Overexpression of lncRNA ITGB2-AS1 Predicts Adverse Prognosis in Acute Myeloid Leukemia

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Research

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Abstract

Background

In recent years, lncRNA *ITGB2-AS1* has been found to play important roles in the occurrence and development of human solid tumors. However, its role in hematological diseases, especially acute myeloid leukemia (AML), remains unclear. Therefore, the aim of this study was to identify the expression pattern of *ITGB2-AS1* in AML patients and to further explore its clinical significance.

Methods

*ITGB2-AS1* expression was analyzed in public datasets (including TCGA and GSE63270) and further validated in our cohort of 109 AML patients using real-time quantitative PCR (RQ-PCR).

Results

The level of *ITGB2-AS1* was up-regulated among two independent cohorts (TCGA, *P*<0.05; GSE63270, *P*<0.05), which was confirmed by our own data (*P*<0.05). Clinically, high *ITGB2-AS1* expression was associated with older age (*P*=0.023) and lower complete remission (CR) rate (*P*=0.005). Multivariate analysis identified that high *ITGB2-AS1* expression was an independent prognostic factor not only for CR rate (*P*=0.027) but also for overall survival (OS) time (*P*=0.011). *ITGB2-AS1* was found positively correlated with *ITGB2* expression in both TCGA (R=0.74, *P*<0.001) and our own data (R=0.881, *P*<0.001). Similarly, high *ITGB2* expression was associated with older age (*P*=0.02) and lower CR rate (*P*=0.015). Moreover, high *ITGB2* expression also predicted worse OS (*P*=0.028).

Conclusion

*ITGB2-AS1* is overexpressed in AML and predicts poor prognosis in AML.

1. Introduction

Acute myeloid leukemia (AML) is a highly heterogeneous disease in cytogenetics and molecular biology, which is characterized by poor differentiation and uncontrolled proliferation of immature myeloid progenitor cells [1]. At present, genetic abnormalities such as chromosomal aberrations and gene mutations are considered as the most powerful prognostic information [2]. However, AML patients with moderate cytogenetic risk perform differently in terms of chemotherapy consolidation, which means that more new markers involved in leukemogenesis and molecular stratification need to be further improved in order to better classify risks and ultimately find better treatments [3].

With the application of next-generation sequencing technology, thousands of LncRNA have been discovered in many solid tumors. Recent evidence suggests that these LncRNAs play a crucial role in gene regulation, thereby affecting various aspects of cell homeostasis, including proliferation, survival, migration, or genome stability [4]. LncRNA *ITGB2-AS1*, up-regulated in pancreatic cancer, breast cancer,
osteosarcoma, and ovarian cancer, plays an important role in promoting the proliferation, invasion, migration and metastasis of cancer cells, and is associated with poor prognosis [5-10]. ITGB2, as a gene on the ITGB2-AS1 complementary chain, has also been found to be involved in tumor adhesion, invasion, angiogenesis and specific immune response [11]. In addition, beta 2-integrin-derived signaling has been revealed to induce survival and proliferation of neonatal AML cells by activating the Syk/STAT signaling axis [12]. However, the expression and clinical significance of ITGB2-AS1 and ITGB2 remain unknown in AML. Herein, this study was aimed to explore the expression pattern and clinical impact of ITGB2-AS1 and ITGB2 in the context of known molecular prognosticators in AML, and found that ITGB2-AS1 can serve as a biomarker for prognosis prediction.

2. Materials And Methods

2.1 Patients and samples

To analyze the prognostic impact of ITGB2-AS1 in AML patients, three independent cohorts with survival information were included in this study: (1) TCGA datasets from GEPIA (http://gepia.cancer-pku.cn/detail.php), OncoLnc (http://www.oncolnc.org) and cBioPortal (http://www.cbioportal.org/); (2) The validation cohort consisted of 62 AML patients and 42 normal controls (GSE63270). Detailed information of the two cohorts are described in Additional Methods. (3) An independent cohort of 109 AML patients enrolled and treated in the People's Hospital affiliated to Jiangsu University from 2005 to 2016. All participants provided informed consents, and the study was approved by the Institutional Review Board of the Affiliated People's Hospital of Jiangsu University. BM mononuclear cells (BMMNCs) were isolated using lymphocyte separation medium (Beijing Solarbio Science & Technology Co., Ltd., Beijing, China).

2.2 RNA isolation and reverse transcription

Total RNA was extracted from BMNC using Trizol reagent (Invitrogen Life Technologies, USA) as described previously [13-17]. 2 ug of total RNA were reverse transcribed into cDNA using 10 umol/l random primers, 200 U MMLV reverse transcriptase, 0.5 mmol/l dNTP, 10 mmol/l dithiothreitol, and 25 U RNase inhibitors.

2.3 RT-qPCR

ITGB2-AS1 expression was detected by real-time quantitative PCR (RT-qPCR) using AceQ qPCR SYBR Green Master Mix (Vazyme Biotech Co., Piscataway, NJ, USA) on a 7500 Thermo cycler (Applied Biosystems, CA). PCR primers were designed using Primer Premier 6 (Premier Biosoft, Palo Alto, CA, USA). The primers for ITGB2-AS1 expression were 5′- TTGCTGTCAAAGCATGCCAC -3′ (forward) and 5′-AAGGCAGCCCACACTTTTCT -3′ (reverse). The primers for ITGB2 expression were 5′-GATGACGGCTTCCATTTCGC -3′ (forward) and 5′-TGGGGATGATCTCGGTGAGT -3′ (reverse). Reaction conditions and PCR cycling were conducted as previously described [13-17] except for the optimized
primer annealing temperatures (60 °C). The relative quantification was calculated using the ΔΔCT method and normalized to the ABL1 housekeeping gene.

2.4 Karyotype and gene mutation detection

By conventional R-banding method, karyotype was analyzed at the time of initial diagnosis. Risk classification based on the karyotype findings has been done as previously described [13-17]. Mutations in C-KIT, NPM1, DNMT3A, N/K-RAS, and U2AF1 were detected by high-resolution melting analysis, whereas FLT3-ITD and CEBPA mutations were detected by direct DNA sequencing.

2.5 Statistical and bioinformatics analyses

SPSS software version 20.0 (IBM Corporation, Armonk, NY, USA) was used to carry out the statistical analysis. Receiver operating characteristic (ROC) curve and area under the ROC were applied to assess the value of ITGB2-AS1 and ITGB2's expression. Besides, Pearson's chi-squared analysis was conducted to determine the difference of categorical variables between ITGB2-AS1 high group and ITGB2-AS1 low group. Through Kaplan–Meier method and Cox regression analysis, the effect of ITGB2-AS1 expression on prognosis was analyzed. Logistic regression analysis was used to identify the independent risk factors on complete remission (CR). In all tests, \( P<0.05 \) was defined as statistically significant. R script was used for plotting gene volcano maps co-expressed with ITGB2-AS1. Details of bioinformatics and receiver operating characteristic (ROC) curve were shown in Additional Methods.

3. Results

3.1 Expression pattern of ITGB2-AS1 and ITGB2 in AML

By using the GEPIA data (http://gepia.cancer-pku.cn/detail.php), we found that the expression of ITGB2-AS1 was significantly increased in AML patients compared with normal BM samples (Fig. 1a, \( P<0.001 \)). A similar result was also found in another dataset (GSE63270; Fig. 1b, \( P<0.001 \)). In order to confirm the results, we further analyzed the expression of ITGB2-AS1 in our cohort of 109 AML patients and 31 controls. ITGB2-AS1 expression was consistently up-regulated in whole cohort AML, Non-M3-AML and CN-AML compared with controls (Fig. 1c; \( P<0.0003, =0.001, \) and \( <0.0001, \) respectively). Next, we identified the positive correlation between ITGB2-AS1 and 37 genes from 18107 genes using cBioPortal (Fig. 3a, \( R>0.7, P<0.05 \)). Among them, ITGB2 attracted our attention because of its special position on chromosome. We analyzed the expression of ITGB2 in the GSE63270 dataset (Figure. 2b, \( P<0.001 \)), the online website GEPIA (Fig. 2a, \( P<0.001 \)) as well as our cohorts (Fig. 2c, \( P=0.0009, =0.0014, \) and \( <0.0001, \) respectively), and found that ITGB2 was also upregulated in AML. Furthermore, the positive correlation was confirmed between ITGB2 and IGB2-AS1 expression in our cohort (Fig. 3b).

3.2 Association between ITGB2-AS1 expression and clinical characteristics
109 AML patients of our cohort were divided into two subgroups (ITGB2-AS1\textsuperscript{high} and ITGB2-AS1\textsuperscript{low}) according to the median level of ITGB2-AS1 transcript. The comparison of clinical/laboratory characteristics between the two subgroups was shown in Table1. No significant differences were observed in peripheral blood counts, BM blasts, FAB classification, cytogenetics, and common gene mutations ($P>0.05$). However, ITGB2-AS1\textsuperscript{high} patients were older than those ITGB2-AS1\textsuperscript{low} patients ($P=0.023$). Moreover, CR rate was significantly lower in ITGB2-AS1\textsuperscript{high} patients than in ITGB2-AS1\textsuperscript{low} patients ($P=0.005$).

3.3 Association between ITGB2 expression and clinical characteristics

The whole cohort of AML patients was also divided into two subgroups according to the median level of ITGB2 transcript (ITGB2\textsuperscript{high} and ITGB2\textsuperscript{low}) (Table2). Consistent with the results of ITGB2-AS1, significant differences in age and CR rate were also revealed between the two subgroups ($P=0.015$ and $=0.02$, respectively).

3.4 Effect of ITGB2-AS1 and ITGB2 expression on chemotherapy response in AML

Among our cohort, 88 patients had available follow-up data. We found that ITGB2-AS1\textsuperscript{high} patients had a lower CR rate ($P=0.005$, Table 1). Additionally, clinical characteristics in patients with and without CR were further compared. Significant differences were found in ITGB2-AS1 expression, age, WBCs, platelets, BM blast, and risk group ($P<0.05$, Table 3). However, there was no significant difference in the expression of ITGB2 in patients with and without CR ($P=0.065$, Table 3). Logistic regression analysis including the most predictive factors was further performed, which revealed that ITGB2-AS1 expression was an independent risk factor affecting CR in whole-cohort AML patients ($P=0.027$, Table4).

3.5 Association between ITGB2-AS1 expression and prognosis in AML patients

To further explore the prognostic relevance of ITGB2-AS1 expression, we investigated the correlation between ITGB2-AS1 expression and clinical outcomes in two independent AML cohorts. ITGB2-AS1\textsuperscript{high} patients in TCGA dataset had significantly reduced OS (Fig. 4a, $P=0.012$), which was validated in our cohort (Fig. 4b, 4c and 4d). Our data also demonstrated that ITGB2-AS1\textsuperscript{high} patients had significantly reduced LFS (Fig. 4e, $P=0.043$). Moreover, Cox regression analysis also confirmed that ITGB2-AS1 expression independently affected the OS ($P=0.019$, Table5; $P=0.026$, Table6) and leukemia-free survival (LFS) ($P=0.005$, Table7) in our cohort.

3.6 Association between ITGB2 expression and prognosis in AML patients

Similar results were shown in AML patient with ITGB2 over expression, though the high expression of ITGB2 was not an independent prognostic risk factor ($P=0.589$, Table5), it tended to indicate poor prognosis. By using the OncoLnc, we found that ITGB2\textsuperscript{high} patients in TCGA dataset had significantly reduced OS (Fig. 5a, $P<0.010$), which was confirmed in our whole patient cohort (Fig. 5b, $P=0.020$), but
not in non-M3 AML (Fig. 5c, \( P=0.106 \)) and CN-AML (Fig. 5d, \( P=0.094 \)). In addition, the expression of \textit{ITGB2} in AML patients had the trend affecting on LFS (Fig. 5e, \( P=0.078 \)).

4. Discussion

Over the past decades, the importance of non-coding RNA has received increasing attention [18]. Numerous studies have found that IncRNAs play important roles in the proliferation, differentiation and apoptosis of cells [19-23]. For example, the expression of \textit{PVT1} can induce apoptosis and necrosis of AML cells by downregulating the expression of c-Myc [24]. Recent studies have shown that IncRNA \textit{UCA1} and \textit{CRNDE} also play an important role in the proliferation and differentiation of AML cells [25, 26]. The study of Zhang et al. showed that \textit{HOTAIRM1} affects the differentiation and maturation of myeloid cells by regulating the expression level of the annexin gene, and downregulation of \textit{HOTAIRM1} expression will prevent all-trans retinoic acid (ATRA)-induced granulocyte differentiation [27]. Therefore, gaining insight into the role of IncRNA in AML may provide opportunities for early diagnosis and therapeutic targeting of AML.

The roles of \textit{ITGB2-AS1} in tumorigenesis has just been explored in a few solid tumors [5-10]. Initially, \textit{ITGB2-AS1} was found overexpressed while its promoter was highly methylated in pancreatic cancer [5]. At a similar time, Liu et al identified that \textit{ITGB2-AS1} is upregulated and associated with poor survival in breast cancer [6]. Their further studies disclosed that \textit{ITGB2-AS1} could induce \textit{ITGB2} expression in breast cancer cells and then promote the migration and invasion. Then, upregulation of \textit{ITGB2-AS1} and prognostic relevance was discovered in osteosarcoma, ovarian cancer and pancreatic cancer [7-9].

As far as we know, this is the first study on \textit{ITGB2-AS1} in leukemia. We found that and \textit{ITGB2-AS1} was significantly up-regulated in AML patients compared to controls. Moreover, we revealed that \textit{ITGB2-AS1} overexpression may have an adverse impact on chemotherapy response, which was confirmed by the lower CR rate. Furthermore, we also confirmed the adverse effect of \textit{ITGB2-AS1} overexpression on survival. All these results indicate that \textit{ITGB2-AS1} can add additional prognostic information by stratifying molecularly defined patients into more homogeneous groups and help to select better treatment strategies. Without doubt, prospective studies are needed to confirm the prognostic prediction of \textit{ITGB2-AS1} overexpression before it can be clinically used in AML.

Integrin family has been shown to be involved in leukemogenesis [28, 29]. Our previous studies disclosed the clinical relevance of two members of integrin family, \textit{ITGA2} and \textit{ITGBL1} [30, 31]. In this study, we demonstrated for the first time that \textit{ITGB2} is also overexpressed in AML patients. In addition, we also found the positive correlation between \textit{ITGA2-AS1} with \textit{ITGB2} in AML. The effects of \textit{ITGB2} overexpression on chemotherapy response and survival were found by univariate analysis, but not by multivariate analysis. More cases should be investigated to reveal the significance of \textit{ITGB2} aberration in AML. Further functional studies of \textit{ITGB2} and \textit{ITGB2-AS1} in leukemia are also needed.

In conclusion, our results indicate that \textit{ITGB2-AS1} is overexpressed in AML and is an independent poor prognostic factor in AML. Furthermore, \textit{ITGB2} expression is also upregulated in AML and is associated
with ITGB2-AS1 expression.

**Abbreviations**

IncRNA: long non-coding RNA  
AML: acute myeloid leukemia  
BM: bone marrow  
PB: peripheral blood  
OS: overall survival  
LFS: leukemia-free survival time  
CR: complete remission  
RT-qPCR: real-time quantitative PCR  
TCGA: The Cancer Genome Atlas  
BMMNCs: Bone Marrow Mononuclear Cells  
WBC: white blood cell  
CN: cytogenetically normal

**Declarations**

**Ethics approval and consent to participate**

The study was approved by the Clinical Research Ethics Committee of the Affiliated People’s Hospital of Jiangsu University.

**Consent for publication**

Written informed consent was obtained from all enrolled individuals before their participation.

**Availability of data and materials**

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

**Competing interests**
The authors declare that they have no competing interests.

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**Authors’ Contributions**

QJ and Y-l Z designed the study and wrote the paper; Y-l Z performed all experiments; Y-l Z and Z-j X analyzed the data; Z-j X, J-d Z, and T-j Z were involved in the delivery of the clinical data; J L, J-c M, J Q and D-m Y offered technique and language support. All authors read and approved the final manuscript.

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**References**

[1] Döhner H, Weisdorf DJ, Bloomfield CD. Acute Myeloid Leukemia. The New England journal of medicine. 2015;373:1136-52.

[2] Döhner H, Estey E, Grimwade D, Amadori S, Appelbaum FR, Büchner T, et al. Diagnosis and management of AML in adults: 2017 ELN recommendations from an international expert panel. Blood. 2017;129:424-47.

[3] Ley TJ, Miller C, Ding L, Raphael BJ, Mungall AJ, Robertson AG, et al. Genomic and epigenomic landscapes of adult de novo acute myeloid leukemia. The New England journal of medicine. 2013;368:2059-74.

[4] Huarte M. The emerging role of IncRNAs in cancer. Nature medicine. 2015;21:1253-61.

[5] Giulietti M, Righetti A, Principato G, Piva F. LncRNA co-expression network analysis reveals novel biomarkers for pancreatic cancer. Carcinogenesis. 2018;39:1016-25.

[6] Liu M, Gou L, Xia J, Wan Q, Jiang Y, Sun S, et al. LncRNA ITGB2-AS1 Could Promote the Migration and Invasion of Breast Cancer Cells through Up-Regulating ITGB2. Int J Mol Sci. 2018;19.

[7] Dai J, Xu LJ, Han GD, Jiang HT, Sun HL, Zhu GT, et al. Down-regulation of long non-coding RNA ITGB2-AS1 inhibits osteosarcoma proliferation and metastasis by repressing Wnt/beta-catenin signalling and predicts favourable prognosis. Artif Cells Nanomed Biotechnol. 2018;46:S783-S90.
[8] Li N, Zhan X. Identification of clinical trait-related IncRNA and mRNA biomarkers with weighted gene co-expression network analysis as useful tool for personalized medicine in ovarian cancer. The EPMA journal. 2019;10:273-90.

[9] Yang M, Qin Q, Zhu J, Guo Y, Yin T, Wu H, et al. Long noncoding RNA ITGB2-AS1 promotes growth and metastasis through miR-4319/RAF1 axis in pancreatic ductal adenocarcinoma. J Cell Physiol. 2020.

[10] Ghafouri-Fard S, Taherian-Esfahani Z, Dashti S, Kholghi Oskooei V, Taheri M, Samsami M. Gene expression of indoleamine and tryptophan dioxygenases and three long non-coding RNAs in breast cancer. Epma j. 2020;114:104415.

[11] Bednarczyk M, Stege H, Grabbe S, Bros M. β2 Integrins-Multi-Functional Leukocyte Receptors in Health and Disease. International journal of molecular sciences. 2020;21.

[12] Oellerich T, Oellerich MF, Engelke M, Münch S, Mohr S, Nimz M, et al. β2 integrin-derived signals induce cell survival and proliferation of AML blasts by activating a Syk/STAT signaling axis. Blood. 2013;121.

[13] Zhou J-D, Zhang T-J, Li X-X, Ma J-C, Guo H, Wen X-M, et al. Epigenetic dysregulation of ID4 predicts disease progression and treatment outcome in myeloid malignancies. Journal of cellular and molecular medicine. 2017;21:1468-81.

[14] Zhou J-D, Wang Y-X, Zhang T-J, Li X-X, Gu Y, Zhang W, et al. Identification and validation of SRY-box containing gene family member methylation as a prognostic and predictive biomarker in myeloid malignancies. Clinical epigenetics. 2018;10:92.

[15] Zhang T-J, Zhou J-D, Zhang W, Lin J, Ma J-C, Wen X-M, et al. overexpression promotes leukemogenesis and predicts unfavorable prognosis in acute myeloid leukemia. Clinical epigenetics. 2018;10:47.

[16] Xu Z-J, Ma J-C, Zhou J-D, Wen X-M, Yao D-M, Zhang W, et al. Reduced protocadherin17 expression in leukemia stem cells: the clinical and biological effect in acute myeloid leukemia. Journal of translational medicine. 2019;17:102.

[17] Sun G-K, Tang L-J, Zhou J-D, Xu Z-J, Yang L, Yuan Q, et al. DOK6 promoter methylation serves as a potential biomarker affecting prognosis in de novo acute myeloid leukemia. Cancer medicine. 2019;8:6393-402.

[18] Liu Y, Cheng Z, Pang Y, Cui L, Qian T, Quan L, et al. Role of microRNAs, circRNAs and long noncoding RNAs in acute myeloid leukemia. 2019;12:51.

[19] Yang L, Zhou J-D, Zhang T-J, Ma J-C, Xiao G-F, Chen Q, et al. Overexpression of IncRNA predicts adverse prognosis in acute myeloid leukemia. Cancer management and research. 2018;10:4999-5007.
[20] Liu Y, Cheng Z, Pang Y, Cui L, Qian T, Quan L, et al. Role of microRNAs, circRNAs and long noncoding RNAs in acute myeloid leukemia. Journal of hematology & oncology. 2019;12:51.

[21] Wang C-H, Li Q-Y, Nie L, Ma J, Yao C-J, Chen F-P. LncRNA ANRIL promotes cell proliferation, migration and invasion during acute myeloid leukemia pathogenesis via negatively regulating miR-34a. The international journal of biochemistry & cell biology. 2020;119:105666.

[22] Wang X, Yang J, Guo G, Feng R, Chen K, Liao Y, et al. Novel lncRNA-IUR suppresses Bcr-Abl-induced tumorigenesis through regulation of STAT5-CD71 pathway. Molecular cancer. 2019;18:84.

[23] Zhao C, Wang S, Zhao Y, Du F, Wang W, Lv P, et al. Long noncoding RNA NEAT1 modulates cell proliferation and apoptosis by regulating miR-23a-3p/SMC1A in acute myeloid leukemia. Journal of cellular physiology. 2019;234:6161-72.

[24] Zeng C, Yu X, Lai J, Yang L, Chen S, Li Y. Overexpression of the long non-coding RNA PVT1 is correlated with leukemic cell proliferation in acute promyelocytic leukemia. J Hematol Oncol. 2015;8:126.

[25] Hughes JM, Legnini I, Salvatori B, Masciarelli S, Marchioni M, Fazi F, et al. C/EBPα-p30 protein induces expression of the oncogenic long non-coding RNA UCA1 in acute myeloid leukemia. Oncotarget. 2015;6:18534-44.

[26] Wang Y, Zhou Q, Ma JJ. High expression of lnc-CRNDE presents as a biomarker for acute myeloid leukemia and promotes the malignant progression in acute myeloid leukemia cell line U937. Eur Rev Med Pharmacol Sci. 2018;22:763-70.

[27] Zhang X, Weissman SM, Newburger PE. Long intergenic non-coding RNA HOTAIRM1 regulates cell cycle progression during myeloid maturation in NB4 human promyelocytic leukemia cells. RNA Biol. 2014;11:777-87.

[28] Johansen S, Brenner AK, Bartaula-Brevik S, Reikvam H, Bruserud Ø. The Possible Importance of β3 Integrins for Leukemogenesis and Chemoresistance in Acute Myeloid Leukemia. Int J Mol Sci. 2018;19.

[29] Sison EAR, Kurre P, Kim YM. Understanding the bone marrow microenvironment in hematologic malignancies: A focus on chemokine, integrin, and extracellular vesicle signaling. Pediatr Hematol Oncol. 2017;34:365-78.

[30] Lian XY, Zhang W, Wu DH, Ma JC, Zhou JD, Zhang ZH, et al. Methylation-independent ITGA2 overexpression is associated with poor prognosis in de novo acute myeloid leukemia. 2018;233:9584-93.

[31] Lian XY, Ma JC, Zhou JD, Zhang TJ, Wu DH, Deng ZQ, et al. Hypermethylation of ITGBL1 is associated with poor prognosis in acute myeloid leukemia. 2019;234:9438-46.

Tables
Table 1. Association between *ITGB2-AS1* expression and clinical characteristics
| Patient's parameters | ITGB2-AS1 expression |  |
|----------------------|----------------------|---|
|                      | High (n=54)          | Low (n=55) | P-value  |
| sex, male/female     | 28/26                | 35/20      | 0.241    |
| Median age, years (range) | 58(20-84)          | 52(24-84)  | 0.023    |
| Median WBC, ×10^9/l (range) | 51.4(0.3-528)      | 34.4(0.3-207.9) | 0.239   |
| Median hemoglobin, g/l (range) | 80.70(49-135)       | 84.02(34-141) | 0.411    |
| Median platelets, ×10^9/l (range) | 58 (7-382)        | 52 (3-415)  | 0.328    |
| BM blasts, % (range)  | 46.6(1-97.5)        | 46.6(3-92) | 0.958    |
| Cytogenetics         |                      |           | 0.578    |
| Normal               | 30(55.6%)            | 25(45.5%)  |          |
| t(15,17)             | 9(16.7%)             | 9(16.4%)   |          |
| t(8,21)              | 1(1.9%)              | 6(10.9%)   |          |
| Inv(16)              | 1(1.9%)              | 0          |          |
| +8                   | 2(3.7%)              | 2(3.6%)    |          |
| -7/del(7)            | 1(1.9%)              | 0          |          |
| Others               | 4(7.4)               | 6(10.9)    |          |
| Complex              | 4(7.4%)              | 4(7.4%)    |          |
| No data              | 2(3.7%)              | 2(3.6%)    |          |
| FAB class classifications |                  |           | 0.152    |
| M0                   | 0                    | 1(1.8%)    |          |
| M1                   | 0                    | 1(1.8%)    |          |
| M2                   | 15(27.8%)            | 22(40.0%)  |          |
| M3                   | 10(18.5%)            | 10(18.2%)  |          |
| M4                   | 15(27.8%)            | 6(10.9%)   |          |
| M5                   | 5(9.3%)              | 6(10.9%)   |          |
| gene mutation        |                      |           |          |
| CEBPA (+/–)          | 4/35                 | 5/32       | 0.466    |
| NPM1 (+/–)           | 1/38                 | 4/33       | 0.194    |
| FLT3-ITD (+/–)       | 2/37                 | 5/32       | 0.256    |
| C-KIT (+/–)          | 1/38                 | 2/35       | 0.610    |
|                      | N/K-RAS (+/−) | IDH1/2 (+/−) | U2AF1 (+/−) | DNMT3A (+/−) | CR (−/+)|
|----------------------|--------------|-------------|-------------|--------------|---------------|
|                      | 3/29         | 1/38        | 1/38        | 2/37          | 27/17        |
|                      | 1/27         | 0/37        | 1/37        | 4/33          | 13/31        |
|                      | 0.616        | -           | 1.000       | 0.425         | 0.005        |

**Abbreviations:** BM, bone marrow; CR, complete remission; FAB, French-American-British; WBC, white blood cells.

**Table 2. Association between ITGB2 expression and clinical characteristics**
| Patient's parameters |  | ITGB2 expression |  |
|----------------------|----------------|------------------|---|
|                      | High (n=55)   | Low (n=54)       | P-value |
| Sex, male/female     | 28/27         | 35/19            | 0.176 |
| Median age, years (range) | 58 (20-84) | 51 (22-84)       | 0.015 |
| Median WBC, ×10 9/l (range) | 49.9 (0.3-528) | 35.0 (0.3-207.9) | 0.292 |
| Median hemoglobin, g/l (range) | 80 (49-135) | 85 (34-141)      | 0.105 |
| Median platelets, ×109/l (range) | 56 (4-383) | 52 (3-415)        | 0.355 |
| BM blasts, % (range) | 45.6 (1-97.5) | 46.6 (3-92)      | 0.457 |
| Cytogenetics         |               |                  | 0.092 |
| Normal               | 31 (56.4%)    | 24 (44.4%)       |       |
| t(15,17)             | 0             | 9 (16.7%)        |       |
| t(8,21)              | 2 (3.6%)      | 5 (9.3%)         |       |
| Inv(16)              | 1 (1.8%)      | 0                |       |
| +8                   | 2 (3.6%)      | 2 (3.7%)         |       |
| Others               | 4 (7.3%)      | 6 (11.1%)        |       |
| Complex              | 4 (7.3%)      | 4 (7.4%)         |       |
| No data              | 2 (3.6%)      | 2 (3.7%)         |       |
| FAB class classifications |        |                  | 0.160 |
| M0                   | 0             | 1 (1.9%)         |       |
| M1                   | 0             | 1 (1.9%)         |       |
| M2                   | 15 (27.3%)    | 22 (40.7%)       |       |
| M3                   | 10 (18.2%)    | 10 (18.5%)       |       |
| M4                   | 15 (27.3%)    | 6 (11.1%)        |       |
| M5                   | 5 (9.1%)      | 6 (11.1%)        |       |
| gene mutation        |               |                  |       |
| CEBPA (+/−)          | 5/35          | 4/32             | 1.00  |
| NPM1 (+/−)           | 1/39          | 4/32             | 0.184 |
| FLT3-ITD (+/−)       | 2/38          | 5/31             | 0.246 |
| C-KIT (+/−)          | 1/39          | 2/34             | 0.601 |
| Abbreviations: BM, bone marrow; CR, complete remission; FAB, French-American-British; WBC, white blood cells |

Table 3. Comparison of clinical manifestations and laboratory features between CR and non-CR in AML patients receiving induction therapy

|   |   |   |
|---|---|---|
| N/K-RAS (+/−) | 3/29 | 1/27 | 0.616 |
| IDH1/2 (+/−) | 1/39 | 0/36 | − |
| U2AF1 (+/−) | 1/39 | 1/36 | 1.00 |
| DNMT3A (+/−) | 2/38 | 4/32 | 0.414 |
| CR (−/+ | 19/26 | 29/14 | 0.02 |
| Patient's parameters | Complete remission |  |
|----------------------|--------------------|---|
|                      | Yes (n=48)         | No (n=40) | P-value |
| ITGB2-AS1 expression | 13.92(0.08-194.46) | 18.84(0.17-23.26) | 0.033 |
| ITGB2 expression     | 14.86(0.10-104.88) | 14.44(0.69-142.17) | 0.065 |
| sex, male/female     | 23/25              | 27/13     | 0.085 |
| Median age, years (range) | 50(24-78)       | 59(20-77) | 0.001 |
| Median WBC, ×10⁹/l (range) | 34.8(0.3-528)   | 59.2(0.4-207.5) | 0.001 |
| Median hemoglobin, g/l (range) | 83(34-135)       | 82(49-121) | 0.899 |
| Median platelets, ×10⁹/l (range) | 40(3-192)        | 64(9-415) | 0.018 |
| BM blasts, % (range) | 39.7(1-97.5)      | 52.2(6.5-92.0) | 0.032 |
| Cytogenetics         |                    |          | 0.034 |
| Normal               | 21(43.8%)          | 21(52.5%) |       |
| t(15,17)             | 13(27.1%)          | 3(7.5%)  |       |
| t(8,21)              | 7(14.6%)           | 0        |       |
| Inv(16)              | 0                  | 1(2.5%)  |       |
| +8                   | 1(2.1%)            | 2(5%)    |       |
| -7/del(7)            | 0                  | 1(2.5%)  |       |
| Others               | 2(4.2%)            | 4(10%)   |       |
| Complex              | 3(6.3%)            | 4(10%)   |       |
| No data              | 1(2.1%)            | 3(7.5%)  |       |
| FAB class classifications |                  |          | 0.034 |
| M0                   | 0                  | 1        |       |
| M1                   | 0                  | 1        |       |
| M2                   | 19                 | 16       |       |
| M3                   | 14                 | 4        |       |
| M4                   | 8                  | 13       |       |
| M5                   | 4                  | 5        |       |
| gene mutation        |                    |          |       |
| CEBPA (+/−)          | 4/27               | 5/32     | 1.000 |
| NPM1 (+/−)           | 2/29               | 2/35     | 1.000 |
FLT3-ITD (+/−) 3/28 3/34 1.000
DNMT3A (+/−) 3/28 3/34 1.000

AML, acute myeloid leukemia; BM, bone marrow; CR, complete remission; WBC, white blood cell.

**Table 4. Univariate and multivariate analyses of variables for complete remission in whole-cohort AML patients**

| Variables                  | CR | Univariate analysis | Multivariate analysis |
|----------------------------|----|---------------------|-----------------------|
|                            |    | OR (95% CI)         | P-Value               | OR (95% CI) | P-Value |
| Age                        |    | 0.195(0.076-0.497)  | 0.001                 | 0.337(0.121-0.939) | 0.037 |
| WBC                        |    | 0.994(0.987-1.002)  | 0.143                 | 0.638(0.209-1.952) | 0.431 |
| ITGB2-AS1 expression       |    | 0.264(0.109-0.641)  | 0.003                 | 0.330(0.123-0.880) | 0.027 |
| ITGB2 expression           |    | 0.353(0.148-0.842)  | 0.019                 | 492849290.2(0.000-) | 0.999 |
| Cytogenetic risk           |    | 0.387(0.194-0.770)  | 0.007                 | 0.464(0.220-0.978) | 0.043 |
| CEBPA mutation             |    | 1.055(0.257-4.324)  | 0.941                 | -            | -      |
| NPM1 mutation              |    | 0.829(0.110-6.251)  | 0.855                 | -            | -      |
| FLT3-ITD (+/−)             |    | 0.824(0.154-4.404)  | 0.820                 | -            | -      |
| DNMT3A (+/−)               |    | 0.824(0.154-4.404)  | 0.820                 | -            | -      |

**Notes:** Variables including WBC (≥30×109 vs 60 years), ITGB2-AS1 expression (low vs high), ITGB2 expression (low vs high), risk classification (favorable vs intermediate vs poor), and gene mutations (mutant vs wild type). Multivariate analysis includes variables with $P<0.200$.

AML, acute myeloid leukemia; CR, complete remission; OR, odds ratio; WBC, white blood cell.

**Table 5. Univariate and multivariate analyses of prognostic factors for overall survival in whole-AML patients**
## Table 6. Univariate and multivariate analyses of prognostic factors for overall survival in non-M3 AML patients

| Variables                  | OS                        | Univariate analysis | Multivariate analysis |
|---------------------------|---------------------------|---------------------|-----------------------|
|                           |                           | HR (95% CI)         | P-Value               | HR (95% CI)         | P-Value               |
| Age                       | 2.772(1.587-4.843)        | 0.000               | 0.923(0.366-2.325)    | 0.864               |
| WBC                       | 1.001(0.999-1.004)        | 0.217               | -                     | -                   |
| ITGB2-AS1 expression      | 2.121(1.326-3.391)        | 0.010               | 2.317(1.149-4.670)    | 0.019               |
| ITGB2 expression          | 1.861(1.076-3.218)        | 0.026               | 0.668(0.154-2.887)    | 0.589               |
| Cytogenetic risk          | 2.327(1.629-3.323)        | 0.000               | 2.229(1.429-3.475)    | 0.000               |
| CEBPA mutation            | 1.346(0.558-3.250)        | 0.508               | -                     | -                   |
| NPM1 mutation             | 1.101(0.338-3.591)        | 0.873               | -                     | -                   |
| FLT3-ITD (+/−)            | 0.880(0.312-2.483)        | 0.809               | -                     | -                   |
| C-KIT (+/−)               | 0.047(0.000-62.202)       | 0.404               | -                     | -                   |
| N/K-RAS (+/−)             | 2.988(1.036-8.618)        | 0.043               | 21.444(0.333-6.261)   | 0.623               |
| IDH1/2 (+/−)              | 6.958(0.870-55.647)       | 0.067               | 6.021(0.730-49.632)   | 0.095               |
| U2AF1 (+/−)               | 5.674(1.272-25.318)       | 0.023               | 5.538(1.222-25.102)   | 0.026               |
| DNMT3A (+/−)              | 1.526(0.593-3.923)        | 0.381               | -                     | -                   |

Notes: Variables including WBC (≥30×10⁹ vs 60 years), ITGB2-AS1 expression (low vs high), ITGB2 expression (low vs high), risk classification (favorable vs intermediate vs poor), and gene mutations (mutant vs wild type). Multivariate analysis includes variables with \( P<0.200 \).

AML, acute myeloid leukemia; HR, hazard ratio; OS, overall survival; WBC, white blood cell.
| Variables          | OS                                      | Univariate analysis | Multivariate analysis |
|--------------------|-----------------------------------------|---------------------|-----------------------|
|                    |                                         | HR (95% CI)         | P-Value               | HR (95% CI)         | P-Value               |
| Age                |                                         | 1.693(0.974-43.027) | 0.076                 | 0.765(0.308-1.902)  | 0.565                 |
| WBC                |                                         | 1.736(0.973-3.099)  | 0.062                 | 0.765(0.308-1.905)  | 0.565                 |
| **ITGB2-AS1**      | **expression**                          | 1.871(1.040-3.365)  | 0.036                 | 2.231(1.100-4.522)  | 0.026                 |
| **ITGB2**          | **expression**                          | 1.586(0.886-2.838)  | 0.120                 | 0.795(0.169-3.745)  | 0.772                 |
| Cytogenetic risk   |                                         | 1.914(1.259-2.993)  | 0.003                 | 2.301(1.470-3.603)  | 0.000                 |
| CEBPA mutation     |                                         | 1.138(0.467-2.774)  | 0.776                 | -                    | -                     |
| NPM1 mutation      |                                         | 0.880(0.267-2.899)  | 0.834                 | -                    | -                     |
| FLT3-ITD (+/–)     |                                         | 0.910(0.313-2.646)  | 0.863                 | -                    | -                     |
| C-KIT (+/–)        |                                         | 0.045(0.000-32.094) | 0.355                 | -                    | -                     |
| N/K-RAS (+/–)      |                                         | 2.821(0.967-8.233)  | 0.058                 | 1.487(0.342-6.464)  | 0.597                 |
| IDH1/2 (+/–)       |                                         | 8.824(1.031-75.542) | 0.047                 | 6.097(0.737-50.410) | 0.093                 |
| U2AF1 (+/–)        |                                         | 6.441(1.398-29.678) | 0.017                 | 5.573(1.266-25.340) | 0.026                 |
| DNMT3A (+/–)       |                                         | 1.265(0.488-3.282)  | 0.629                 | -                    | -                     |

**Notes:** Variables including WBC (≥30×10^9 vs 60 years), ITGB2-AS1 expression (low vs high), ITGB2 expression (low vs high), risk classification (favorable vs intermediate vs poor), and gene mutations (mutant vs wild type). Multivariate analysis includes variables with $P<0.200$.

AML, acute myeloid leukemia; HR, hazard ratio; OS, overall survival; WBC, white blood cell.

**Table 7. Univariate and multivariate analyses of prognostic factors for leukemia-free survival in whole-AML patients**
| Variables                              | LFS                     |                   |                |                |
|---------------------------------------|-------------------------|------------------|----------------|----------------|
|                                       |                         | Univariate analysis |                | Multivariate analysis |
|                                       |                         | HR (95% CI) | P-Value | HR (95% CI) | P-Value |
| Age                                   | 2.528(1.413-4.488)      | 0.002           | 1.148(0.526-2.506) | 0.728          |
| WBC                                   | 2.136(1.215-3.754)      | 0.008           | 1.200(0.611-2.356) | 0.597          |
| ITGB2-AS1 expression                  | 2.052(1.161-3.628)      | 0.013           | 2.724(1.347-5.509) | 0.005          |
| ITGB2 expression                      | 1.825(1.038-3.206)      | 0.037           | 0.793(0.175-3.588) | 0.764          |
| Cytogenetic risk                      | 1.981(1.381-2.842)      | 0.000           | 1.960(1.281-3.000) | 0.002          |
| CEBPA mutation                        | 1.133(0.472-2.717)      | 0.780           | -              | -              |
| NPM1 mutation                         | 1.024(0.315-3.333)      | 0.968           | -              | -              |
| FLT3-ITD (+/-)                        | 0.998(0.355-2.906)      | 0.997           | -              | -              |
| C-KIT (+/-)                           | 0.046(0.00-71.024)      | 0.412           | -              | -              |
| N/K-RAS (+/-)                         | 2.457(0.847-7.127)      | 0.098           | 2.145(0.729-6.310) | 0.166          |
| IDH1/2 (+/-)                          | 2.235(0.304-16.441)     | 0.430           | -              | -              |
| U2AF1 (+/-)                           | 2.283(0.541-9.631)      | 0.261           | -              | -              |
| DNMT3A (+/-)                          | 1.357(0.530-3.471)      | 0.525           | -              | -              |

**Notes:** Variables including WBC (≥30×10⁹ vs 60 years), ITGB2-AS1 expression (low vs high), ITGB2 expression (low vs high), risk classification (favorable vs intermediate vs poor), and gene mutations (mutant vs wild type). Multivariate analysis includes variables with \( P < 0.200 \).

AML, acute myeloid leukemia; HR, hazard ratio; LFS, leukemia-free survival; WBC, white blood cell.

**Figures**
**Figure 1**

ITGB-AS1 over expression in AML a. ITGB2-AS1 expression in controls and AML patients from TCGA datasets using the GEPIA (http://gepia.cancer-pku.cn/detail.php). b. Box plot showing ITGB2-AS1 expression differences in normal controls and AML patients, from GEO: GSE63270, calculated using the Mann-Whitney test. c. ITGB2-AS1 expression differences in normal controls, whole-cohort AML patients, non-M3 AML patients, and CN-AML patients, calculated using the Mann-Whitney test.
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Genes related to ITGB2-AS1 a. Volcano Map showing the correlation between 18107 genes and ITGB2-AS1, data from TCGA (downloaded from website GEPIA), plotted used R script (details of programming code in additional files). The 37 genes annotated in the graph were significantly positively correlated with ITGB2-AS1 (R>0.7, P<0.05). b. The positive correlation between ITGB2 and IGB2-AS1 expression in AML patients in our cohort (R=0.8811, P<0.01).
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Prognostic value of ITGB2-AS1 expression in AML a. The impact of ITGB2-AS1 expression on overall survival of AML patients from TCGA datasets using the GEPIA (http://gepia.cancer-pku.cn/detail.php). b-d. Kaplan-Meier curves of overall survival (OS) in our cohort b. For whole-cohort AML c. For non-M3 AML d. For CN-AML e. Kaplan-Meier curves of leukemia-free (LFS) survival for whole-cohort AML
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Supplementary Files

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