Expression, Prognosis, and Functional Analysis: *KDM5B* in Acute Myeloid Leukaemia (Non-M3)

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ABSTRACT

Objective: To investigate the value of Lysine Demethylase 5B (*KDM5B*) in the prognosis and immunity of acute myeloid leukaemia (AML).

Study Design: A case-control study.

Place and Duration of the Study: Department of Haematology, The First Affiliated Hospital of Guangxi Medical University, Nanning, Guangxi, China, from 2013 to 2024.

Methodology: Bioinformatic methods were used to compare the expression of *KDM5B* between 135 individuals with AML and 70 individuals without AML in the TCGA database. In order to confirm the findings, bone marrow specimens underwent real-time polymerase chain reaction analysis by the Mann-Whitney U test. A comprehensive assessment was conducted to explore the interplay among *KDM5B* expression levels, clinical profiles, and the overall survival prognosis in AML patients. Furthermore, the underlying mechanism of *KDM5B* in AML pathogenesis was delved into utilising GSEA. To assess the impact of *KDM5B* expression on the immune landscape within tumours, the ESTIMATE and CIBERSORT computational methodologies were employed to evaluate its role in tumour immune infiltration.

Results: *KDM5B* expression was notably increased in AML patients and linked to a poor prognosis. *KDM5B* expression was correlated with NPM1 mutation in bone marrow samples. Additionally, high *KDM5B* expression was a poor prognostic factor for overall survival. GSEA showed that high *KDM5B* expression was related to the immune system. Analysis of immune infiltration revealed a correlation between elevated *KDM5B* expression and decreased stromal and immune scores, accompanied by altered infiltration patterns of diverse immune cell types. Furthermore, immune checkpoint markers were correlated with low *KDM5B* expression.

Conclusion: *KDM5B* is highly expressed in AML and correlates with poor prognosis. *KDM5B* may be involved in AML by affecting the tumour micro-environment, thus being a potential biological target in AML.

Key Words: *KDM5B, Acute myeloid leukaemia, Immune infiltration, Prognostic factor.*

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INTRODUCTION

Acute myeloid leukaemia (AML) is a vastly heterogeneous malignancy, distinguished by its multifaceted prognosis outcomes.[1] AML has a high incidence among adults particularly older people, reaching 4 per 100,000 population; the incidence rises with age.[2] Advancements in diagnostic methodologies and therapeutic strategies have led to notable improvements in the survival rates among AML patients. Nevertheless, the prognosis for elderly individuals remains bleak. Therefore, elucidating the underlying mechanisms that drive AML progression will facilitate a more nuanced evaluation of disease risk and the selection of tailored therapeutic approaches commensurate with the risk profile.

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Numerous molecular targets and signalling pathways have received extensive attention in the field of AML pathogenesis and therapeutic research. *KDM5B*, a vital constituent of the histone demethylase superfamily, is distinguished by its JmjC domain. This enzyme encodes a protein capable of demethylating histone H3 lysine 4 residues (H3K4),[3] thereby influencing transcriptional repression. Research reports indicate that *KDM5B* is expressed highly in tumours and contributes significantly to tumour progression of hepatocellular carcinoma,[4] prostate cancer,[5] and lung cancer.[6] In addition, *KDM5B* is associated with poorer OS and is a prognostic biomarker.[7] Recently, Shokri *et al*. have found that *KDM5A/5B* knockdown resulted in reduced HL-60 cell viability, in addition to altered cell cycle distribution and sub-G1 accumulation, apoptosis induction was observed in both knockdown cells of AML as well.[8] Huang *et al*. showed that *KDM5B* is highly expressed in clinical AML samples and demonstrated that silencing *KDM5B* induces apoptosis in primary human AML cells *via* the miR-140-3p/BCL2 axis.[9] However, *KDM5B* has also been reported to suppress anti-proliferative and tumour-suppressor genes in AML. *KDM5B*, a direct target of *EZH2*, has been reported to act as a negative regulator by altering *H3K4me3* of key

genes associated with leukaemia stem cell maintenance in MLL-rearranged AML.[10,11] These controversial results were the impetus for further investigation into the functional role of *KDM5B* in AML.

On the other hand, it has been found that *KDM5B* can be used as a highly druggable target in breast cancer.[12] The use of epigenetic modulators such as demethylating agents can significantly increase the remission rate and improve the prognosis of AML patients. In a phase II trial, relapsed/refractory AML patients achieved encouraging results from PD-1 inhibitors and azacitidine.[13] This suggests that the combination of epigenetic modulators and immunotherapy has a promising future in AML. The aim of this study was to explore the expression of *KDM5B* in adult AML and the relationship between the expression level of *KDM5B* and prognosis. To further investigate the mechanism of *KDM5B* in adult AML, the role of *KDM5B* in the tumour micro-environment was investigated using biosignature analysis, thereby providing a strategy for therapeutic intervention in AML.

METHODOLOGY

The standardised pan-cancer dataset was sourced from the UCSC database. RNA-seq data for 135 non-M3 AML samples were retrieved from TCGA-LAML project, while data for 70 healthy individuals were obtained from the GTEx database. For verification, a case-control study was designed. The bone marrow specimens of 72 adult AML patients and 30 healthy individuals were collected between 2013 and 2021 from the Department of Haematology, The First Affiliated Hospital of Guangxi Medical University, Guangxi, China.

AML inclusion criteria were initially diagnosed as non-M3 AML and with no prior chemotherapy. Patients with a combination of other malignancies, myeloproliferative neoplasms transformed into AML, or treatment-related AML were excluded. Inclusion criteria for healthy individuals were those without abnormal haematology and bone marrow (BM) morphology and no major infectious diseases. In both groups, routine BM punctures were conducted and approximately 4 ml of BM was extracted. Regular telephone follow-ups were conducted from August 2013 to May 2024. The treatment protocol of the patients in this study strictly followed the NCCN Guidelines for the diagnosis and treatment of AML. All participants provided signed-knowledgeable permission, conforming to the Declaration of Helsinki.

To isolate bone marrow mono-nuclear cells, a density gradient centrifugation process employing a lymphocyte separation medium (Solaibao, China) was employed. Subsequently, Trizol reagent (Invitrogen, USA) was introduced to the samples. The primer sequences designed for *KDM5B* were: Forward primer 5'-AATAGAACCCGAGGAGACAACG-3' and reverse primer 5'-GACAGACATACAGGTCCACAGCA-3'. β-actin was utilised as an internal control, with the forward primer 5'-TGCGCCAATCAGCTACTTCT-3' and reverse primer 5'-TCAGGATTAAGCTCTGCAGCTA-3'. The relative expression of *KDM5B* was quantified utilising the comparative $2^{-\Delta\Delta ct}$ method.

Cell lines originating from leukaemia, including THP-1, MOLM-13, MV4-11, and SKM-1, as well as normal bone marrow stromal HS-5 cells, were acquired from the Guangxi Medical University in Guangxi, China. The Kaplan-Meier plotter database was utilised, incorporating GSE12417 (GPL97 and GPL570, n = 242) and GSE1159 (GPL96, n = 260). The area under the curve (AUC) for *KDM5B* expression was assessed using receiver operator characteristic analysis. Statistical analyses were performed using SPSS (version 26.0; SPSS Inc., Chicago, IL, USA) and GraphPad Prism software (version 9.5.0; Inc., La Jolla, CA, USA). The Kolmogorov-Smirnov test and the Shapiro-Wilk's test were used to test the normality of the data. Normal data were compared by the parametric t-test or the Mann-Whitney U-test, Pearson's Chi-square test, and Fisher's exact probabilities. Proportional hazard analysis was performed using the Xiantao tool available from https://www.xiantaozi.com/ in conjunction with the survival and rms R packages. Cox-regression was used to evaluate *KDM5B* expression along with clinical factors for predicting AML patients' overall survival. Statistically significant clinicopathological variables ($p < 0.05$) from the univariate analysis were subsequently subjected to multivariate analysis.

Using the clusterProfiler feature within the Xiantao platform, AML patients from GSE12417 (GPL97, n = 163) dataset were stratified into low and high *KDM5B* expression groups, with the median expression serving as the cut-off point. Subsequently, enrichment analysis was performed against the MSigDB library, with statistical significance ($p < 0.05$) and FDR of <0.25. Employing the R (version 4.4.1)/Estimate package, based on the *KDM5B* expression signature in the AML micro-environment, the scores were systematically calculated for TCGA-LAML (non-M3). Additionally, the CIBERSORT algorithm was utilised to quantify the presence of 22 distinct immune cell subtypes. A subsequent analysis employed the Wilcoxon rank-sum test to contrast immune cell enrichment scores between *KDM5B* high and low expression cohorts. Additionally, Spearman's correlation analysis elucidated the link between *KDM5B* expression and a spectrum of immune cell types.[14,15] A panel of 47 immune checkpoint-related genes, previously identified through research, was analysed for differential expression patterns.[16] Finally, the findings were presented using the ggplot2 package.

RESULTS

Using bioinformatic methods, the expression of *KDM5B* was analysed in pan-cancers. In comparison with healthy individuals, *KDM5B* was proved to be significantly differentially expressed in 28 types of tumours ($p < 0.001$, Figure 1A). Upon contrasting the TCGA and GTEx databases, a notable upregulation of *KDM5B* expression was observed in AML patients, as compared to healthy subjects ($p < 0.001$, Figure 1B). Utilising RT-PCR, a substantial elevation in *KDM5B* mRNA levels was demonstrated among AML patients, relative to the control group ($p < 0.001$, Figure 1C). Notably, the expression pattern of *KDM5B* across various risk strata of AML patients diverged significantly from that of healthy individuals ($p < 0.001$, Figure 1D). When *KDM5B* expression was examined in normal human bone marrow stromal cells and diverse leukaemia cell lines *via* qPCR, it was found that AML-derived THP - 1 cells exhibited significantly higher *KDM5B* expression than other cell lines ($p < 0.001$, Figure 1E).

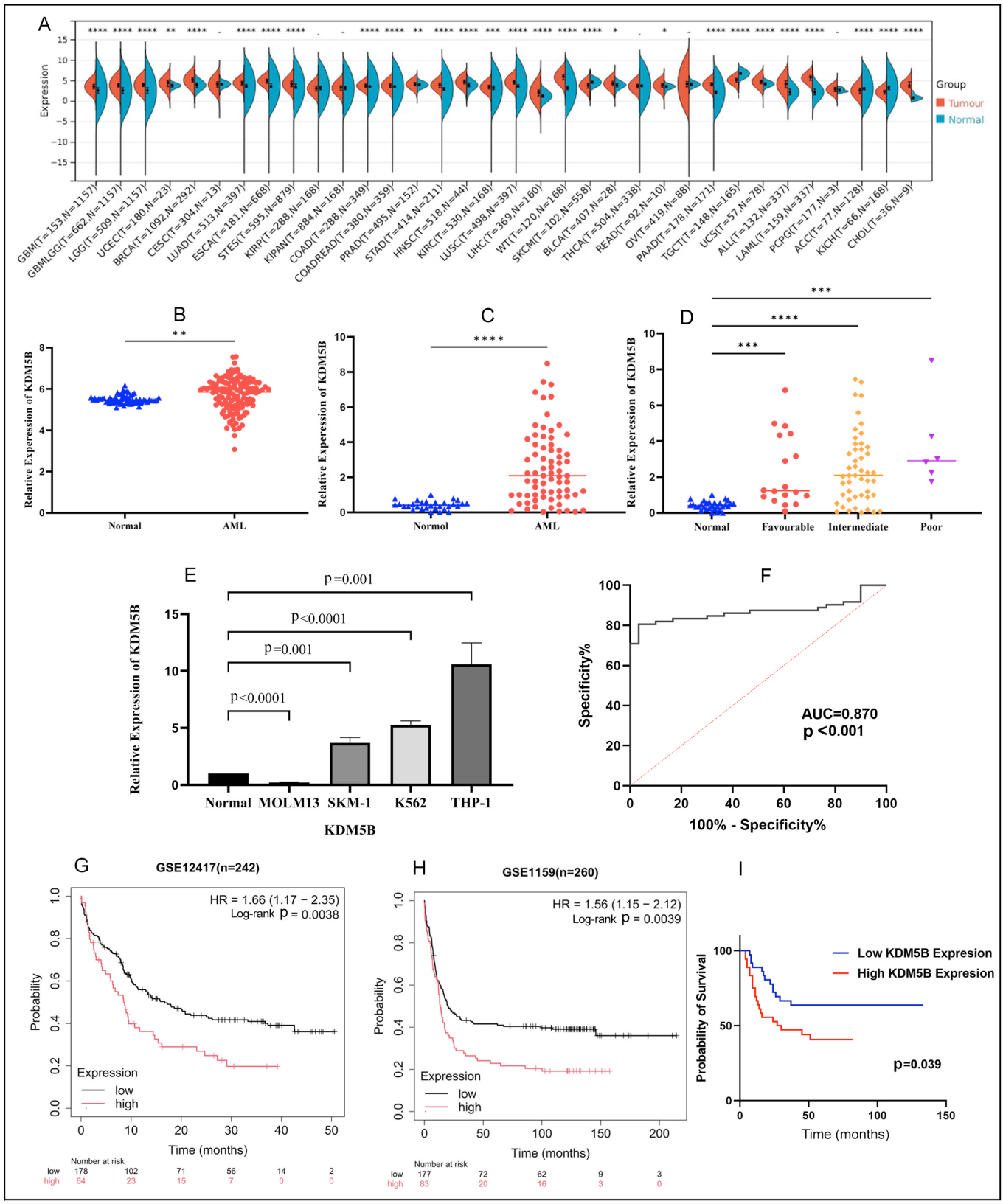

Figure 1: Expression of *KDM5B* in pan-cancers and AML. (A) Expression of *KDM5B* in pan-cancers. (B) Comparison of *KDM5B* expression in normal GTEx database and primary AML of TCGA. (C) Comparison of *KDM5B* expression levels in BM samples. (D) Relationship between *KDM5B* expression level and prognostic risk stratification. (E) The expression of *KDM5B* in different leukaemia cell lines. (F) ROC analysis of the diagnostic effect of *KDM5B* on AML. (G, H) Kaplan-Meier survival curves for AML patients of GSE12417 and GSE1159. (I) Kaplan-Meier survival curves for AML patients which were divided into two groups based on the median value of *KDM5B* expression level. *p <0.05, **p <0.01, ***p <0.001, ****p <0.0001, respectively.

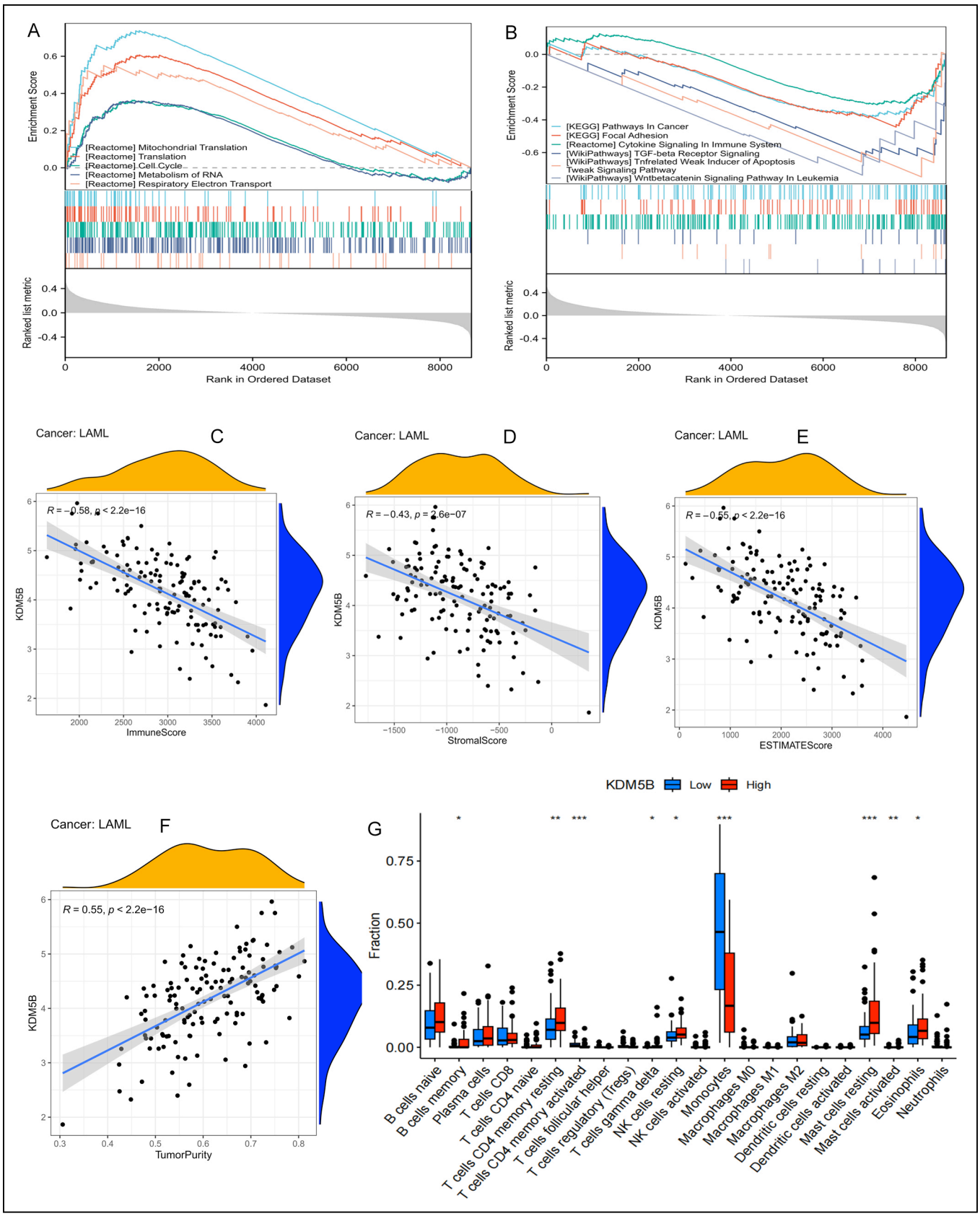

Figure 2: (A) GSEA of samples with high expression of *KDM5B*. (B) GSEA of samples with low expression of KDM5B. (C) Correlation between the expression of *KDM5B* and immune score. (D) Correlation between the expression of KDM5B and stromal score. (E) Correlation between the expression of *KDM5B* and estimate score. (F) Correlation between the expression of *KDM5B* and tumour purity. (G) Comparison of immune cell enrichment scores in high and low *KDM5B* expression groups. ∗p <0.05, ∗∗p <0.01, ∗∗∗p <0.001.

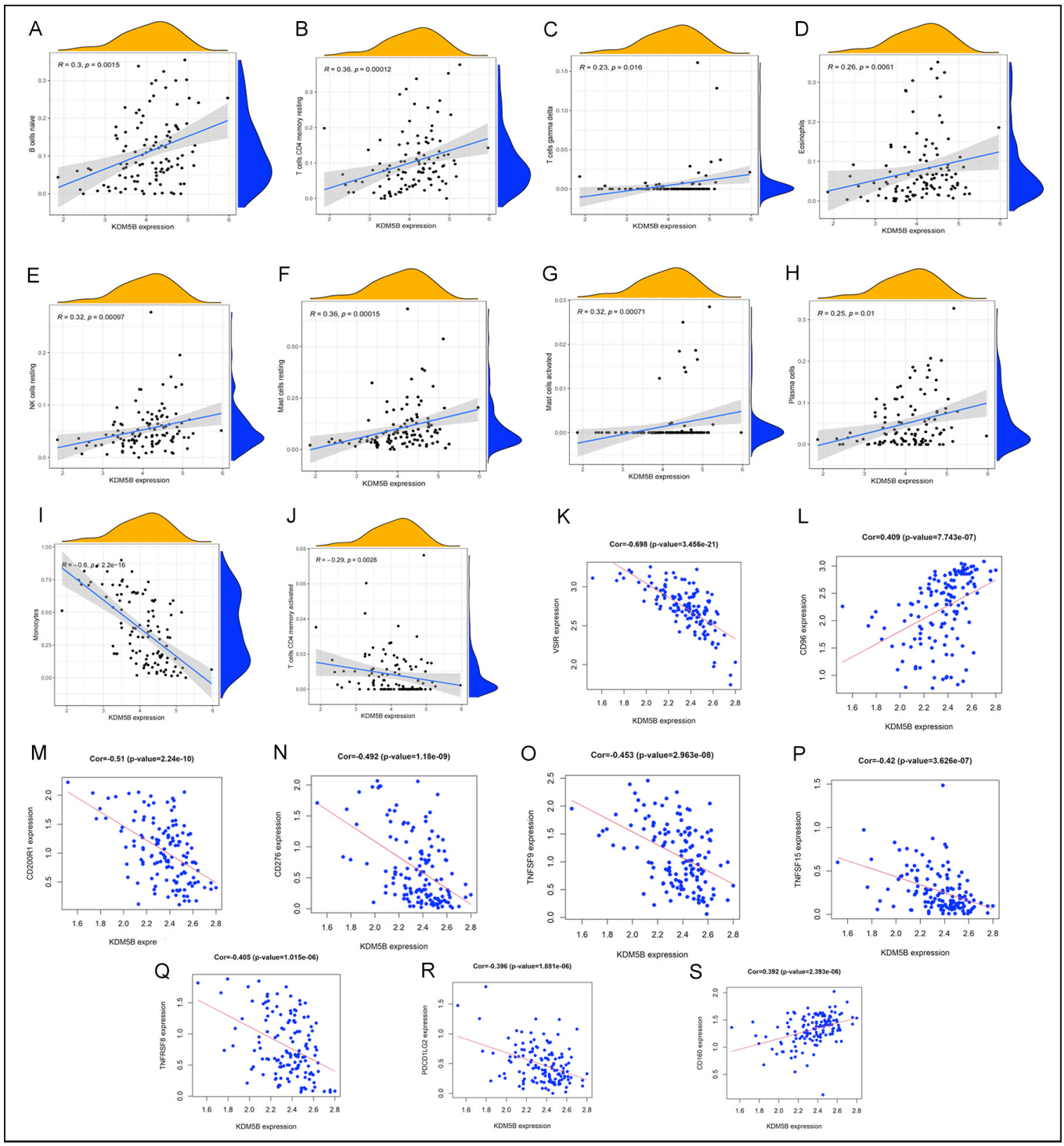

Figure 3: (A) The associations between *KDM5B* expression levels and the infiltration patterns of naive B cells (B) The associations between *KDM5B* expression levels and the infiltration patterns of resting CD4 memory T cells. (C) The associations between *KDM5B* expression levels and the infiltration patterns of gamma delta T cells. (D) The associations between *KDM5B* expression levels and the infiltration patterns of eosinophils. (E) The associations between *KDM5B* expression levels and the infiltration patterns of resting NK cells. (F) The associations between *KDM5B* expression levels and the infiltration patterns of resting mast cells. (G) The associations between *KDM5B* expression levels and the infiltration patterns of activated mast cells. (H) The associations between *KDM5B* expression levels and the infiltration patterns of plasma cells. (I) The associations between *KDM5B* expression levels and the infiltration patterns of monocytes. (J) The associations between *KDM5B* expression levels and the infiltration patterns of activated CD4 memory T cells. (K) The correlations between *KDM5B* expression and immune checkpoint of *VSIR*. (L) The correlations between *KDM5B* expression and immune checkpoint of *CD86*. (M) The correlations between *KDM5B* expression and immune checkpoint of *CD200R1*. (N) The correlations between *KDM5B* expression and immune checkpoint of *CD276*. (O) The correlations between *KDM5B* expression and immune checkpoint of *TNFSF9*. (P) The correlations between *KDM5B* expression and immune checkpoint of *TNFSF15*. (Q) The correlations between *KDM5B* expression and immune checkpoint of *TNFRSF8*. (R) The correlations between *KDM5B* expression and immune checkpoint of *PDCD1LG2*. (S) The correlations between *KDM5B* expression and immune checkpoint of *CD160*.

Table I: Comparison of clinical and molecular characteristics with KDM5B expression in BM samples.

Clinical characteristics	KDM5 Blow (n = 36)	KDM5B High (n = 36)	p-value	Method
Age, (years), median (IQR)	36.5 (29, 47)	31.5 (26,44)	0.203	Wilcoxon
Gender, n (%)			0.471	Chi-square test
Male	16 (22.2%)	13 (18.1%)		
Female	20 (27.8%)	23 (31.9%)		
Haemoglobin (g/L), mean ± sd.	77.8 ± 19.2	76.1 ± 18.4	0.818	T-test
Leucocyte (×109), median (IQR)	24.3 (9.2, 62.9)	14.1 (6.5, 56.0)	0.197	Wilcoxon
Platelet (×109), median (IQR)	34.2(18.2, 98.3)	41.0 (20.7,73.3)	0.964	Wilcoxon
BM blasts (%), median (IQR)	63.8 (33.5, 82.0)	66.3 (50.0, 75.2)	0.593	Wilcoxon
Cytogenetic abnormalities			0.458	Chi-square test
Normal	25(34.7%)	22(30.6%)		
Abnormal	11(15.3%)	14(34.7%)		
FAB classifications, n (%)			0.168	Fisher's exact probabilities
M1	1 (1.4%)	5 (6.9%)		
M2	11 (15.3%)	11 (15.3%)		
M4	10 (13.9%)	12 (16.7%)		
M5	14 (19.4%)	7 (9.7%)		
M6	0 (0%)	1 (1.4%)		
Cytogenetics risk, n (%)			0.191	Fisher's exact probabilities
Favourable	11 (15.3%)	7 (9.7%)		
Intermediate	24 (33.3%)	24 (33.3%)		
Poor	1 (1.4%)	5 (6.9%)		
IDH1/IDH2 mutation, n (%)			>0.99	Chi-square test
Mutation	4 (5.6%)	4 (5.6%)		
Wild type	32 (44.4%)	32 (44.4%)		
CEBPA mutation, n (%)			0.772	Chi-square test
Mutation	7 (9.7%)	8 (11.1%)		
Wild type	29 (40.3%)	28 (38.9%)		
NPM1 mutation, n (%)			0.011	Chi-square test
Mutation	10 (13.9%)	2 (2.8%)		
Wild type	26 (36.1%)	34 (47.2%)		
FLT3 mutation, n (%)			0.571	Chi-square test
Mutation	9 (12.5%)	7 (9.7%)		
Wild type	27 (37.5%)	29 (40.3%)		
DNMT3 mutation, n (%)			0.326	Chi-square test
Mutation	7 (9.7%)	4 (5.6%)		
Wild type	29 (40.3%)	32 (44.4%)		
WTI mutation, n (%)			0.437	Chi-square test
Mutation	12 (16.7%)	9 (12.5%)		
Wild type	24 (33.3%)	27 (37.5%)		
HSCT, n (%)			0.458	Chi-square test
Yes	25 (34.7)	22 (30.6)		
No	11(15.3)	14 (19.4)		
Complete remission, n (%)			0.339	Chi-square test
Yes	13 (18.1)	17 (23.6)		
No	23 (31.9)	19 (26.4)		

These results suggested that *KDM5B* acts as an oncogene in AML. Additionally, the area under the curve (AUC) for distinguishing AML from normal conditions was 0.870, with a 95% confidence interval (CI) ranging from 0.800 to 0.940 ($p < 0.001$, Figure 1F), indicating the potential of *KDM5B* as a diagnostic biomarker for AML.

The correlation between the expression of *KDM5B* and clinical features is shown in Table I. The clinical features of AML patients were derived from 72 BM samples, which were categorised into high and low *KDM5B* expression groups based on median expression levels, each comprising 36 individuals. The expression level of *KDM5B* is negatively correlated with the NPM1 mutation ($p = 0.011$, Table I). However, clinical parameters such as gender, age, haemoglobin, peripheral blood leucocyte count, platelets, FAB typing, *etc*. were not significantly different between the two groups. To assess the prognostic implications of *KDM5B* expression, survival analyses were conducted utilising the GSE12417 and GSE1159 datasets, demonstrating that patients with high *KDM5B* expression exhibited shorter survival durations ($p < 0.005$, Figure 1G, H). This finding was corroborated by plotting survival curves for the 72 patients, which confirmed a notably lower overall survival (OS) rate in the high *KDM5B* expression group compared to the low expression group ($p = 0.039$, Figure 1I). To determine whether *KDM5B* is an independent dangerous element for the prognosis of AML patients, a Cox univariate analysis was performed, incorporating *KDM5B* expression alongside potential clinical predictors. This analysis identified high *KDM5B* expression, haematopoietic stem cell transplantation (HSCT), and complete remission as prognostic indicators for unfavourable OS (Table II).

Table II: Univariate and multivariate analysis of overall survival for AML patients.

Variables	Total (n)	Univariate analysis		Multivariate analysis	
		Hazard ratio (95% CI)	p-value for univariate analysis	Hazard ratio (95% CI)	p-value for multivariate analysis
KDM5B	72				
Low	36	Reference		Reference	
High	36	2.045 (1.023 - 4.089)	0.043	2.046 (1.018 - 4.114)	0.044
Gender	72				
Female	43	Reference			
Male	29	0.708 (0.345 - 1.453)	0.347		
Age	72				
>35	25	Reference			
≤34	47	1.414 (0.676 - 2.958)	0.358		
Leucocyte	72				
>20	34	Reference			
≤20	38	1.191 (0.605 - 2.345)	0.613		
Haemoglobin	72				
>60	55	Reference			
≤60	17	0.919 (0.416 - 2.031)	0.834		
Platelet	72				
≤50	43	Reference			
>50	29	1.158 (0.588 - 2.280)	0.671		
BM blasts	72				
>50	40	Reference			
≤60	32	0.623 (0.311 - 1.247)	0.181		
IDH1/IDH2	72				
Wild	64	Reference			
Mutated	8	0.723 (0.221 - 2.366)	0.591		
CEBPA	72				
Wild	57	1.052 (0.458 - 2.418)	0.904		
Mutated	15	Reference			
NPM1	72				
Wild	60	Reference			
Mutated	12	0.588 (0.207 - 1.670)	0.319		
FLT3	72				
Wild	56	1.239 (0.512 - 2.996)	0.635		
Mutated	16	Reference			
DNMT3	72				
Wild	61	Reference			
Mutated	11	0.756 (0.266 - 2.147)	0.600		
WTI	72				
Wild	51	2.257 (0.933 – 5.458)	0.071		
Mutated	21	Reference			
HSCT	72				
No	42	Reference		Reference	
Yes	30	0.379 (0.177 - 0.814)	0.013	0.634 (0.282 - 1.429)	0.272
Complete remission	72				
No	44	Reference		Reference	
Yes	28	9.428 (4.182 - 21.254)	<0.001	7.929 (3.391 - 18.537)	<0.001

Subsequent multivariate Cox-regression analysis showed that *KDM5B* expression levels (p = 0.044, Table II) and complete remission (p <0.001, Table II) were reliable predictors for OS. Consequently, these findings underscore the crucial role of *KDM5B* in the prognosis and progression of AML.

To further explore the function of *KDM5B*, gene chip expression data from patients with non-M3 AML (GSE12417, n = 163) and GSEA analyses were performed between high and low *KDM5B* expression groups to identify core signalling mechanisms in AML. Within the group featuring high *KDM5B* expression, significant enrichment was observed in mitochondrial translation, general translation processes, cell cycle regulation, RNA metabolism, and respiratory electron transport chains. Conversely, the low *KDM5B* expression group predominantly displayed enrichment in immune and oncogenic pathways, encompassing cancer biology, focal adhesion, cytokine signalling within the immune system, TGF-β receptor signalling cascades, TNF-related weak inducer of apoptosis (TWEAK) signalling, and *Wnt-β-catenin* signalling pathways implicated in leukaemia as depicted in Figure 2 (A, B). These findings prompted an investigation of the role of *KDM5B* in immunity against AML.

The complex interaction between *KDM5B* expression and the tumour micro-environment (TME) within the context of AML was investigated to elucidate its role in modulating the tumour's immune response, as per previous studies.[17] Analysis revealed a negative correlation between *KDM5B* expression and immunity scores (p <0.001, Figure 2C), stromal scores (p <0.001, Figure 2D), and estimated scores (p

<0.001, Figure 2E) in AML patients, while positively correlated with tumour purity (p <0.001, Figure 2F). This suggests that elevated *KDM5B* expression corresponds to reduced immune infiltration. To quantify the specific immune cell subsets involved, the CIBERSORT algorithm was applied, revealing significant enrichment of multiple immune cell types in the high *KDM5B* expression group (Figure 2G), particularly naive B cells, resting CD4 memory T cells, gamma delta T cells, eosinophils, resting NK cells, resting and activated mast cells, and plasma cells. Conversely, *KDM5B* upregulation inversely correlated with monocytes and activated CD4 memory T cells (Figure 3A-J). These findings suggest that *KDM5B* influences patient survival through interaction with immune infiltration in AML. To gain further insights into the immunomodulatory role of *KDM5B*, its relationship with 47 immune checkpoints was investigated. Notably, *KDM5B* expression inversely correlated with the majority of immunomodulatory genes (Figure 3K-S), including *VSIR, CD86, CD200R1, CD276, TNFSF9, TNFSF15, TNFRSF8, PDCD1LG2,* and *CD160*. This implies that lower *KDM5B* expression levels may be associated with higher expression of immune checkpoint markers, suggesting patients with reduced *KDM5B* expression may exhibit a more favourable response to anti-cancer immunotherapy.

DISCUSSION

The current treatments for AML are based on chemotherapy and HSCT, which has greatly improved the survival rate, but relapses and drug resistance are still a difficulty in therapy.[18] The pathogenic mechanisms of AML are not completely elucidated. Immune escape is considered an important element that affects long-term disease-free survival and relapses in AML patients.[19] The prevention or reversal of immunological evasion to improve the remedial outcome of AML and reduce recurrence is a goal for researchers. It has been reported that inhibition of *KDM5B* can promote the expression of *STING* and promote the recognition and killing of mouse pancreatic cancer cells by CD8 T cells, thereby improving anti-tumour activity and regulating the immune micro-environment.[20]

This study examined the level of *KDM5B*, explored the prognostic significance and potential mechanism in AML using the TCGA dataset and collected samples. The results revealed that *KDM5B* expression was significantly increased in individuals afflicted with AML and was correlated with diminished OS, suggesting that *KDM5B* acts as an oncogene. Multivariate analysis indicated that *KDM5B* expression could be a reliable predictor of OS, which indicated that *KDM5B* potentially exerts a crucial influence on the survival time of AML. Furthermore, the authors analysed the biological functions of *KDM5B* by GSEA, and *KDM5B* expression was correlated with cytokine signalling in the immune system, cell cycle, and cancer pathway. This suggests that *KDM5B* may be an independent prognostic factor influencing tumorigenesis and tumour immunology in AML progression.

Recent studies have shown that the tumour micro-environment (TME) is crucial for tumour persistence in AML and that immune cell infiltration is a core component of TME.[21] To investigate the influence of *KDM5B* on the clinical outcome of AML, *KDM5B* expression was analysed in relation to the TME and the infiltration of immune cells. The analysis revealed that a higher degree of immune infiltration was observed in the group with low *KDM5B* expression. Additionally, a positive association was found to be exhibited between the elevated expression level of *KDM5B* and the majority of immune cell infiltration. Hence, it is hypothesised that an intricate interplay between immune infiltration and tumour cell immune evasion exists, having a regulatory influence on TME remodelling.

Immune checkpoints, defined as immunosuppressive molecules residing on immune cells, serve as regulators of immune activation levels.[22] Aberrant expression patterns of these molecules constitute a pivotal factor in the onset of tumours. The tumour cells exploit immune checkpoints as a means to evade immune surveillance, thereby facilitating their survival and proliferation. These findings indicate a robust correlation between *KDM5B* expression and the majority of immune checkpoints in AML. This suggests that *KDM5B* may exert its influence on AML progression by modulating the immune micro-environment, potentially contributing to the disease's immune evasion mechanisms.

Epigenetics is often defined as the reversible chemical modifications of DNA and histones that regulate chromatin accessibility and transcription without altering the DNA sequence.[23] Some epigenetic regulatory elements and modifications play direct roles in the immune pathway. It has been reported that *KDM5B* mediates tumour immune escape by recruiting *SETDB1* to silence reverse transcriptional elements. The knockout of *KDM5B* cannot only inhibit the proliferation of melanoma cells but also enhance their sensitivity to immune checkpoint inhibitors.[24] With the in-depth study of epigenetics in AML, an increasing number of epigenetic medicines have been used for treatment and have shown good applicability. The combined inhibition of enhancer of Zeste Homolog 2 and lysine-specific demethylase 1 has a synergistic effect on the treatment of AML, mainly by affecting mitochondrial respiratory capacity and glycolytic activity, leading to depletion of adenosine triphosphate.[25] Therefore, targeting *KDM5B* may provide new ideas for the development of combined tumour immunity and antitumour drugs for AML.

The study first determined the prognostic value of *KDM5B* in AML patients, providing a novel biomarker for the prognostic assessment of AML patients. Secondly, the relationship between *KDM5B* expression and immune cell infiltration was elucidated by bioinformatic analysis, which deepens the understanding of the AML tumour micro-environment and immune-regulatory mechanisms and provides a potential theoretical basis for combining immunotherapy with other therapies. However, for a heterogeneous disorder, the sample size of this study is relatively small. The sample will be

further expanded for verification to make the results more reliable. Furthermore, the pathways related to the role of *KDM5B* in AML have not been further confirmed and will continue to be explored *in-vitro* and *in-vivo*.

CONCLUSION

The present investigation unveils that *KDM5B* expression is augmented in AML patients, and notably, elevated *KDM5B* levels correlate with unfavourable overall survival outcomes. *KDM5B* expression was associated with tumour immunity for AML and may be a prognostic indicator affecting tumorigenesis and tumour immunology during the progression of AML.

ETHICAL APPROVAL:

The Human Ethics Committee of The First Affiliated Hospital of Guangxi Medical University, Guangxi, China approved this study (Approval No: 2024-E537-01).

PATIENTS' CONSENT:

All patients provided written informed consent.

COMPETING INTEREST:

The authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:

NL, XH, XL, QL, YX: Drafting of the work.
NL, XH, XL, YX: Acquisition and analysis of the data.
NL, ZL: Concept of the idea and design of the work.
All authors approved the final version of the manuscript to be published.

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