Clin. Lab. 2025;71:1-4
©Copyright

ORIGINAL ARTICLE

Clinical Significance of *CD109* Expression and Methylation Patterns in Acute Myeloid Leukemia

Ting-ting Du [1, 2, *], Ming-qiang Chu [2, 3, *], Zi-jun Xu [1, 2, *], Xiang-mei Wen [1, 2], Jing-dong Zhou [2, 3], Wei Zhao [2, 3], Min-jie Zhang [1, 2], Su-wan Liu [1, 2], Jun Qian [2, 3, *], Jiang Lin [1, 2, *]

[*] *These authors contributed equally to this work*
[1] *Laboratory Center, Affiliated People's Hospital of Jiangsu University, Zhenjiang, Jiangsu, P. R. China*
[2] *Zhenjiang Clinical Research Center of Hematology, Zhenjiang, Jiangsu Province, P. R. China*
[3] *Department of Hematology, Affiliated People's Hospital of Jiangsu University, Zhenjiang, Jiangsu, P. R. China*

SUMMARY

Introduction: **The altered expression of *CD109* has been observed in solid tumors of various types, and evidence suggests a correlation between *CD109* expression and development and prognosis of tumors. However, the expression and methylation patterns of *CD109* in acute myeloid leukemia (AML) and their clinical significance remain unclear.**
Methods: ***CD109*** **mRNA expression and promoter methylation were determined in AML patients and leukemia cells. Furthermore, the clinical significance of the findings and the regulatory relationship between expression and methylation of *CD109* were analyzed.**
Results: ***CD109*** **expression was found to be elevated in AML patients, both in publicly available datasets and in our own cohort. Subsequent clinical analysis showed an association between the wild-type form of *NPM1* and higher *CD109* expression. Kaplan–Meier survival analysis revealed that AML patients with higher *CD109* expression had shorter overall survival times. Furthermore, the *CD109* promoter was found to be hypomethylated in AML patients, and further analysis indicated that this hypomethylation led to elevated expression of *CD109*. We also observed that *CD109* mRNA expression and demethylation were markedly decreased in samples from patients with complete remission compared to those from newly diagnosed patients.**
Conclusions: **Our results suggest that *CD109* exhibits elevated expression and hypomethylation in AML, with its expression being regulated by methylation of its promoter region. Furthermore, *CD109* could serve as a prognostic indicator as well as a monitoring tool for the therapeutic outcome in AML.**
(Clin. Lab. 2025;71:1-4. DOI: 10.7754/Clin.Lab.2025.250128)

Correspondence:
Jiang Lin, Senior Technologist
Laboratory Center
Affiliated People's Hospital of Jiangsu University
Zhenjiang, Jiangsu
P. R. China
Email: 2651329493@qq.com

Jun Qian, Senior Physician
Zhenjiang Clinical Research Center of Hematology
Zhenjiang, Jiangsu Province
P. R. China
Email: qianjun0007@hotmail.com

Manuscript accepted January 31, 2025

Supplementary Data

Table S1. Primers for RT-qPCR, RQ-MSP, RQ-USP, BSP, and sequences for construct generation.

Target	**Primers**	
	Forward	**Reverse**
CD109	**CCC ATC AGG CCA ACA CAT CT**	**ACC ACA GCC ATA AGG CAT CC**
CD109-M	**TTT TAT TTT GTT GTT AGG CGC**	**GAT AAA CCC TAC ATC TCG ACG**
CD109-U	**ATT TTT TAT TTT GTT GTT AGG TGT**	**AAT AAA CCC TAC ATC TCA ACA ACA**
CD109-B	**GAG GGG TGG AGT TTT TAA GTT**	**ATA ATC AAA CCT CCA AAC CAA T**
ALU	**TTA GGT ATA GTG GTT TAT ATT TGT AAT TTT AGT A**	**ATT AAC TAA ACT AAT CTT AAA CTC CTA ACC TCA**
ABL1	**TCC TCC AGC TGT TAT CTG GAA GA**	**TCC AAC GAG CGG CTT CAC**

Table S2. Correlations of *CD109* expression with clinicopathological characteristics of AML patients.

Patient characteristics	**AML (TCGA dataset)**		
	Low *CD109* (n = 92)	**High *CD109* (n = 91)**	**p-value**
Gender, male/female	**45/47**	**53/38**	**0.237**
Median age, years (range)	**56 (21- 82)**	**60 (18 - 88)**	**0.170**
Median WBC, × 10^9/L (range)	**13.3 (0.5 - 297.4)**	**27.1 (0.6 - 298.4)**	**0.078**
Median BM blasts, % (range)	**72.5 (30 - 100)**	**72 (30 - 97)**	**0.428**
Median PM blasts, % (range)	**29.5 (0 - 98)**	**49 (0 - 94)**	**0.130**
FAB classification			**< 0.001**
M0	**1**	**14**	**< 0.001**
M1	**19**	**25**	**0.303**
M2	**23**	**18**	**0.479**
M3	**17**	**0**	**< 0.001**
M4	**15**	**21**	**0.270**
M5	**16**	**6**	**0.039**
M6	**1**	**2**	**0.621**
M7	**0**	**3**	**0.121**
No data	**0**	**2**	**0.246**
Karyotype			**< 0.001**
Favorable	**27**	**7**	**< 0.001**
Intermediate	**52**	**53**	**0.881**
Adverse	**10**	**30**	**< 0.001**
IDH1 (+/-)	**11/81**	**6/85**	**0.309**
IDH2 (+/-)	**9/83**	**9/82**	**1.000**
TP53 (+/-)	**1/91**	**15/76**	**< 0.001**
CEBPA (+/-)	**7/75**	**5/74**	**0.767**
NPM1 (+/-)	**33/59**	**15/76**	**0.004**
FLT3-ITD (+/-)	**13/79**	**14/77**	**0.838**
DNMT3A (+/-)	**25/67**	**19/72**	**0.388**
RNUX1 (+/-)	**2/90**	**13/78**	**0.003**

The cutoff point is the median expression value.

Table S3. Correlations of *CD109* expression with clinicopathological characteristics of AML patients.

Patient characteristics	***CD109* expression**		
	Low *CD109* (n = 42)	**High *CD109* (n = 76)**	**p-value**
Gender, male/female	**23/19**	**44/32**	**0.846**
Median age, years (range)	**64 (31.0 - 85.0)**	**64 (22.0 - 87.0)**	**0.734**
Median WBC, × 10^9/L (range)	**16.8 (0.5 - 304.0)**	**17.8 (0.9 - 255.0)**	**0.654**
Median Hb, g/L (range)	**88 (37.0 - 179.0)**	**85.0 (44.0 - 163.0)**	**0.537**
Median PLT, × 10^9/L (range)	**37.5 (4.0 - 185.0)**	**5.0 (5.0 - 607.0)**	**0.320**
Median BM blasts, % (range)	**44.5 (14.5 - 99.0)**	**54.9 (10.8 - 93.5)**	**0.512**
FAB classification			**0.120**
M1	**3**	**12**	**0.251**
M2	**26**	**30**	**0.022**
M4	**7**	**11**	**0.792**
M5	**3**	**9**	**0.535**
No data	**3**	**14**	**0.109**
Cytogenetics			**0.923**
Normal	**19**	**30**	**0.564**
t(8;21)	**5**	**6**	**0.518**
+8	**1**	**1**	**1.000**
5q-	**0**	**2**	**0.538**
-7/del(7)	**1**	**1**	**1.000**
11q23	**0**	**1**	**1.000**
Others	**2**	**4**	**1.000**
Complex	**3**	**9**	**0.535**
No data	**11**	**22**	**0.832**
Karyotype			**0.745**
Favorable	**5**	**6**	**0.518**
Intermediate	**21**	**36**	**0.848**
Adverse	**4**	**12**	**0.411**
Unknown	**12**	**22**	**1.000**
IDH1 (+/-)	**0/31**	**3/54**	**0.549**
IDH2 (+/-)	**6/25**	**5/52**	**0.185**
TET2 (+/-)	**2/29**	**3/54**	**1.000**
TP53 (+/-)	**2/29**	**3/54**	**1.000**
CEBPA (+/-)	**2/29**	**10/47**	**0.201**
NPM1 (+/-)	**13/18**	**11/46**	**0.027**
FLT3 (+/-)	**12/19**	**13/44**	**0.141**
CKIT (+/-)	**5/26**	**3/54**	**0.124**
RAS (+/-)	**3/28**	**8/49**	**0.740**
U2AF1 (+/-)	**0/31**	**2/55**	**0.538**
NRAS (+/-)	**5/26**	**7/50**	**0.747**
KRAS (+/-)	**0/31**	**4/53**	**0.293**
DNMT3A (+/-)	**2/29**	**8/49**	**0.484**
SRSF2 (+/-)	**1/30**	**4/53**	**0.653**
SETBP1 (+/-)	**0/31**	**1/56**	**1.000**
CR (+/-)	**11/10**	**19/28**	**0.296**

The cutoff point is the cutoff value for expression.

Table S4. Correlations of *CD109* methylation with clinicopathological characteristics of AML patients.

Patient characteristics	*CD109* methylation		
	Hypermethylated (n = 30)	Hypomethylated (n = 101)	p-value
Gender, male/female	16/14	57/44	0.835
Median age, years (range)	56 (42 - 81)	59 (18 - 85)	0.797
Median WBC, × 10^9/L (range)	13.6 (0.9 - 154.0)	19.7 (0.4 - 209.6)	0.219
Median Hb, g/L (range)	82 (42.0 - 144.0)	80.0 (32.0 - 141.0)	0.372
Median PLT, × 10^9/L (range)	37.0 (3.0 - 148.0)	42.0 (5.0 - 415.0)	0.358
Median BM blasts, % (range)	37.3 (5.0 - 91.0)	47.5 (15.5 - 94.5)	0.104
FAB classification			0.367
M0	0 (0%)	1 (1%)	1.000
M1	1 (3%)	6 (6%)	1.000
M2	15 (50%)	53 (52%)	0.838
M4	7 (24%)	26 (26%)	0.818
M5	6 (20%)	7 (7%)	0.074
M6	1 (3%)	2 (2%)	0.545
No data	0 (0%)	6 (6%)	0.336
Cytogenetics			0.122
Normal	17 (58%)	57 (56%)	1.000
t(9;22)	0 (0%)	1 (1%)	1.000
t(8;21)	0 (0%)	11(11%)	0.068
inv(16)	1 (3%)	0 (0%)	0.229
+8	1 (3%)	4 (4%)	1.000
5q-	3 (10%)	2 (2%)	0.079
11q23	0 (0%)	1 (1%)	1.000
Others	4 (13%)	12 (12%)	0.761
Complex	4 (13%)	8 (8%)	0.469
No data	0 (0%)	5 (5%)	0.588
Karyotype			0.300
Favorable	1 (3%)	12 (12%)	0.296
Intermediate	23 (77%)	71 (70%)	0.645
Adverse	6 (20%)	13 (13%)	0.377
Unknown	0 (0%)	5 (5%)	0.588
IDH1 (+/-)	2/27	5/75	0.654
IDH2 (+/-)	5/24	8/92	0.166
TET2 (+/-)	0/29	3/97	1.000
TP53 (+/-)	1/28	3/97	1.000
CEBPA (+/-)	1/28	8/92	0.683
NPM1 (+/-)	8/21	23/77	0.626
FLT3 (+/-)	8/21	25/75	0.811
CKIT (+/-)	3/26	7/93	0.693
RAS (+/-)	5/24	23/77	0.615
U2AF1 (+/-)	0/29	6/94	0.336
NRAS (+/-)	5/24	21/79	0.796
KRAS (+/-)	2/27	8/92	1.000
DNMT3A (+/-)	2/27	6/94	1.000
SRSF2 (+/-)	1/28	2/98	0.537
SETBP1 (+/-)	1/28	1/99	0.400
CR (+/-)	12/15	48/38	0.378

The cutoff point is the cutoff value for methylation.