocytes, T cells CD4 memory, Mast cells) that differently expressed in high- and low-risk group ($p < 0.05$).

(F, G) Scatter plot of correlations between tumor mutational burden (TMB) value and the risk score in the 10-gene signature (with the immune score in F; with the stromal score in G).

Figure 8

Drug sensitivity analysis of the 10-gene signature. (Cor > 0 means patients with high expression of this gene may be sensitive to this drug; Cor < 0 means patients with high expression of this gene may be resistant to this drug. $P < 0.05$)

Supplementary Files

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