Clin. Lab. 2026;72:XXX-XXX

ORIGINAL ARTICLE

Expression and Clinical Significance of FOXQ1, MMP11, and CST1 in Colorectal Cancer

Jiaxin Chu [1, 2], Danna Wang [1, 2], Fengle Guo [2], Dandan Li [2], Zheng Li [2], Haofeng Ding [4], Yun Sun [4], Yan Yan [2], Ke Wang [2], Li Ren [3], Junwei Han [3], Bo Zhu [1, 2]

[1] *Department of Pathology, School of Basic Medicine, Bengbu Medical University, Bengbu, Anhui, People's Republic of China*
[2] *The First Affiliated Hospital of Bengbu Medical University, Bengbu, Anhui, People's Republic of China*
[3] *Department of Nuclear Medicine, School of Laboratory Medicine, Bengbu Medical University, Bengbu, Anhui, People's Republic of China*
[4] *School of Clinical Medicine, Bengbu Medical University, Bengbu, Anhui, China*

SUMMARY

Background: **Colorectal cancer (CRC) is associated with a high mortality rate. Previous studies have shown that FOXQ1, MMP11, and CST1 play significant roles in various cancers, influencing the invasion and metastasis of tumors. However, their effects on colorectal cancer have not been fully investigated. The purpose of this research was to examine the expression of FOXQ1, MMP11, and CST1 in colorectal cancer (CRC) and to systematically assess how these factors relate to clinicopathological characteristics and patient survival outcomes.**
Methods: **This study retrospectively gathered paraffin-embedded samples from 110 CRC patients who underwent surgery between 2017 and 2018. Meanwhile, relevant data were obtained from public databases to analyze expression differences of FOXQ1, MMP11, and CST1 between tumor tissues and normal lung tissues. We examined the expression of FOXQ1, MMP11, and CST1 using immunohistochemistry. Furthermore, the associations among FOXQ1, MMP11, CST1, clinical-pathological parameters, and prognosis were systematically analyzed. Further verification of the in vitro results was conducted through qRT-PCR.**
Results: **Expression of FOXQ1, MMP11, and CST1 in patients was high, with 83.6%, 67%, and 74.5%, respectively. Through rigorous quantitative analysis of clinical-pathological parameters, the study confirmed that these biomarkers have a close and clinically significant correlation with the progression of TNM staging and the occurrence of lymph node metastasis ($p < 0.05$). Bioinformatics analysis and qRT-PCR verification both indicated that the expression levels of FOXQ1, MMP11, and CST1 in colorectal cancer (CRC) tissues were significantly higher than those in adjacent non-cancerous tissues.**
Conclusions: **The research data indicate that the abnormal overexpression of FOXQ1, MMP11, and CST1 in CRC tissues is significantly correlated with poor clinical prognosis in patients. There may be a synergistic effect influencing the invasion and metastasis of tumor cells, positioning them as potential novel therapeutic targets for patients with CRC.**
(Clin. Lab. 2026;72:xx-xx. DOI: 10.7754/Clin.Lab.2025.250764)

Correspondence:
Bo Zhu
Department of Pathology
School of Basic Medicine
Bengbu Medical University
Bengbu, Anhui
People's Republic of China
Email: 35736791@qq.com

Junwei Han
Department of Nuclear Medicine
School of Laboratory Medicine
Bengbu Medical University
Bengbu, Anhui
People's Republic of China
Email: 605693422@qq.com

Manuscript accepted August 26, 2025

KEYWORDS

FOXQ1, MMP11, CST1, colorectal cancer, immunohistochemistry, bioinformatics analysis

INTRODUCTION

CRC, a malignant tumor originating from the epithelial cells of the colon and rectum, ranks as the third most common cancer globally and is the second leading cause of cancer-related mortality [1]. According to epidemiological data, approximately 1.8 million new cases and 881,000 deaths are attributed to CRC annually worldwide [2]. Advances in early diagnosis and interventional therapies have significantly prolonged the survival of CRC patients. Nevertheless, for those diagnosed at advanced stages, the mortality rate remains alarmingly high due to the cancer's aggressive invasiveness and metastatic potential, which can result in tumor recurrence or metastasis even after intensive treatment [3]. To date, current therapeutic strategies have not substantially reduced the mortality rate among CRC patients, and there remains a paucity of effective long-term prognostic indicators in clinical practice [4,5]. Consequently, the identification of novel diagnostic biomarkers for CRC holds critical importance for improving clinical diagnosis, treatment, and prognosis evaluation [6]. Recent studies indicate that FOXQ1, CST1, and MMP11 play pivotal roles in the progression of various malignancies. However, the expression profiles of FOXQ1, CST1, and MMP11 in CRC tissues and their potential clinical implications remain largely unexplored. This study aimed to investigate the expression of FOXQ1, CST1, and MMP11 in CRC, so as to provide a theoretical basis for clarifying their roles in CRC development and evaluating their clinical prognostic value and to offer new insights for the early detection and management of CRC.

MATERIALS AND METHODS

Materials and reagents

The following materials and reagents were used: human colorectal cancer cells HCT116 (HCT116); human normal colon epithelial cells NCM460 (NCM460) (Shanghai Cell Bank, Chinese Academy of Sciences); DMEM high glucose culture medium (PunoSai); FOXQ1 antibody (Proteintech); MMP11 and CST1 antibody (Abcam).

Methods

The cell culture of the HCT116 and NCM460 cell lines was conducted in a controlled humidity environment at 37°C, utilizing a culture medium composed of 10% fetal bovine serum and 1% penicillin-streptomycin mixture. Passaging was performed when the cell confluence rate reached 70% - 80%.

Patients

This study screened 110 paraffin-embedded tissue samples of colorectal cancer (CRC) diagnosed between 2017 and 2018 from the pathological archive of the First Affiliated Hospital of Bengbu Medical University as the research subjects.

The study was conducted in strict accordance with the principles of the Helsinki Declaration, and the enrolled patients underwent systematic clinical evaluation, histopathological analysis, survival follow-up, and survival prognosis analysis. Normal intestinal mucosa 5 cm from the tumor edge served as negative controls to eliminate possible confounding factors. Among the enrolled patients, there were 70 males (63.6%), aged 28 to 82 years (median age 61.5 years), and all cases met the criteria for primary treatment, without receiving any form of neoadjuvant chemotherapy or radiotherapy before surgery. The patients' clinical pathological data are shown in Table 1.

IHC

Sections of 4 μm-thick tissue were deparaffinized using xylene and rehydrated in graded alcohols. Non-specific epitopes were blocked with rabbit serum within 30 minutes and subsequently incubated overnight with primary antibody (FOXQ1: 1:500, 26, 23718-1-AP, Proteintech, CST1:1:1,000, AB124281, Abcam and MMP11:1:1,000, AB53143, Abcam) in a humidified chamber at 4°C. Sections were incubated for 50 minutes with HRP-labeled secondary antibodies of the same species, washed with PBS, and dropped with freshly prepared DAB chromogen solution. When observing a tissue section under a microscope, positive staining appears brownish-yellow, the color development was terminated by rinsing the sections with tap water, and the nuclei were counterstained with hematoxylin for 3 minutes, dehydrated, and mounted. Pictures were collected of positive staining.

Scoring criteria

Two senior pathologists independently assessed the immunohistochemical sections. For FOXQ1, CST1, and MMP11 proteins, the immunohistochemical scores were calculated based on two criteria: the percentage of positive tumor cells (scored as 0 for < 10%, 1 for 11 - 50%, 2 for 51 - 75%, and 3 for > 75%) and staining intensity (scored as 0 for no staining, 1 for pale yellow, 2 for tan, and 3 for brown). The final score was obtained by multiplying these two individual scores. Samples with a total score of ≥ 3 were classified as positive, whereas those with a lower score were designated as negative.

Statistical analyses

SPSS 26.0 facilitated statistical analysis, with a chi-squared test examining the associations between FOXQ1, CST1, MMP11, and clinicopathological factors. By using Kaplan-Meier analysis, researchers can accurately evaluate and identify the risk factors affect-

Table 1. Relationship between FOXQ1, CST1, and MMP11 expression and clinicopathologic features in CRC.

Clinicopath-ological	FOXQ1		High expres-sion	p-value	CST1		High expres-sion	p-value	MMP11		High expres-sion	p-value
	Posi-tive	Nega-tive			Posi-tive	Nega-tive			Posi-tive	Nega-tive		
Gender												
Male	56	14	80%	0.175	52	18	74.3%	0.982	47	23	67.1%	0.982
Female	36	4	90%		30	10	75%		27	13	67.5%	
Age (years)												
≤ 60	44	11	80%	0.28	40	15	72.7%	0.543	35	20	72.7%	0.543
> 60	48	7	87.2%		42	13	76.3%		39	16	76.3%	
LN metastases												
Yes	58	3	95%	0.002	54	7	88.5%	0.002	48	13	78.7%	0.002
No	34	15	69.3%		28	21	57.1%		26	23	53%	
STNM stage												
I	20	10	66.75	0.047	15	15	50%	0.009	16	14	53.3%	0.023
II	68	8	89.5%		65	11	85.5%		57	19	75%	
III + IV	4	0	100%		2	2	50%		1	3	25%	
Tumor location												
Rectum	50	10	83.3%	0.82	44	16	73.7%	0.958	40	20	66.7%	0.981
Colon	42	8	84%		38	12	76%		34	16	68%	
Tumor size (cm)												
< 5.0	44	10	81.5%	0.562	40	16	71.4%	0.332	38	18	67.9%	0.833
≥ 5.0	48	8	85.7%		42	12	77.8%		36	18	66.7%	
Depth of invasion												
Invasion of the serosa	48	10	82.8%	0.69	43	15	74.1%	0.989	42	16	72.4%	0.081
No invasion of the serosa	44	8	84.6%		39	13	75%		32	20	61.5%	

Table 2. Multivariate Cox regression model analysis of survival outcomes.

Clinicopathological	B	SE	Wald	df	p	Exp (B)	95.0% CI for Exp (B)	
							Lower	Upper
Age (years)	0.445	0.42	1.121	1	0.29	1.561	0.685	3.557
Gender	-0.203	0.418	0.234	1	0.628	0.817	0.36	1.854
LN metastases	1.223	0.556	4.845	1	0.028	3.399	1.143	10.103
Tumor size	-0.147	0.392	0.141	1	0.707	0.863	0.4	1.861
Depth of invasion	-0.069	0.41	0.028	1	0.867	0.934	0.418	2.084
MMP11	0.65	0.313	4.306	1	0.038	1.915	1.037	3.539
FOXQ1	0.658	0.296	4.946	1	0.026	1.932	1.081	3.45
CST1	1.187	0.353	11.334	1	0.001	3.277	1.642	6.541

MMP11 Matrix Metalloproteinase 11.

ing prognosis. Statistical significance was set at $p < 0.05$.

Follow-up

The follow-up process commenced on the date when a clear diagnosis of CRC was established through postoperative pathology. It was carried out via outpatient

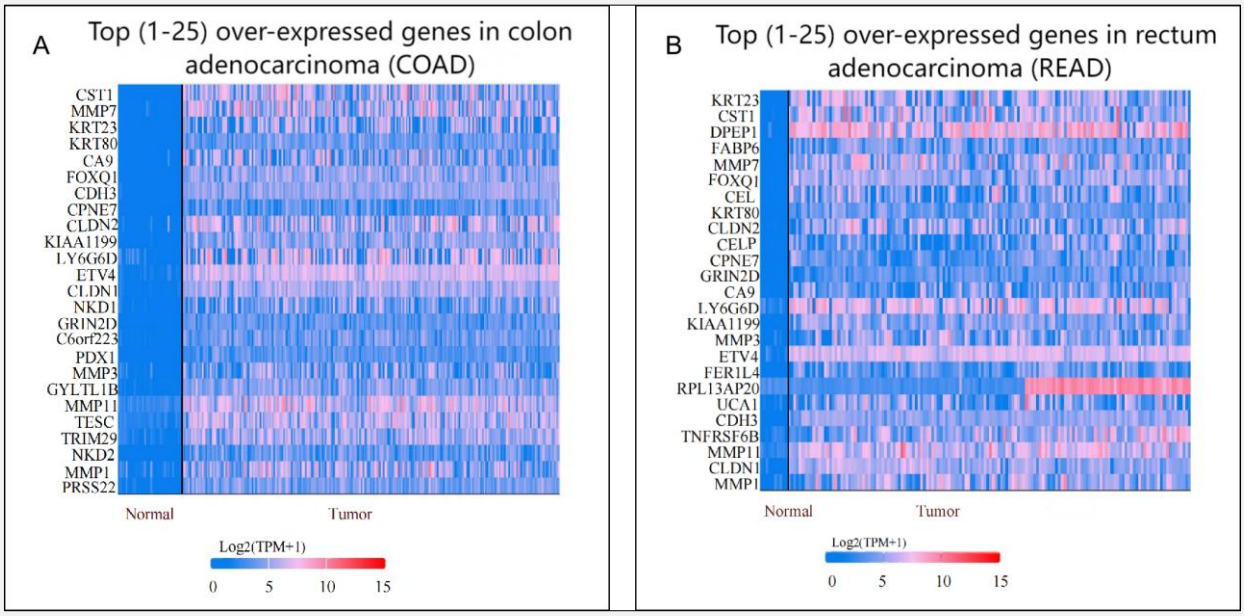

Figure 1. A Highly expressed factor in colon cancer. B Highly expressed factor in rectal cancer.

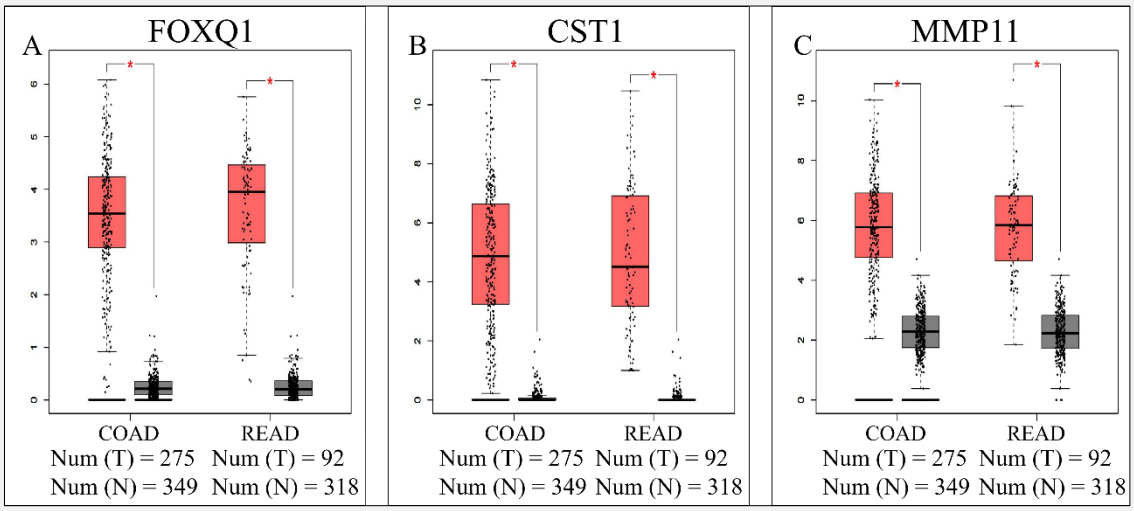

Figure 2. Expression of FOXQ1, CST1, and MMP11 in colon cancer, rectal cancer tissues, and normal tissues.

reexaminations or telephone follow-ups. The follow-up assessments encompassed the patients' survival status, as well as any recurrence or progression of the disease. The endpoint of the follow-up was defined as either the death of the patient or the conclusion of the follow-up period. The final deadline for follow-up was April 2024.

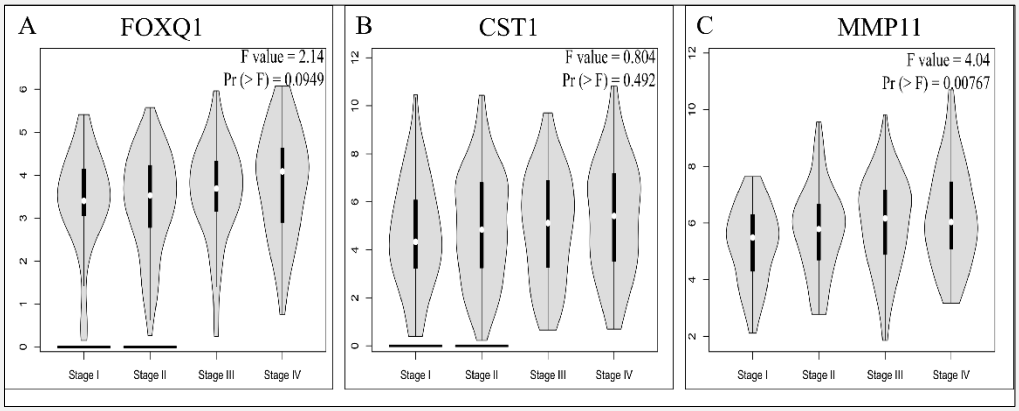

Figure 3. Relationship between FOXQ1, CST1, and MMP11 and colorectal cancer staging.

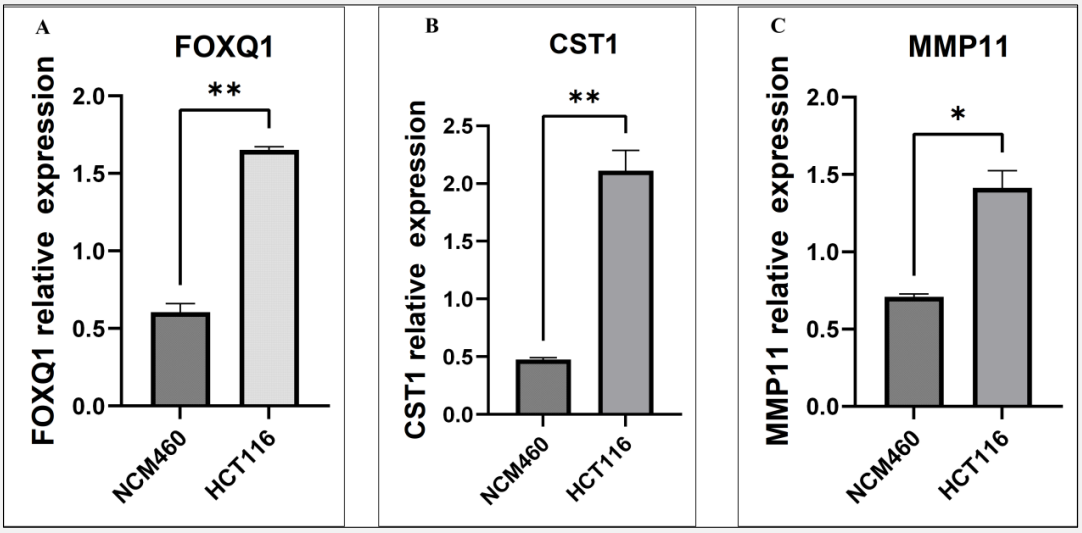

Figure 4. A FOXQ1 expression results in normal colon cells and colorectal cancer cells (p < 0.01). B CST1 expression results in normal colon cells and colorectal cancer cells (** p < 0.01). C) MMP11 expression results in normal colon cells and colorectal cancer cells (* p < 0.05).**

qRT-PCR

After isolating CRC cells using the total RNA extraction kit, reverse transcription was performed with the cDNA first strand synthesis kit, and then qRT-PCR was conducted using the 2 × Taq PCR MasterMix. The specific detailed steps for the qRT-PCR experiment were followed according to the reagent instructions. Primer sequences were the following:

GAPDH
F: 5′-ACCCACTCCTCCACCTTTGAC-,
R: 5′-CTGTTGCTGTAGCCAAATTCG-3′.
CST1
F: 5′-CGGGTGGCATCTATAACGCA-3′,
R: 5′-GTCTGTTGCCTGGCTCTTAGT-3′.
FOXQ1
F: 5′- TGACTTCAACAGCGACACCCA-3′,

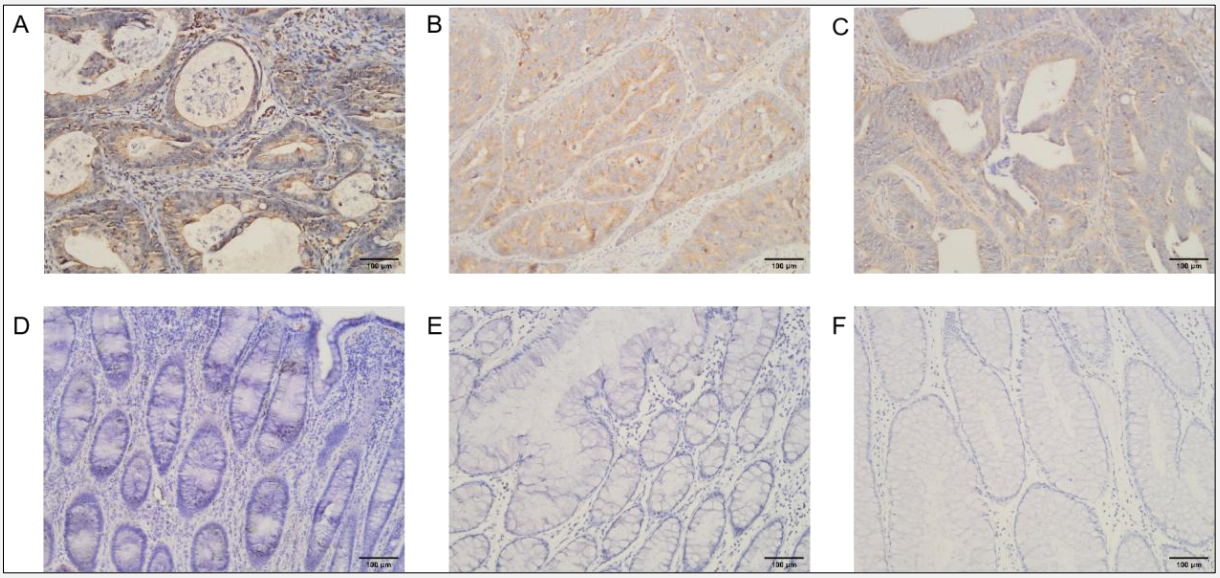

Figure 5. A Expression of FOXQ1 in colorectal cancer tissues. B Expression of CST1 in colorectal cancer tissues. C Expression of FOXQ1 in colorectal cancer tissues. D Expression of FOXQ1 in colorectal normal tissues. E Expression of MCST1 in colorectal normal tissues. F Expression of MMP11 in colorectal normal tissues (x 200).

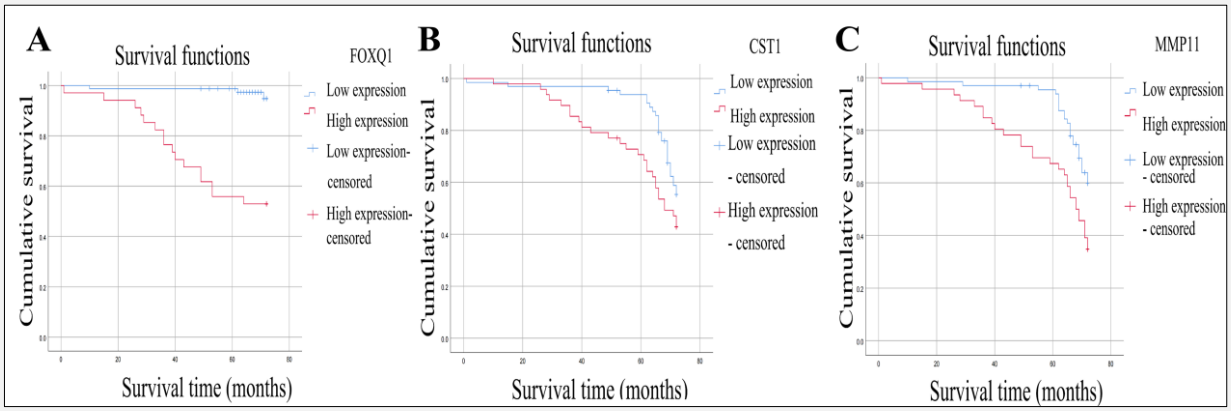

Figure 6. A Impact of FOXQ1 expression on the patients' overall survival. B Impact of CST1 expression on the patients' overall survival. C Impact of MMP11 expression on the patients' overall survival.

R: 5′-CACCCTGTTGCTGTAGCCAAA-3′.
MMP11
F: 5′-GAGAAGACGGACCTCACCTACA-3′,
R: 5′-CTCAGTAAAGGTGAGTGGCGTC-3′.

Data source and processing

The gene expression data from tumor tissues of colorectal cancer patients were obtained from the processed TCGA public database, which was downloaded from the GEPIA database (http://gepia.cancer-pku.cn/). This

dataset includes gene expression data from 275 tumor tissue samples of colorectal carcinoma (COAD) patients and 349 normal tissue samples, in addition to gene expression data from 92 tumor tissue samples of rectal carcinoma (READ) patients and 318 normal tissue samples. Data analysis utilized Ualcan (http://ualcan.path.uab.edu), an analysis and mining tool based on the TCGA database and clinical proteomics tumor analysis. This tool analyzes relative gene expression between tumor and normal tissues and among tumor subgroups classified by sample type, individual tumor staging, major subtypes, and other clinical pathological features. All public data were used in accordance with TCGA and GEO data access policies, and this study did not require additional ethical approval.

RESULTS

FOXQ1, MMP11, and CST1 expressions in database

The expression levels of important factors present in CRC and normal tissues were examined with the aid of Ualcan (Figure 1). In the TCGA database, FOXQ1, CST1, and MMP11 exhibited significantly higher expression levels compared to adjacent non-tumor tissues ($p < 0.05$) (Figure 2). By using GEPIA, we further analyzed the associations between FOXQ1, CST1, MMP11, and CRC staging. The data revealed that MMP11 expression was notably linked to CRC staging ($p < 0.05$) (Figure 3).

Survival analysis was performed using the GSE72970 dataset. The optimal cutoff values for CST1 and MMP11 were determined as 7.44 and 10.85, respectively, and Kaplan-Meier (KM) survival curves were generated for both genes. As the GSE72970 dataset did not include the FOXQ1 gene, the TCGA dataset was utilized for the survival analysis of FOXQ1. The optimal cutoff value for FOXQ1 was set at 6.08, and the corresponding KM survival curve was plotted (Figure 7).

Expression of FOXQ1, MMP11, and CST1 in colon cancer and human normal colon cells

The results of the qRT-PCR experiments demonstrated that FOXQ1, CST1, and MMP11 were significantly upregulated in the CRC cell line HCT116 compared to the human normal colon epithelial cell line NCM460 (Figure 4).

The expression levels of FOXQ1, CST1, and MMP11 were examined in CRC tissues and corresponding normal tissues through clinical sample analysis

Immunohistochemical staining showed that FOXQ1, CST1, and MMP11 proteins were negative in normal colorectal mucosa. In cancerous tissues, FOXQ1 and CST1 exhibited positive expression, primarily localized in the cytoplasm and cell membrane, while MMP11 was predominantly distributed in the cytoplasm with partial localization in the nucleus. Immunohistochemistry results revealed that the positivity rates of FOXQ1, CST1, and MMP11 in CRC tissues were 83.6% (92/110), 74.5% (82/110), and 67% (73/110), respectively. In para-carcinoma tissues, the positivity rates were significantly lower: 38.2% (42/110) for FOXQ1, 24.5% (27/110) for CST1, and 30% (33/110) for MMP11. Collectively, these findings indicate that the positive expression rates of FOXQ1, CST1, and MMP11 proteins were significantly higher in cancerous tissues compared to para-carcinoma tissues (χ^2 = 47.726, 55.005, and 30.586, $p < 0.005$, 0.005, and 0.005) (Figure 5).

The following investigation will examine the relationship between FOXQ1, MMP11, and CST1 protein expression, as well as the clinicopathological features of CRC tissues

A statistical analysis of the clinicopathological characteristics of 110 CRC patients yielded the following results (Table 1): positive expression of FOXQ1, MMP11, and CST1 was correlated with TNM stage and the presence or absence of lymph node metastasis ($p < 0.05$). The study found no correlation between the protein expression of FOXQ1, CST1, and MMP11 and gender, age, tumor size, or depth of invasion among different CRC patients ($p > 0.05$). Similarly, our study did not identify any significant relationships between MMP11 protein expression and factors including gender, age, tumor size, or infiltration depth of CRC patients ($p > 0.05$) (Table 1). According to the Cox multivariate regression, we can obtain that FOXQ1, CST1, and MMP11 can serve as independent prognostic factors (Table 2). A longitudinal study was conducted on 110 CRC patients, with follow-up periods ranging from 2 to 72 months (Figure 6). The figure illustrates the association between FOXQ1, CST1, and MMP11 protein expression and patient survival prognosis. The analysis revealed that patients with positive FOXQ1, CST1, and MMP11 expression exhibited a significantly lower survival rate compared to those with negative expression.

DISCUSSION

Colorectal cancer (CRC) ranks as the second leading cause of cancer-related mortality globally [7]. Inhibiting tumor invasion and metastasis has emerged as a critical strategy for improving patient survival outcomes [8]. In recent years, FOXQ1 (Forkhead Box Q1), CST1 (Cystatin SN), and MMP11 (Matrix Metalloproteinase 11) have been increasingly recognized as key regulators involved in the initiation and progression of CRC [9,10]. Accumulating evidence indicates that these three genes are significantly upregulated in advanced CRC and are closely associated with adverse clinical outcomes, suggesting their potential as biomarkers for disease progression [11,12].

FOXQ1 is a member of the FOX transcription factor superfamily, located on human chromosome 6p23-25. It is broadly expressed across multiple human tissues and

plays a pivotal role in tumorigenesis by promoting cell proliferation, migration, invasion, and epithelial-mesenchymal transition (EMT) [13]. In the context of CRC, FOXQ1 overexpression not only enhances tumor cell growth and tumorigenic potential but also suppresses apoptosis, thereby facilitating tumor progression [14]. Mechanistically, FOXQ1 exerts its oncogenic effects through the activation of multiple signaling pathways, including the PI3K/AKT and Wnt/β-catenin pathways, and by modulating downstream target genes such as MMPs and VEGF, thereby synergistically promoting a metastatic phenotype [15].

CST1, a member of the cysteine protease inhibitor family, was initially identified in the submandibular gland, gallbladder, and uterus, and has since been found to be overexpressed in various malignant tumors [16,17]. In CRC, elevated CST1 expression correlates positively with advanced TNM stage and lymph node metastasis and is associated with poorer patient survival [18]. Functionally, CST1 promotes tumor invasion and metastasis by inhibiting cysteine protease activity, which disrupts extracellular matrix (ECM) remodeling. Moreover, CST1 contributes to tumor progression by modulating tumor-associated inflammation and immune microenvironment and by activating the PI3K/AKT signaling pathway [19,20].

MMP11, a member of the matrix metalloproteinase family, was first identified in breast cancer and has since been shown to be overexpressed in multiple malignancies, including CRC, where its expression is linked to poor clinical outcomes [21,22]. MMP11 facilitates tumor cell invasion by degrading ECM components such as collagen and fibronectin, thereby compromising tissue integrity. Additionally, it influences immune cell infiltration within the tumor microenvironment and enhances EMT, further promoting metastasis [23]. Clinical data demonstrate that MMP11 expression levels in CRC tissues are significantly correlated with TNM stage, lymph node metastasis, and overall survival, with high expression predicting the shortest survival duration [24].

In this study, we retrospectively evaluated the immunohistochemical expression of FOXQ1, CST1, and MMP11 in tumor tissues from 110 CRC patients. Our results revealed significantly higher expression levels of these proteins in cancerous tissues compared to adjacent normal mucosa (FOXQ1: 83.6%, CST1: 74.5%, MMP11: 67%), consistent with previous findings [25-27].

Notably, FOXQ1, CST1, and MMP11 do not act in isolation but may form a cooperative regulatory network through shared signaling pathways such as PI3K/AKT, thereby synergistically promoting EMT and metastatic phenotypes [28,29]. For instance, FOXQ1 transcriptionally regulates MMP11 expression [30], while CST1 indirectly modulates MMP11 activity by inhibiting cysteine proteases. Collectively, these interactions contribute to the formation of a tumor-promoting microenvironment [31].

From a clinical perspective, this study underscores the potential of combining FOXQ1, CST1, and MMP11 as a biomarker panel for prognostic evaluation in CRC. Their expression levels can aid in individualized risk stratification, particularly for patients with advanced TNM stages or lymph node metastasis, where high expression may warrant more aggressive therapeutic interventions. Furthermore, targeting these molecules and their downstream signaling pathways, such as PI3K/AKT, may offer novel therapeutic strategies for advanced CRC. Future research should focus on validating their clinical utility and exploring their potential as therapeutic targets.

CONCLUSION

In summary, the FOXQ1-CST1-MMP11 axis promotes CRC metastasis through cross-talk and synergistic effects. The elucidation of its mechanism not only deepens the understanding of CRC invasive behavior but also provides theoretical basis and practical paths for prognostic assessment and targeted therapy.

Source of Funds:
This work was supported by the Natural Science Research Project of Anhui Educational Committee (2023 AH051998), 2022 Bengbu Medical College Science and Technology Project Natural Science Category (2022byzd021), Bengbu Medical University Postgraduate Scientific Research and Innovation Plan Project (Byycx24067), and 2024 Bengbu Medical University Science and Technology Project Natural Science Category (2024byzd135).

Ethical Approval Statement:
This study was approved by the Ethics Committee of Bengbu Medical University (Lunke PiZi (2024) No. 161).

Declaration of Interest:
No conflicts of interest concerning this article were declared.

References:

1. Brody H. Colorectal cancer. Nature 2015;521(7551):S1. (PMID: 25970450)

2. Baidoun F, Elshiwy K, Elkeraie Y, et al. Colorectal Cancer Epidemiology: Recent Trends and Impact on Outcomes. Curr Drug Targets 2021;22(9):998-1009. (PMID: 33208072)

3. Yan X, Wang Y, Ma A, Li H. The role of health economic evidence in clinical practice guidelines for colorectal cancer: a comparative analysis across countries. J Comp Eff Res 2025;14(4): e240226. (PMID: 39969114)

4. Piawah S, Venook AP. Targeted therapy for colorectal cancer metastases: A review of current methods of molecularly targeted therapy and the use of tumor biomarkers in the treatment of metastatic colorectal cancer. Cancer 2019;125(23):4139-47. (PMID: 31433498)

5. Patel SG, Karlitz JJ, Yen T, Lieu CH, Boland CR. The rising tide of early-onset colorectal cancer: a comprehensive review of epidemiology, clinical features, biology, risk factors, prevention, and early detection. Lancet Gastroenterol Hepatol 2022;7(3):262-74. (PMID: 35090605)

6. Zygulska AL, Pierzchalski P. Novel Diagnostic Biomarkers in Colorectal Cancer. Int J Mol Sci 2022;23(2):852. (PMID: 35055034)

7. Dekker E, Tanis PJ, Vleugels JLA, Kasi PM, Wallace MB. Colorectal cancer. Lancet 2019;394(10207):1467-80. (PMID: 31631858)

8. Buccafusca G, Proserpio I, Tralongo AC, Rametta Giuliano SR, Tralongo P. Early colorectal cancer: diagnosis, treatment and survivorship care. Crit Rev Oncol Hematol 2019;136:20-30. (PMID: 30878125)

9. Yang W-D, Zhang Z-H, Zhao M-Y, et al. P300-dependent acetylation of the FOXQ1 complex activates super-enhancers to promote colorectal cancer proliferation and metastasis. Commun Biol 2025;8(1):1016. (PMID: 40624346)

10. Liu C, Mei T. Circ_0001821 Potentiates Cell Growth, Metastasis, and Stemness in Colorectal Cancer by Regulating miR-339-3p/CST1. Biochem Genet 2023;61(4):1451-69. (PMID: 36633774)

11. Wang J, Zhang Y, Chen X, et al. Single-Cell Transcriptomics Reveals Cellular Heterogeneity and Drivers in Serrated Pathway-Driven Colorectal Cancer Progression. Int J Mol Sci 2024;25(20): 10944. (PMID: 39456726)

12. Debaugnies M, Rodríguez-Acebes S, Blondeau J, et al. RHOJ controls EMT-associated resistance to chemotherapy. Nature 2023;616(7955):168-75. (PMID: 36949199)

13. Gao M, Shih I-M, Wang T-L. The role of forkhead box Q1 transcription factor in ovarian epithelial carcinomas. Int J Mol Sci 2012;13(11):13881-93. (PMID: 23203039)

14. Yang M, Liu Q, Dai M, et al. FOXQ1-mediated SIRT1 upregulation enhances stemness and radio-resistance of colorectal cancer cells and restores intestinal microbiota function by promoting β-catenin nuclear translocation. J Exp Clin Cancer Res 2022;41(1): 70. (PMID: 35183223)

15. Liu JY, Wu XY, Wu GN, Liu F-K, Yao X-Q. FOXQ1 promotes cancer metastasis by PI3K/AKT signaling regulation in colorectal carcinoma. Am J Transl Res 2017;9(5):2207-18. (PMID: 28559972)

16. Zhang J-J, Cao C-X, Wan L-L, et al. Forkhead Box q1 promotes invasion and metastasis in colorectal cancer by activating the epidermal growth factor receptor pathway. World J Gastroenterol 2022;28(17):1781-97. (PMID: 35633908)

17. Bayik D, Lathia JD. Cancer stem cell-immune cell crosstalk in tumour progression. Nat Rev Cancer 2021;21(8):526-36. (PMID: 34103704)

18. Zhang L, Wang D, Zhang L, Zhu L. CST1 promoted gastric cancer development by activating the AKT pathway. Clinics (Sao Paulo) 2025;80:100561. (PMID: 39721372)

19. Liu Y, Yao J. Research progress of cystatin SN in cancer. Onco Targets Ther 2019;12:3411-9. (PMID: 31118691)

20. Yang X, Wang G, You J, et al. High Expression of Cancer-IgG Is Associated With Poor Prognosis and Radioresistance via PI3K/AKT/DNA-PKcs Pathway Regulation in Lung Adenocarcinoma. Front Oncol 2021;11:675397. (PMID: 34150640)

21. Liu M, Huang L, Liu Y, et al. Identification of the MMP family as therapeutic targets and prognostic biomarkers in the microenvironment of head and neck squamous cell carcinoma. J Transl Med 2023;21(1):208. (PMID: 36941602)

22. Pan C, Dai J, Wei Y, et al. Matrix Metalloproteinase 11 Promotes Migration and Invasion of Colorectal Cancer by Elevating Slug Protein. Int J Med Sci 2024;21(11):2170-88. (PMID: 39239548)

23. Gorodetska I, Lukiyanchuk V, Gawin M, et al. Blood-based detection of MMP11 as a marker of prostate cancer progression regulated by the ALDH1A1-TGF-β1 signaling mechanism. J Exp Clin Cancer Res 2025;44(1):105. (PMID: 40122809)

24. Jiang J, Liu H-L, Tao L, et al. Let-7d inhibits colorectal cancer cell proliferation through the CST1/p65 pathway. Int J Oncol 2018;53(2):781-90. (PMID: 29845224)

25. Liu Q, Cao Y, Wei X, et al. Nuclear isoform of RAPH1 interacts with FOXQ1 to promote aggressiveness and radioresistance in breast cancer. Cell Death Dis 2023;14(12):803. (PMID: 38062011)

26. Zhong W, Liu Y, Zhang L, et al. Combination of serum CST1 and HE4 for early diagnosis of endometrial cancer. PeerJ 2023; 11:e16424. (PMID: 38077439)

27. Soleimani S, Pouresmaeili F, Salahshoori Far I. Evaluation of lncRNAs as Potential Biomarkers for Diagnosis of Metastatic Triple-Negative Breast Cancer through Bioinformatics and Machine Learning. Iran J Biotechnol 2024;22(3):e3853. (PMID: 39737204)

28. Martin-Morales L, Manzano S, Rodrigo-Faus M, et al. Germline gain-of-function MMP11 variant results in an aggressive form of colorectal cancer. Int J Cancer 2023;152(2):283-97. (PMID: 36093604)

29. Wang Z, Guo X, Li X, et al. Cancer-associated fibroblast-derived MMP11 promotes tumor progression in pancreatic cancer. Cancer Sci 2025;116(3):643-55. (PMID: 39639765)

30. Qiang J, Zhao C, Shi L-Q, et al. BRD9 promotes the progression of gallbladder cancer via CST1 upregulation and interaction with FOXP1 through the PI3K/AKT pathway and represents a therapeutic target. Gene Ther 2024;31(11-12):594-606. (PMID: 39306629)

31. Ali H, AbdelMageed M, Olsson L, et al. Detection of lymph node metastasis in colon cancer by ectopically expressed fibroblast markers FOXQ1 and THBS2. Front Oncol 2023;13:1297324. (PMID: 38156105)

32. Malvia S, Bagadi SAR, Pradhan D, et al. Study of Gene Expression Profiles of Breast Cancers in Indian Women. Sci Rep 2019; 9(1):10018. (PMID: 31292488)