Int J Clin Exp Pathol 2024;17(1):1-12
www.ijcep.com /ISSN:1936-2625/IJCEP0154207

Original Article

Comprehensive analysis of EML2 as a prognostic biomarker in colon cancer

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Received November 1, 2023; Accepted January 2, 2024; Epub January 15, 2024; Published January 30, 2024

Abstract: Background: Echinoderm microtubule-associated protein-like 2 (EML2), a gene located on 19q13.32, is overexpressed in various cancers and has been identified as a prognostic factor. However, the function and carcinogenic mechanism of EML2 in colon cancer is yet to be explored. Methods: This study aimed to demonstrate the relationship between EML2 expression and colon cancer using The Cancer Genome Atlas (TCGA) database. The EML2 expression, including GSE33113 and GSE39923, was validated in colon cancer in the Gene Expression Omnibus (GEO) database. The Receiver Operating Characteristic (ROC) curves were used to assess the feasibility of EML2 as a distinguishing factor from the area under the curve (AUC) scores. In addition, Cox regression and logistic regression analyses were conducted to evaluate the factors linked to the prognosis of colon cancer. Moreover, the STRING tool was used to establish the EML2 binding protein network. The enrichment analysis cluster Profiler of the R package was utilized to investigate the function of EML2. The relationship between the immune infiltration and EML2 expression level in colon cancer was investigated by the R package Gene Set Variation Analysis (GSVA) and the single sample Gene Set Enrichment Analysis (ssGSEA) method in the Tumor Immune Estimation Resource (TIMER) database. Results: Pan-cancer data analysis revealed that EML2 expression was higher in most cancers, including colon cancer. This outcome was in line with the findings of the GEO database. The ROC curve demonstrated that EML2 can serve as a diagnostic biomarker for colon cancer (AUC = 0.738). High EML2 expression was associated with poorer overall survival (OS; $P = 0.004$). Moreover, the results of the enrichment and immune infiltration analysis revealed that high EML2 expression correlated with regulation of the infiltration level of GTPase binding and some immune cell types like NK cells and NK CD56 bright cells. Conclusion: The findings revealed that colon cancer tissues had a higher EML2 expression than normal colon epithelial tissues. This phenomenon was significantly associated with poor prognosis and altered immune cell infiltration. Consequently, EML2 has shown the capacity to serve as a prognostic biomarker for patients diagnosed with colon cancer.

Keywords: EML2, biomarker, colon cancer, prognosis, immune infiltration

Introduction

In the United States, colorectal cancer is the fourth most commonly diagnosed cancer and the second leading cause of cancer-related death. In 2020, there were an estimated 104,610 new cases of colon cancer, with 53,200 deaths [1]. The main factors contributing to the development of colorectal cancer are consumption of alcohol and tobacco, obesity, diabetes, and a family history of the disease. Recent studies have also suggested that infection with pathogens such as *H. pylori* and *Fusarium spp.* increases the risk of colorectal cancer [2-4]. If detected early, colon cancer can be cured by surgical resection; however, its later stages can be treated by chemotherapy. Cytotoxic drugs and biologic agents are utilized in the management of advanced stages of colon cancer [5]. Mortality associated with colon cancer has been declining for many years and is currently less than 50% of the peak mortality [6, 7]. This notable enhancement has been accomplished by early detection and prevention of cancer [8]. Hence, there is a need to find more accurate biomarkers that can effectively diagnose colon cancer at an early stage and can be efficiently used for disease surveillance.

Echinoderm microtubule-associated protein-like 2 (EML2) is a tumor-associated gene located on the chromosome 19q13.32 [9, 10]. Its primary biologic functions are related to cancer

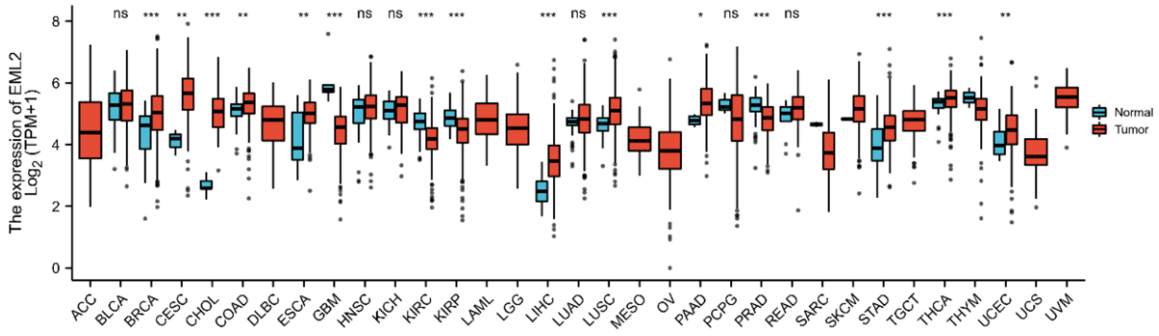


Figure 1. EML2 expression in normal and tumor tissues of TCGA and GTEx databases.

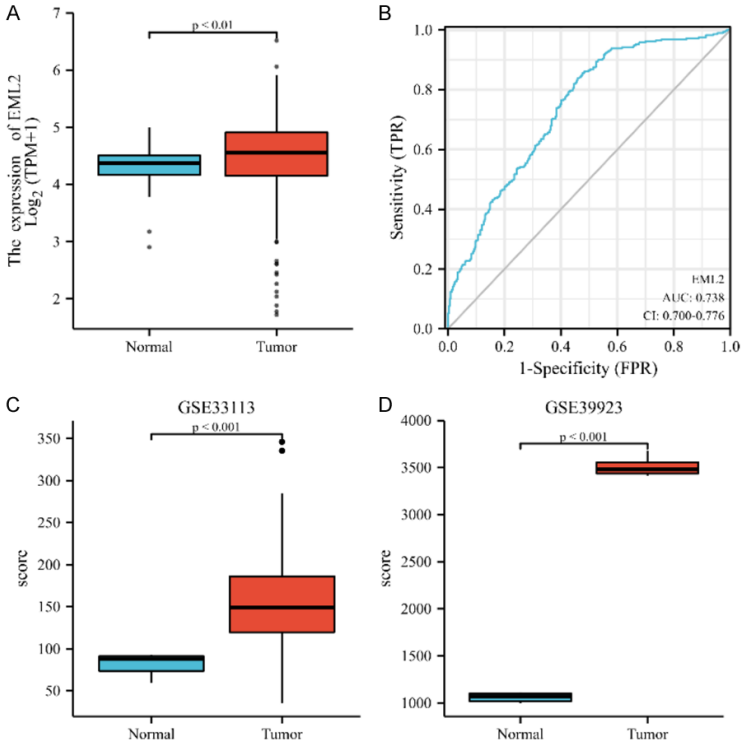


Figure 2. EML2 expression in the GEO database. A. EML2 expression in normal and tumor tissues in colon cancer. B. ROC curve of EML2 in colon cancer. The X-axis represents false-positive rates, and the Y-axis represents true-positive rates. C. EML2 expression in normal colon tissues and colon cancer epithelial component from GSE3313. D. EML2 expression in normal colon epithelial and colon cancer tissues from GSE39929.

cell progression, immune response, cell growth, cell proliferation, apoptosis, and cell chemotaxis [11-14]. It has been demonstrated that EML2 is overexpressed in nasopharyngeal carcinomatosis and can be used to predict adverse outcome [11]. However, a correlation between EML2 and colon cancer has not been investigated yet. Therefore, this study aimed to examine the expression of EML2 in colon cancer tissues and its clinical value.

Materials and methods

Analysis of RNA sequencing data collection

The expression of EML2 in pan-cancer was determined using relevant data from The Cancer Genome Atlas (TCGA) database (https://portal.gdc.com). The eligible samples from the TCGA database were screened for further analysis of EML2 expression in tumor tissues. The combined analysis of TCGA and genotypic tissue expression (GTEx) databases was used for normal tissue samples. GSE33113 and GSE39923 (obtained *via* Gene Expression Omnibus [GEO]) were used to obtain colon cancer microarray data.

Analysis of gene set enrichment and correlation

The top 100 genes that showed a high positive association with EML2 were screened for enrichment analysis. The EnrichGO function in the R package "clusterProfifiler" was used for gene ontology (GO) enrichment, and the EnrichKEGG function was used for the Kyoto Encyclopedia of Genes and Genomes (KEGG) analysis. Additionally, the correlation between EML2 and other mRNAs in colon cancer was analyzed using data from TCGA.

Analysis of survival prognosis

The R package "survival" (version 4.0.3) was used to obtain an overall survival (OS) plot for

Table 1. Analysis of the association between EML2 expression and clinicopathologic features of colon cancer based on the TCGA database

Characteristic	Low expression of EML2	High expression of EML2	*P* value
N	239	239	
T stage, n (%)			0.012
T1	6 (1.3%)	5 (1%)	
T2	53 (11.1%)	30 (6.3%)	
T3	157 (32.9%)	166 (34.8%)	
T4	22 (4.6%)	38 (8%)	
N stage, n (%)			0.074
N0	152 (31.8%)	132 (27.6%)	
N1	53 (11.1%)	55 (11.5%)	
N2	34 (7.1%)	52 (10.9%)	
M stage, n (%)			0.077
M0	182 (43.9%)	167 (40.2%)	
M1	26 (6.3%)	40 (9.6%)	
Pathologic stage, n (%)			0.108
Stage I	48 (10.3%)	33 (7.1%)	
Stage II	96 (20.6%)	91 (19.5%)	
Stage III	64 (13.7%)	69 (14.8%)	
Stage IV	26 (5.6%)	40 (8.6%)	
Age, n (%)			0.926
≤ 65	96 (20.1%)	98 (20.5%)	
> 65	143 (29.9%)	141 (29.5%)	
Residual tumor, n (%)			0.938
R0	178 (47.6%)	168 (44.9%)	
R1	2 (0.5%)	2 (0.5%)	
R2	13 (3.5%)	11 (2.9%)	
CEA level, n (%)			0.445
≤ 5	102 (33.7%)	94 (31%)	
> 5	50 (16.5%)	57 (18.8%)	
Perineural invasion, n (%)			0.712
No	59 (32.6%)	76 (42%)	
Yes	18 (9.9%)	28 (15.5%)	
Lymphatic invasion, n (%)			0.932
No	137 (31.6%)	129 (29.7%)	
Yes	85 (19.6%)	83 (19.1%)	
Colon polyps present, n (%)			0.713
No	78 (31.3%)	84 (33.7%)	
Yes	39 (15.7%)	48 (19.3%)	
Neoplasm type, n (%)			1.000
Colon adenocarcinoma	239 (50%)	239 (50%)	
Rectum adenocarcinoma	0 (0%)	0 (0%)	
OS event, n (%)			0.014
Alive	199 (41.6%)	176 (36.8%)	
Dead	40 (8.4%)	63 (13.2%)	
Age, meidan (IQR)	69 (58.5, 77)	69 (58, 78)	0.783

EML2. A cutoff value of 50% was used to split the cohort into two groups based on their level of expression: a high- and a low-expression group. The R package (version 4.0.3) "ROC"

Table 2. Analysis of the association between the expression of EML2 and clinicopathological features by logistic regression

Characteristic	Total (N)	Odds Ratio (OR)	*P* value
T stage (T3 & T4 vs. T1 & T2)	477	1.921 (1.214-3.078)	0.006
N stage (N1 & N2 vs. N0)	478	1.416 (0.982-2.046)	0.063
M stage (M1 vs. M0)	415	1.677 (0.986-2.895)	0.059
Pathologic stage (Stage III & Stage IV vs. Stage I & Stage II)	467	1.406 (0.974-2.035)	0.069
Primary therapy outcome (PR & CR vs. PD & SD)	250	0.671 (0.304-1.460)	0.316
Gender (Male vs. Female)	478	0.935 (0.653-1.339)	0.714
Race (White vs. Asian & Black or African American)	306	0.715 (0.416-1.213)	0.217
Age (> 65 vs. ≤ 65)	478	0.966 (0.670-1.392)	0.852
BMI (≥ 25 vs. < 25)	256	0.785 (0.464-1.320)	0.363
Residual tumor (R1 & R2 vs. R0)	374	0.918 (0.418-1.990)	0.829
CEA level (> 5 vs. ≤ 5)	303	1.237 (0.772-1.987)	0.377
Perineural invasion (Yes vs. No)	181	1.208 (0.614-2.420)	0.588
Lymphatic invasion (Yes vs. No)	434	1.037 (0.704-1.527)	0.854
History of colon polyps (Yes vs. No)	408	0.727 (0.482-1.092)	0.125
Colon polyps present (Yes vs. No)	249	1.143 (0.678-1.933)	0.617

was used for analysis, and "ggplot2" visualization was used to assess the value of EML2 in predicting the prognosis of patients with colon cancer.

Analysis of immune cell infiltration

The single sample Gene Set Enrichment Analysis (ssGSEA) approach in the R package Gene Set Variation Analysis (GSVA; version 4.0.3) and the Tumor Immunology Estimation Resource (TIMER) database (http://timer.cistrome.org/) was used to investigate the molecular characterization of tumor-immune interactions in colon cancer. The Wilcoxon rank and Spearman rank correlation tests were used to calculate *p*-values to explore the correlation between EML2 expression and the abundance of tumor-infiltrating immune cells.

Results

Analysis of mRNA expression of EML2

The expression of EML2 was analyzed in 33 types of cancer. The results showed that EML2 was overexpressed in most of the cancer types, including bladder urothelial carcinoma (BLCA), breast invasive carcinoma (BRCA), cervical squamous cell carcinoma, and endocervical adenocarcinoma (CESC), cholangiocarcinoma (CHOL), colon adenocarcinoma (COAD), esophageal carcinoma (ESCA), head and neck squamous cell carcinoma (HNSC), kidney chromophobe (KICH), liver hepatocellular carcinoma (LIHC), lung adenocarcinoma (LUAD), lung squamous cell carcinoma (LUSC), pancreatic adenocarcinoma (PAAD), rectum adenocarcinoma (READ), skin cutaneous melanoma (SKCM), stomach adenocarcinoma (STAD), thyroid carcinoma (THCA), and uterine corpus endometrial carcinoma (UCEC). However, a low expression of EML2 was observed in glioblastoma multiforme (GBM), kidney renal papillary cell carcinoma (KIRP), kidney renal clear cell carcinoma (KIRC), pheochromocytoma and paraganglioma (PCPG), prostate adenocarcinoma (PRAD), sarcoma (SARC), and thymoma (THYM) (**Figure 1**).

Furthermore, the expression of EML2 was evaluated in colon cancer, including GSE33113 and GSE39923, and the overexpression of EML2 in colon cancer tissues was confirmed (**Figure 2A-D**). The feasibility of using EML2 expression to distinguish between colon cancer tissues and normal colon tissues was assessed using receiver operating characteristic (ROC) curves. The area under the ROC curve (AUC), which evaluates the quality of the test, was 0.738.

Clinical relevance of the EML2 expression

The characteristics of 478 patients with primary colon cancer with both clinical and gene expression data were downloaded from the TCGA database. A cutoff value of 50% was used as the dividing threshold, and the patients

Table 3. Univariate and multivariate Cox analysis of prognostic factors for colon cancer

Characteristics	Total (N)	Univariate analysis		Multivariate analysis	
		Hazard ratio (95% CI)	*P* value	Hazard ratio (95% CI)	*P* value
T stage	476				
T1 & T2	94	Reference			
T3 & T4	382	3.072 (1.423-6.631)	0.004	9761 (0.000-5893)	0.693
N stage	477				
N0	283	Reference			
N1 & N2	194	2.592 (1.743-3.855)	< 0.001	2046 (0.000-1568)	0.146
M stage	414				
M0	348	Reference			
M1	66	4.193 (2.683-6.554)	< 0.001	5631 (0.144-2199)	0.109
Pathologic stage	466				
Stage I & Stage II	267	Reference			
Stage III & Stage IV	199	2.947 (1.942-4.471)	< 0.001	1.000 (0.000-7666)	1.000
Gender	477				
Female	226	Reference			
Male	251	1.101 (0.746-1.625)	0.627		
Age	477				
≤ 65	194	Reference			
> 65	283	1.610 (1.052-2.463)	0.028	7703 (2252-2635)	< 0.001
CEA level	302				
≤ 5	195	Reference			
> 5	107	3.128 (1.788-5.471)	< 0.001	1.024 (0.000-1431)	0.997
Residual tumor	373				
R0	345	Reference			
R1 & R2	28	4.364 (2.401-7.930)	< 0.001	3456 (4461-2678)	< 0.001
Perineural invasion	181				
No	135	Reference			
Yes	46	1.940 (0.982-3.832)	0.056	0.000 (0.000-0.003)	0.004
Lymphatic invasion	433				
No	265	Reference			
Yes	168	2.450 (1.614-3.720)	< 0.001	0.011 (0.000-954.889)	0.439
EML2	477				
Low	238	Reference			
High	239	1.703 (1.135-2.555)	0.010	0.000 (0.000-0.288)	0.033

were divided into a high-EML2 expression group (n = 239) and a low-EML2 expression group (n = 239). The correlation between the EML2 expression and the clinicopathologic characteristics of patients was explored. The results showed that EML2 expression was significantly associated with the T stage (P = 0.012) and OS event (P = 0.014) *via* the chi-square test or Fisher's exact test (**Table 1**).

The logistic regression method was used to analyze further the relationship between the EML2 expression and the clinicopathologic characteristics of colon cancer. The results showed that the expression of EML2 was significantly associated with the T stage (P = 0.004; **Table 2**).

Relationship between EML2 expression and survival prognosis of colon cancer patients

The univariate and multivariate Cox analyses of prognostic factors were done in patients with colon cancer. In univariate Cox analysis of EML2, T3 & T4 stage (P = 0.004), N1 & N2 stage (P < 0.001), M1 stage (P < 0.001), Stage

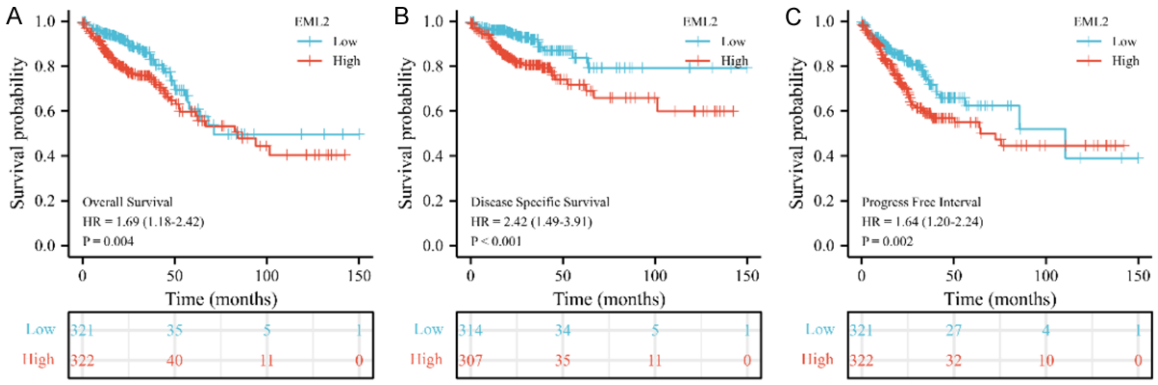


Figure 3. Association between EML2 expression and overall survival (OS), disease specific survival (DSS), and progression free interval (PFI) in colon cancer patients. A. Association between EML2 expression and OS in colon cancer patients. B. Association between EML2 expression and DSS in colon cancer patients. C. Association between EML2 expression and PFI in colon cancer patients.

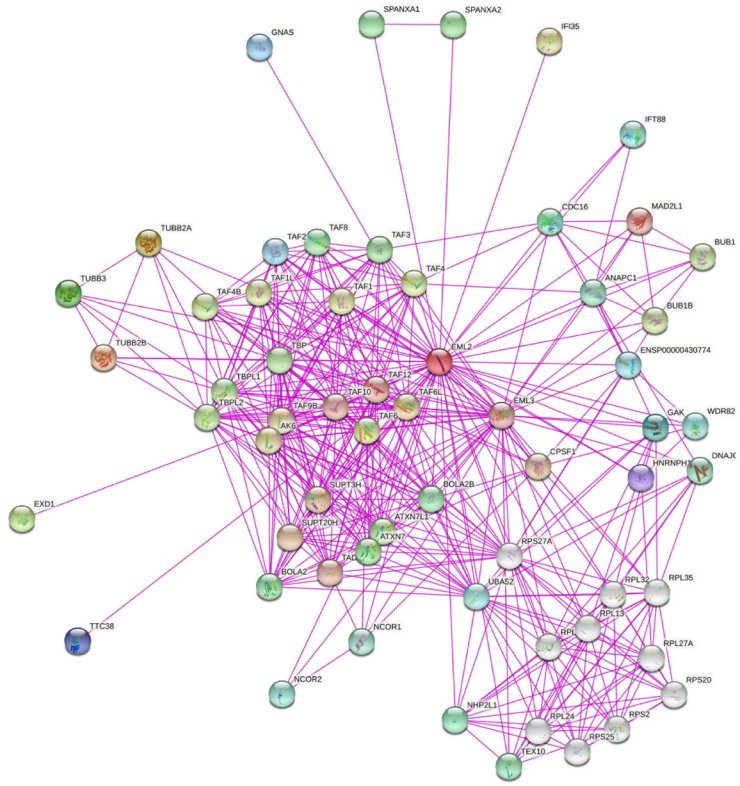


Figure 4. EML2-binding proteins obtained by the STRING tool.

III & Stage IV ($P < 0.001$), Age > 65 ($P = 0.028$), CEA level > 5 ($P < 0.001$), R1 & R2 ($P < 0.001$), lymphatic invasion ($P < 0.001$), and elevated EML2 expression ($P = 0.01$) were found to be associated with OS in patients with colon cancer. In the multivariate Cox model, age > 65 ($P < 0.001$), R1 & R2 ($P < 0.001$), perineural invasion ($P = 0.04$), and elevated EML2 expression ($P = 0.033$) were related to a worse prognosis of the disease (**Table 3**).

Furthermore, the relationship between EML2 expression and OS was investigated in patients with colon cancer. Based on the Kaplan-Meier (KM) plot, patients in the higher EML2 expression group showed poorer prognosis than the ones in the lower EML2 expression group (HR = 1.69, 95% CI: 1.18-2.42, $P = 0.004$; **Figure 3**).

Correlation and EML2-related gene enrichment analysis

This study only targeted protein binding at the physical level. A total of 60 experimentally supported EML2-bindable proteins from the STRING network were analyzed (**Figure 4**).

EML2 expression-related genes were subjected to correlation pathway analysis to explore the function of EML2 further. The top 100 most positively correlated genes of EML2 were analyzed using GO and KEGG functions in the "clusterProfifile" R package. The GO analysis data showed that EML2 was associated with the binding of cell adhesion molecules, small GTPase, Ras GTPase, and Rho GTPase (**Figure 5A**). The

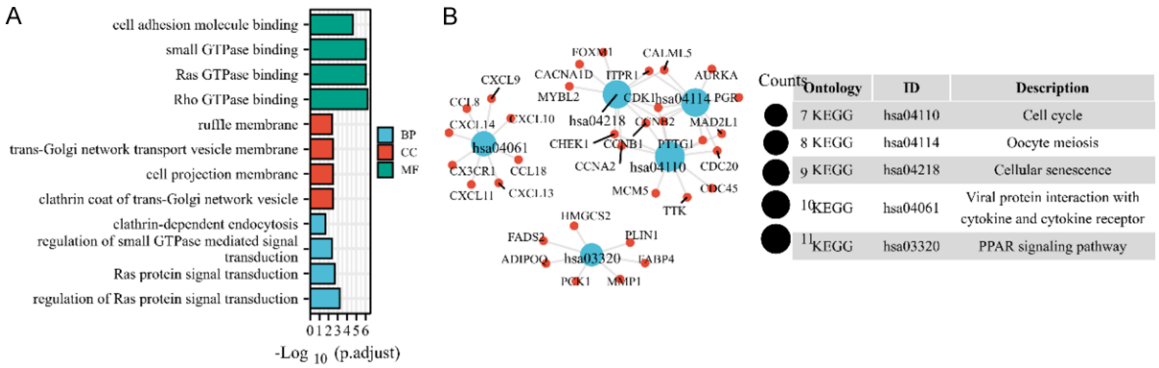
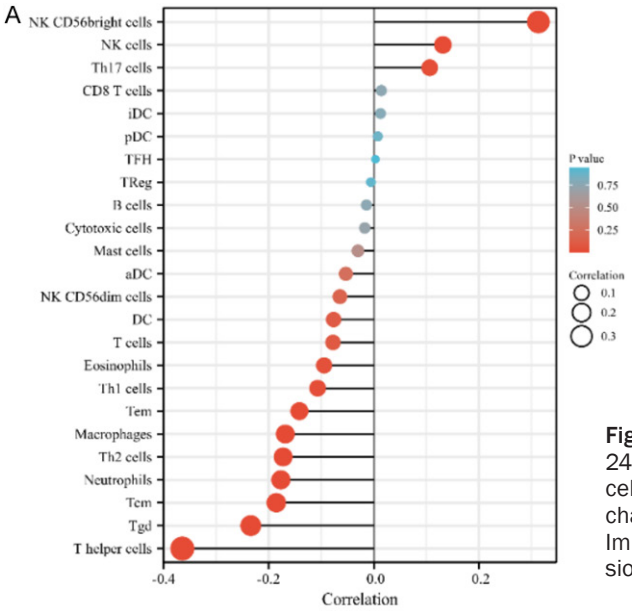


Figure 5. Function and pathway enrichment analysis of EML2 in colon cancer. A. Significant Gene Ontology terms of the top 100 genes most positively associated with EML2. B. Significant KEGG pathway of the top 100 genes most positively associated with EML2.



B

Molecular	cell	P value(Spearman)
EML2	NK CD56bright cells	<0.001
EML2	NK cells	<0.001
EML2	T helper cells	<0.001
EML2	Tcm	<0.001
EML2	Tgd	<0.001
EML2	Neutrophils	0.004
EML2	Th2 cells	0.017
EML2	Tem	0.018
EML2	Macrophages	0.030

Figure 6. Lollipop chart of EML2 expression levels in 24 immune cells and significant infiltration of immune cells associated with EML2 expression. A. Lollipop chart of EML2 expression level in 24 immune cells. B. Immune cell infiltration associated with EML2 expression, $P < 0.05$, represents a significant result.

KEGG analysis data revealed that the "Peroxisome proliferator-activated receptors (PPARs) signaling pathway" was probably related to the carcinogenic mechanism of EML2 (**Figure 5B**).

Association of EML2 expression with immune cell infiltration

The ssGSEA with Spearman's r in the R package was used to analyze the associations between EML2 expression levels and 24 immune cell types to assess in-depth whether EML2 expression was associated with immune cell infiltration. EML2 expression had a significant correlation with natural killer (NK) CD56 bright cells, NK cells, T helper cells, Tcm, Tgd, neutrophils, Th2 cells, Tem, and macrophages (**Figure 6**).

The results further demonstrated that EML2 expression was positively correlated with infiltration of NK CD56 bright cells ($r = 0.340$, $P < 0.001$; **Figure 7A**) and NK cells ($r = 0.223$, $P < 0.001$; **Figure 7B**). On the contrary, EML2 expression was negatively correlated with that of T helper cells (**Figure 7C**; $r = -0.328$, $P < 0.001$), Tcm (**Figure 7D**; $r = -0.159$, $P < 0.001$), Tgd (**Figure 7E**; $r = -0.185$, $P < 0.001$), neutrophils (**Figure 7F**; $r = 0.132$, $P = 0.004$), Th2 cells (**Figure 7G**; $r = -0.109$, $P = 0.017$), Tem (**Figure 7H**; $r = -0.108$, $P = 0.018$), and macrophages (**Figure 7I**; $r = -0.099$, $P = 0.030$).

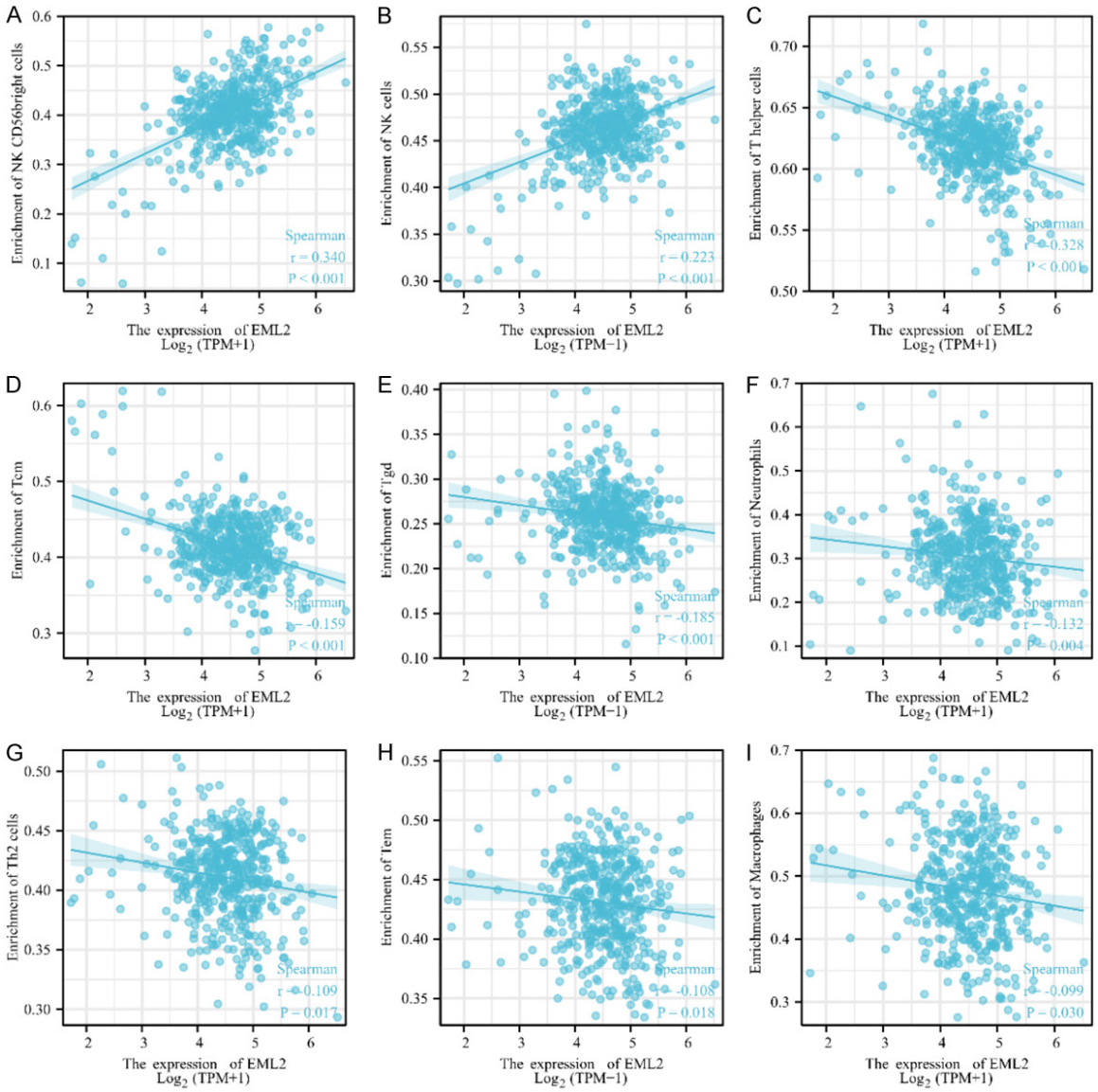


Figure 7. Correlation between EML2 expression and immune cell infiltration. A. Correlation between EML2 expression and NK CD56 bright cells. B. Correlation between EML2 expression and NK cells. C. Correlation between EML2 expression and T helper cells. D. Correlation between EML2 expression and Tcm. E. Correlation between EML2 expression and Tgd. F. Correlation between EML2 expression and Neutrophils. G. Correlation between EML2 expression and Th2 cells. H. Correlation between EML2 expression and Tem. I. Correlation between EML2 expression and Macrophages.

The results also showed that when EML2 was divided into high- and low-expression groups, there was a significant difference in the level of immune cell infiltration, including NK CD56 bright cells, NK cells, T helper cells, Tcm, Tgd, neutrophils, and Th2 cells ($P < 0.05$) (**Figure 8A-G**), while Tem and macrophages did not differ (**Figure 8H**, **8I**).

Finally, the association between immune cell infiltration and clinical survival in patients with colon cancer was analyzed by TIMER. The evaluation showed that high levels of NK cells and $CD4^+$ T cells were significantly associated with poorer prognosis in patients with colon cancer ($P < 0.05$; **Figure 9A**, **9B**).

Discussion

Despite recent progress, colon cancer remains one of the most common causes of death in humans worldwide [15]. In recent years, target-

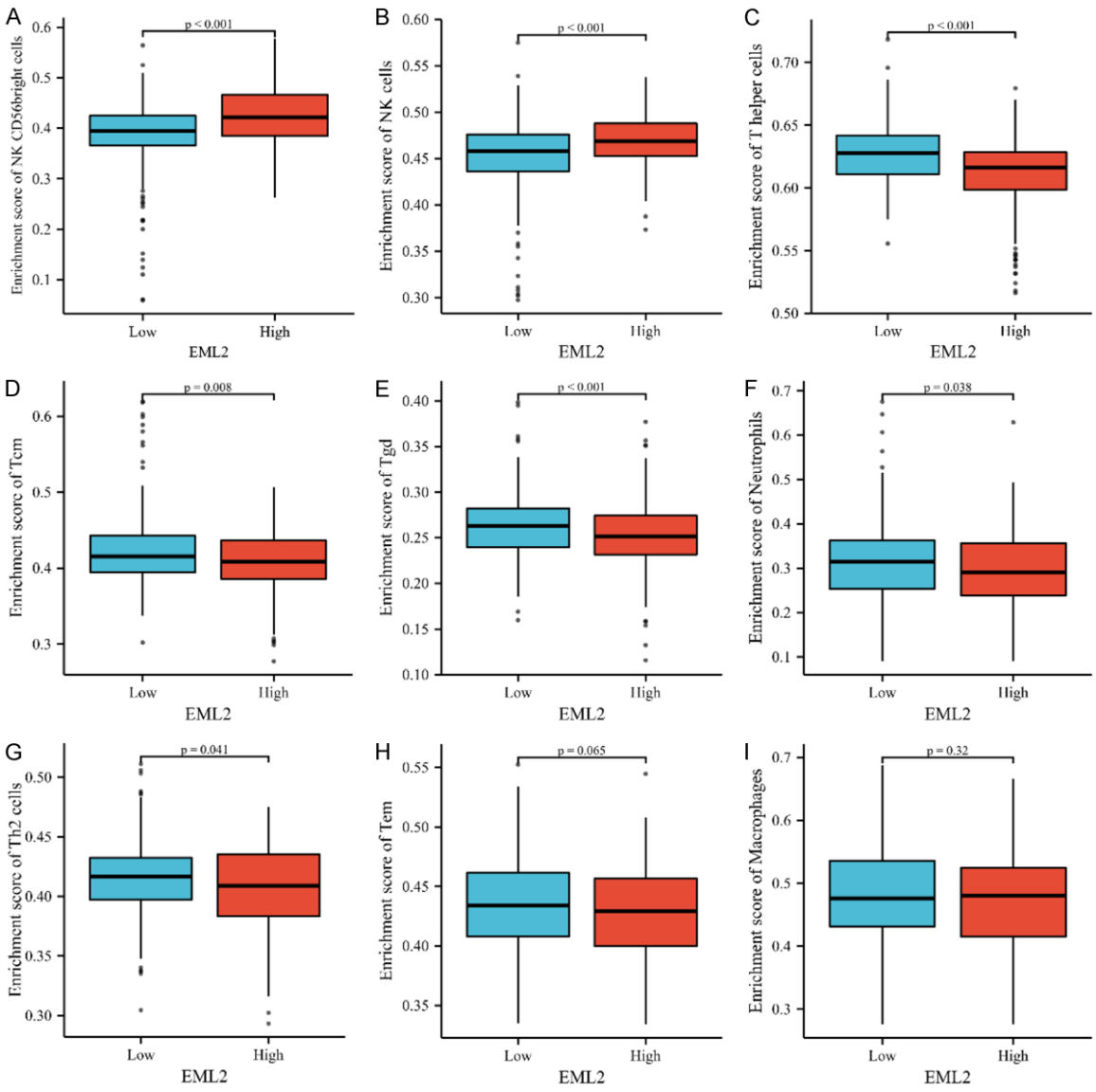


Figure 8. Comparison of immune cells between high- and low-EML2 expression groups. A. Histogram showing the difference of NK CD56 bright cells infiltration level between high- and low-EML2 expression groups. B. Histogram showing the difference in NK cells infiltration level between high- and low-EML2 expression groups. C. Histogram showing the difference of T helper cells infiltration level between high- and low-EML2 expression groups. D. Histogram showing the difference in Tcm infiltration level between high- and low-EML2 expression groups. E. Histogram showing the difference of Tgd infiltration level between high- and low-EML2 expression groups. F. Histogram showing the difference of Neutrophils infiltration level between high- and low-EML2 expression groups. G. Histogram showing the difference in Th2 cell infiltration level between high- and low-EML2 expression groups. H. Histogram showing the difference of Tem infiltration level between high- and low-EML2 expression groups. I. Histogram showing the difference of Macrophages infiltration level between high- and low-EML2 expression groups.

ed therapies have significantly improved overall survival (OS) in patients with colon cancer [16]. However, the worldwide yearly death rate continues to be elevated, underscoring the need to identify novel biomarkers and employ them for timely detection, prediction, and management of colon cancer. Previous studies have reported that EML2 is overexpressed in various types of cancers. To the best of the authors' knowledge, the relationship between EML2 expression and colon cancer has not yet been explored [9, 11]. Thus, in this study, the mechanisms of EML2 in promoting colon cancer and its feasibility as a molecular biomarker were explored.

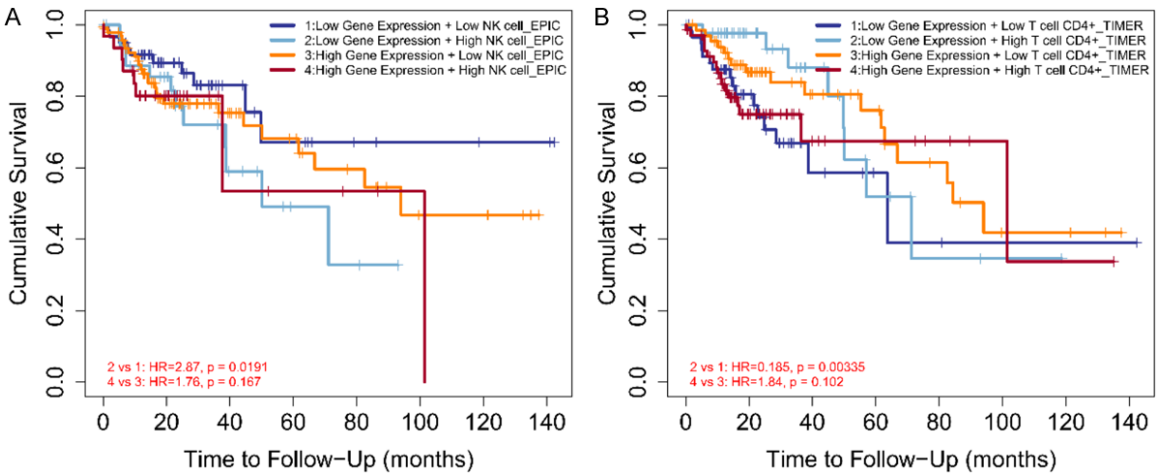


Figure 9. Impact of immune cell infiltration on prognosis in colon cancer patients. A. Clinical survival outcome of colon cancer patients in the high-NK cell group. B. Clinical survival outcome of colon cancer patients in the high-T cell $CD4^+$ group.

In the pan-cancer analysis, EML2 was found to be upregulated in most cancer types. Further exploration revealed that high expression of EML2 was associated with reduced OS in colon cancer patients. Logistic regression was performed to assess the relationship between EML2 expression levels and clinicopathologic characteristics of colon cancer. The results showed that EML2 was significantly associated with the clinical stage of the disease. In addition, univariate and multivariate Cox analyses showed that EML2 was an independent factor for predicting prognosis. These results, as well as the ROC analyses, suggested that EML2 may be a promising prognostic bioindicator.

Increasing evidence suggests that the cellular and acellular components in the tumor microenvironment (TME) reprogram tumor initiation, growth, invasion, metastasis, and response to therapies [17]. In recent times, cancer research and treatment has shifted from a cancer-centric paradigm to a TME-centric paradigm. The primary biologic function of EML2 is mainly involved in the immune response, as revealed by the Gene enrichment analysis. Further, EML2 expression was associated with immune cell infiltration. Thus, it was hypothesized that EML2 might influence the tumor microenvironment by altering the ratio of specific immune cell types, promoting tumor progression and metastasis.

This study showed a significant positive correlation between the NK cells, NK CD56 bright cells, and EML2 expression. NK cells are a crucial component of the tumor microenvironment. They can be subdivided into the following two types based on their CD56 expression: CD56 bright NK cells are generally associated with immunomodulatory properties and pro-inflammatory cytokine production. In contrast, CD56 dim NK cells perform cytotoxic functions [18, 19]. In the early stages of tumor development, NK cells exhibit effector properties. However, in the later stages, these cells show impaired cytotoxic capacity, become dysfunctional, senescent, and are eventually depleted [20, 21]. Recent studies have demonstrated that EML2 may actively stimulate the immune system and decrease tumor size in mouse models [22]. Thus, EML2 may play a key role in maintaining the TME.

Moreover, increased levels of NK cells and CD4 infiltration were associated with poor prognosis in colon cancer and are consistent with similar findings in related research [23, 24]. The mechanisms of the TME are complex. Other kinds of immune cells may also influence the survival and development of tumor cells. These include T helper cells, Tcm, Tgd, neutrophils, Th2 cells, Tem, and macrophages. Further studies are required to explore the relationship between EML2 expression and immune cell infiltration.

In summary, this study demonstrates that upregulation of EML2 expression in colon cancer can be associated with poor prognosis. Furthermore, by influencing immune cell infiltration levels, EML2 was found to be involved in the development of colon cancer. Not only does this study reveal the role of EML2 in colon cancer progression, but it also identifies it as a prognostic biomarker. Thus, the findings of this study provide new insights into the pathological basis of colon cancer. However, additional prospective analyses and randomized clinical trials are essential to clarify the underlying molecular mechanisms and clinical relevance of colon cancer.

Importantly, this is the first study to explore the relationship between EML2 expression and colon cancer. However, it has some limitations. All the data analyzed by bioinformatic methods in this study were downloaded directly from public databases and require further experimental validation. Furthermore, it is necessary to get extended follow-ups and gather further patient data in order to corroborate EML2 conclusively as a prognostic indicator for the survival of patients. Regardless, this study lays the foundation for a detailed analysis of the relevance of EML2 to colon cancer and the immune microenvironment.

Acknowledgements

The authors would like to acknowledge the supports from the Armed Police Force High-level Scientific and Technological Talent Fund.

Disclosure of conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a conflict of interest.

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